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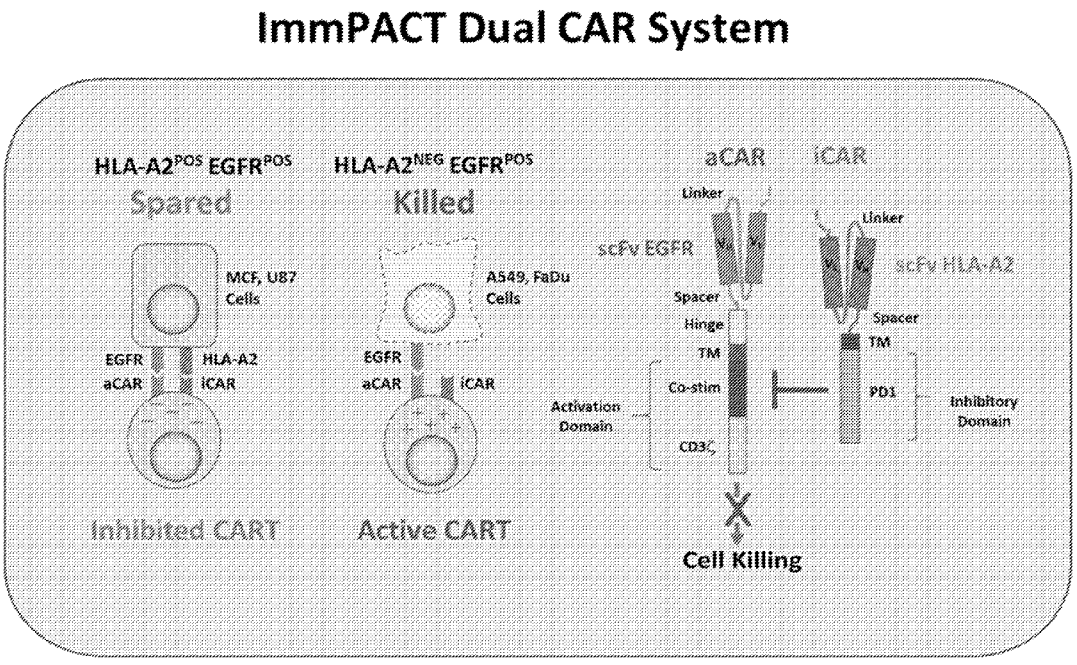

FIG. 16A

(57) Abstract: The invention relates to the field of cancer immunotherapy by employing bicistronic inhibitory chimeric antigen receptor (iCAR)/activating chimeric antigen receptor (aCAR) constructs for use in cancer treatment therapies. The invention further relates to bicistronic inhibitory chimeric antigen receptor (iCAR)/activating chimeric antigen receptor (aCAR) constructs that limit off-target effects when used in cancer treatment therapies.

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BICISTRONIC INHIBITORY CHIMERIC ANTIGEN RECEPTOR (ICAR)/ACTIVATING CHIMERIC ANTIGEN RECEPTOR (ACAR) CONSTRUCTS FOR USE IN CANCER THERAPIES

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 63/321,620, which was filed on March 18, 2022, and it also claims the benefit of U.S. Provisional Application No. 63/318,353, which was filed on March 9, 2022.

FIELD OF THE INVENTION

[0002] The invention relates to the field of cancer immunotherapy by employing inhibitory chimeric antigen receptors (iCARs) paired with activating chimeric antigen receptors (aCARs) for use in cancer treatment therapies.

BACKGROUND OF THE INVENTION

[0003] The identification of targetable antigens that are exclusively expressed by tumor cells but not by healthy tissue is undoubtedly the major challenge in cancer immunotherapy today. Clinical evidence that T cells are capable of eradicating tumor cells comes from numerous studies evaluating highly diverse approaches for harnessing T cells to treat cancer (Rosenberg and Restifo, *Science*, 348(6230): 62-68 (2015)). These approaches employ bone marrow transplantation with donor lymphocyte infusion, adoptive transfer of tumor-infiltrating lymphocytes (TILs), treatment with T cells genetically redirected at pre-selected antigens via CARs (Gross and Eshhar, *Annual Review of Pharmacology and Toxicology*, 56:59-83, (2016)) or T cell receptors (TCRs), the use of immune checkpoint inhibitors, BiTEs (bispecific T-cell engager molecules) technologies; Einsele, H., *et al., Cancer,* 126(14):3192-3201 (2020)), or active vaccination. Of these, the use of genetically engineered T cells and different strategies for active immunization entail pre-existing information on candidate antigens which are likely to exert a durable clinical response but minimal adverse effects. Yet, as stated in the title of a review by S. Rosenberg, "Finding suitable targets is the major obstacle to cancer gene therapy" (Rosenberg, *Cancer Gene Therapy*, 21:45–47 (2014))).

[0004] The concept of using chimeric antigen receptors (or CARs) to genetically redirect T cells (or other killer cells of the immune system such as natural killer (NK) cells and cytokine-induced killer cells) against antigens of choice in an MHC-independent manner was first introduced by Gross and Eshhar in the late 1980s (Gross et al., *PNAS*, 86(24):10024-1002 (1989). They are produced synthetically from chimeric genes encoding an extracellular single-

chain antibody variable fragment (scFv) fused through a flexible hinge and transmembrane domain to costimulatory domains and signaling components comprising immunoreceptor tyrosine-based activation motifs of CD3-ζ or FcRγ chains capable of T cell activation. At present, CARs are being examined in dozens of clinical trials and have shown exceptionally high efficacy in B cell malignancies (Dotti et al., 2014; Gill and June, 263(1): 68-89 (2015)); Gross and Eshhar, *Annual Review of Pharmacology and Toxicology*, 56:59-83, 2016). The safety of CAR-T cell therapy is determined, in large part, by its ability to discriminate between the tumor and healthy tissue. A major risk in targeting solid tumors, and the direct cause for adverse autoimmune effects that have been reported in clinical and preclinical studies, is off-tumor, on-target toxicity resulting from extra-tumor expression of the target antigen (dealt with in detail in the review (Gross and Eshhar, 2016b) and (Klebanoff, *et al.*, Nature Medicine 22:26–36 (2016)).

[0005] While undoubtedly intriguing, these previous CAR-based approaches require tuning the affinity of CAR scFv's to selectively bind high antigen levels in tumors while minimizing recognition of lower antigen levels in healthy tissues. In addition, the magnitude of both the activating and costimulatory signals needs to be balanced to allow effective on-target, on-tumor T cell reactivity. It is worth noting that in B cell malignancies, CARs targeted antigen exclusive to B cells and did not require titration of affinity or T cell signaling. For solid tumors, whether such balance can be routinely attained in the clinical setting is questionable.

[0006] Off-tumor reactivity occurs when the tumor antigen targeted by CAR-redirected killer cells is shared with normal tissue. However, if the normal tissue expresses another surface antigen that is not present on the tumor, it can be targeted by inhibitory CARs (iCARs) that contains an inhibitory signaling moiety which when engaged prevents T-cell activation by the activating CAR (aCAR). Co-expression of aCAR and iCAR will therefore direct killer cells to target tumors while sparing normal tissue.

[0007] Instead of an activating domain (such as FcRγ or CD3-ζ), an iCAR possesses a signaling domain derived from an inhibitory receptor which can antagonize T cell activation, such as CTLA-4, PD-1, or NK inhibitory receptors.

[0008] There remains a need in the art for cancer therapies, in particular therapies that comprise iCARs in order to limit off-target effects. The present invention meets that need by providing either co-transduction of monocistronic aCAR and iCAR constructs, or bicistronic constructs comprising such iCARs and which find use in cancer treatment.

BRIEF SUMMARY OF THE INVENTION

[0009] The present invention provides bicistronic iCAR/aCAR constructs or monocistronic aCAR and iCAR constructs for co-transduction and uses thereof.

[0010] The present invention provides a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction comprising:

i. an iCAR portion, wherein the iCAR portion comprises:
    a. an iCAR single chain variable fragment (scFv) component optionally in the VH-VL or VL-VH orientation;
    b. an iCAR hinge domain component;
    c. an iCAR transmembrane (TM) domain component;
    d. an iCAR inhibitory domain component; and
ii. an aCAR portion, wherein the iCAR portion comprises:
    a. an aCAR single chain variable fragment (scFv) component optionally in the VH-VL or VL-VH orientation;
    b. an aCAR hinge domain component;
    c. an aCAR co-stimulatory domain component
    d. an aCAR activation signaling domain; and
iii. a linker that connects the iCAR portion in (i) and the aCAR portion in (ii).

[0011] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the linker connecting the VH-VL or VL-VH in either orientation comprises one or more linker selected from the group consisting of (G4S)X3 linker (SEQ ID NO:81), G4S (SEQ ID NO:153), (G4S)X3 (SEQ ID NO:154), and Whitlow linker (SEQ ID NO:82).

[0012] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen.

[0013] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the HLA antigen is selected from the group consisting of HLA-A2, HLA-A3, HLA-A, HLA-B, HLA-C, HLA-G, HLA-E, HLA-F, HLA-DPA1, HLA-DQA1, HLA-DQB1, HLA-DQB2, HLA-DRB1, and HLA-DRB5.

[0014] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the HLA antigen comprises or consists essentially of HLA-A2.

[0015] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the HLA antigen is HLA-A2.

[0016] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component is selected from the group consisting of BB7.2, 3PF12, 3PF12/C4, 3PF12/F12, 3PF12/B11, W6/32, BBM.1, SN66E3, Ha5C2.A2, MWB1, MWB1-mod, Hz.BB7.2 VH1-69 _A18VK, Hz.BB7.2 VH1-69 (27,30)_A18, Hz.BB7.2 VH1-69 (27,30,48)_A18, Hz.BB7.2 VH1-69 (27,30,67)_A18, Hz.BB7.2 VH1-69 (27,30,69)_A18, Hz.BB7.2 VH1-69 (27,30,67,69)_A18, Hz.BB7.2 VH1-3_A18, Hz.BB7.2 VH1-3(48)_ A18, Hz.BB7.2 VH1-3(67)_A18, Hz.BB7.2 VH1-3(69)_A18, Hz.BB7.2 VH1-3(71)_A18, Hz.BB7.2 VH1-3(73)_A18, MWB1.2, SN66E3.2 and SN66E3.3.

[0017] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component is BB7.2.

[0018] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from BB7.2 (SEQ ID NOs: 37 and 38) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 37 and 38.

[0019] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from Hz.BB7.2 VH1-69_A18VK (SEQ ID NOs: 57 and 58) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 57 and 58.

[0020] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, wherein the iCAR scFv comprises the Vh and Vl from Hz.BB7.2 VH1-69 (27,30)_A18 (SEQ ID NOs: 59 and 60) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 59 and 60.

[0021] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from Hz.BB7.2 VH1-69 (27,30,48) _ A18 (SEQ ID NOs: 61 and 62) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 61 and 62.

[0022] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from Hz.BB7.2 VH1-69 (27,30,67) A18 (SEQ ID NOs: 63 and 64) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 63 and 64.

[0023] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from

Hz.BB7.2 VH1-69 (27,30,69)_A18 (SEQ ID NOs: 65 and 66) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 65 and 66.

[0024] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from Hz.BB7.2 VH1-69 (27,30,67,69)_A18 (SEQ ID NOs: 67 and 68) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 67 and 68.

[0025] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from Hz.BB7.2 VH1-3_A18 (SEQ ID NOs: 69 and 70) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 69 and 70.

[0026] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from Hz.BB7.2 VH1-3(48)_ A18 (SEQ ID NOs: 71 and 72) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 71 and 72.

[0027] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from Hz.BB7.2 VH1-3(67)_A18 (SEQ ID NOs: 73 and 74) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 73 and 74.

[0028] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from Hz.BB7.2 VH1-3(69)_A18 (SEQ ID NOs: 75 and 76) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 75 and 76.

[0029] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from Hz.BB7.2 VH1-3(71)_A18 (SEQ ID NOs: 77 and 78) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 77 and 78.

[0030] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from Hz.BB7.2 VH1-3(73)_A18 (SEQ ID NOs: 79 and 80) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 79 and 80.

[0031] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv is BB7.2 of SEQ ID NO:167.

[0032] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises Hz BB7.2.1 of SEQ ID NO:287.

[0033] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv consists essentially of Hz BB7.2.1 of SEQ ID NO:287.

[0034] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv is Hz BB7.2.1 of SEQ ID NO:287.

[0035] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component is 3PF12.

[0036] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from 3PF12/C4 (SEQ ID NOs: 39 and 40) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 39 and 40.

[0037] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from 3PF12/F12 (SEQ ID NOs: 41 and 42) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 41 and 42.

[0038] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, wherein the iCAR scFv comprises the Vh and Vl from 3PF12/B11 (SEQ ID NOs: 43 and 44) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 43 and 44.

[0039] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv is 3PF12 of SEQ ID NO:168.

[0040] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component is SN66E3.

[0041] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from SN66E3.1 (SEQ ID NOs: 49 and 50) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 49 and 50.

[0042] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv is SN66E3.1 of SEQ ID NO:169.

[0043] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises or consists essentially of SN66E3.2 of SEQ ID NO:285.

[0044] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv is SN66E3.2 of SEQ ID NO:285.

[0045] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from SN66E3.2 (SEQ ID NOs: 165 and 166) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 165 and 166.

[0046] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from SN66E3.3 (SEQ ID NOs: 283 and 284) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 283 and 284.

[0047] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises SN66E3.3 of SEQ ID NO:286.

[0048] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv consists of or consists essentially of SN66E3.3 of SEQ ID NO:286.

[0049] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv is SN66E3.3 of SEQ ID NO:286.

[0050] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component is W6/32.

[0051] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from W6/32 (SEQ ID NOs: 45 and 46) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 45 and 46.

[0052] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component is BBM.1.

[0053] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from BBM.1 (SEQ ID NOs: 47 and 48) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 47 and 48.

[0054] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component is Ha5C2.A2.

[0055] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from Ha5C2.A2 (SEQ ID NOs: 51 and 52) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 51 and 52.

[0056] T In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component is MWB1.

[0057] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from MWB1 (SEQ ID NOs: 53 and 54) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 53 and 54.

[0058] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from MWB1-mod (MWB1.1) (SEQ ID NOs: 55 and 56) or vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NOs: 55 and 56.

[0059] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv comprises the Vh and Vl from MWB1.2 (SEQ ID NOs: 163 and 164).

[0060] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv is MWB1.1 scFvVH_VL (SEQ ID NO:273).

[0061] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv is MWB1.2 scFvVH_VL (SEQ ID NO:274).

[0062] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is selected from a PD-1 hinge, a CD28 hinge, and a CD8 hinge (including a CD8a hinge), a LIR1 Ig3-4 hinge, a LIR1 Ig-4 hinge, a LIR1 52 aa hinge, a LIR1 36 aa hinge, a LIR1 30 aa hinge, a LIR1 26 aa hinge, a LIR1 8 aa hinge, a CD33 hinge, a KIR2DL1 hinge, a PD-1 (47) hinge, a PD-1 (42) hinge, a PD-1 (36) hinge, a PD-1 (30) hinge, a PD-1 (26) hinge, a PD-1 (20) hinge, and an IgG4 hinge.

[0063] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is a PD-1 hinge (SEQ ID NO: 86).

[0064] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is a CD28 hinge (SEQ ID NO: 85).

[0065] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is a CD8 alpha hinge (SEQ ID NO: 84).

[0066] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is a LIR1 Ig3-4 hinge (SEQ ID NO: 87).

[0067] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is a LIR1 Ig-4 hinge (SEQ ID NO: 88).

[0068] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89).

[0069] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component comprises a LIR1 52 aa hinge (SEQ ID NO: 89).

[0070] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is SN66E3.2 of SEQ ID NO:285, and the iCAR hinge domain component comprises a LIR1 52 aa hinge (SEQ ID NO: 89).

[0071] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is SN66E3.2 of SEQ ID NO:285, and the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89).

[0072] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component consists of or consists essentially of a LIR1 52 aa hinge (SEQ ID NO: 89).

[0073] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89).

[0074] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is Hz BB7.2.1 of SEQ ID NO:287, and the iCAR hinge domain component comprises a LIR1 52 aa hinge (SEQ ID NO: 89).

[0075] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is Hz BB7.2.1 of SEQ ID NO:287, and the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89).

[0076] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component comprises a LIR1 36 aa hinge (SEQ ID NO: 90).

[0077] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component consists of or consists essentially of a LIR1 36 aa hinge (SEQ ID NO: 90).

[0078] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is a LIR1 36 aa hinge (SEQ ID NO: 90).

[0079] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component comprises a LIR1 30 aa hinge (SEQ ID NO: 91).

[0080] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component consists of or consists essentially of a LIR1 30 aa hinge (SEQ ID NO: 91).

[0081] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is a LIR1 30 aa hinge (SEQ ID NO: 91).

[0082] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component comprises a LIR1 26 aa hinge (SEQ ID NO: 289).

[0083] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component consists of or consists essentially of a LIR1 26 aa hinge (SEQ ID NO: 289).

[0084] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is a LIR1 26 aa hinge (SEQ ID NO: 289).

[0085] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component comprises a LIR1 8 aa hinge (SEQ ID NO:92).

[0086] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component consists of or consists essentially of a LIR1 8 aa hinge (SEQ ID NO:92).

[0087] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is a LIR1 8 aa hinge (SEQ ID NO:92).

[0088] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is a CD33 hinge (SEQ ID NO: 93).

[0089] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is a KIR2DL1 hinge (SEQ ID NO: 94).

[0090] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is a PD-1 (47) hinge (SEQ ID NO: 290).

[0091] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is a PD-1 (42) hinge (SEQ ID NO: 291).

[0092] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is a PD-1 (36) hinge (SEQ ID NO: 292).

[0093] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is a PD-1 (30) hinge (SEQ ID NO: 293).

[0094] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is a PD-1 (26) hinge (SEQ ID NO: 294).

[0095] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR hinge domain component is a PD-1 (20) hinge (SEQ ID NO: 295).

[0096] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR TM domain component is selected from a PD-1 TM domain, a CD28 TM domain, a CD8 TM domain (including a CD8a TM domain), a LIR1 TM domain, a CD33 TM domain, and a KIR2DL1 TM domain.

[0097] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR TM domain component is a PD-1 TM domain (SEQ ID NO:97).

[0098] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR TM domain component is a CD28 TM domain (SEQ ID NO:96).

[0099] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR TM domain component is a CD8 alpha TM domain (SEQ ID NO:95).

[0100] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98).

[0101] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is SN66E3.2 of SEQ ID NO:285, the iCAR hinge domain component comprises a LIR1 52 aa hinge (SEQ ID NO: 89), and the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98).

[0102] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is SN66E3.2 of SEQ ID NO:285, the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98).

[0103] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen,

wherein said HLA antigen is HLA-A2, the iCAR scFv is Hz BB7.2.1 of SEQ ID NO:287, the iCAR hinge domain component comprises a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98).

[0104] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is Hz BB7.2.1 of SEQ ID NO:287, the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98).

[0105] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR TM domain component is a CD33 TM domain (SEQ ID NO:99).

[0106] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR TM domain component is a KIR2DL1 TM domain (SEQ ID NO:100).

[0107] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is an inhibitory domain from a protein selected from the group consisting of PD-1, KIR2DL1, KIR2DL2, KIR2DL3, KIR2DL4, KIR2DL5A, KIR3DL1, KIR3DL2, KIR3DL3, LAIR1, CD22, CD33, SIGLEC5, SIGLEC6, SIGLEC7, SIGLEC8, SIGLEC9, SIGLEC10, SIGLEC11, SIGLEC12, PECAM1/CD31, CD200R1, FCRL1, FCRL2, FCRL3, FCRL4, FCRL5, SLAMF1, SLAMF5, BTLA, LAG3, 2B4, CD160, CEACAM1, TIM3, VISTA, TIGIT, SIRPalpha, FcγRIIB, CD5, CD300a, CD300f, LIR1, LIR2, LIR3, LIR5, LIR8, Ly9, 2xPD1(G4S), 2xPD1(PD1), PVRIg, and AA2AR.

[0108] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a PD-1 inhibitory domain (SEQ ID NO:101).

[0109] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR component is a KIR2DL1 inhibitory domain (SEQ ID NO:102).

[0110] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR component is a KIR2DL2 inhibitory domain (SEQ ID NO:103).

[0111] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR component is a KIR2DL3 inhibitory domain (SEQ ID NO:104).

[0112] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a KIR2DL4 inhibitory domain (SEQ ID NO:105).

[0113] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a KIR2DL5A inhibitory domain (SEQ ID NO:106).

[0114] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a KIR3DL1 inhibitory domain (SEQ ID NO:107).

[0115] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a KIR3DL2 inhibitory domain (SEQ ID NO:108).

[0116] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a KIR3DL3 inhibitory domain (SEQ ID NO:109).

[0117] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a LAIR1 inhibitory domain (SEQ ID NO:110).

[0118] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a CD22 inhibitory domain (SEQ ID NO:111).

[0119] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a CD33 inhibitory domain (SEQ ID NO:112).

[0120] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a SIGLEC5 inhibitory domain (SEQ ID NO:113).

[0121] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a SIGLEC6 inhibitory domain (SEQ ID NO:114).

[0122] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a SIGLEC7 inhibitory domain (SEQ ID NO:115).

[0123] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a SIGLEC8 inhibitory domain (SEQ ID NO:116).

[0124] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a SIGLEC9 inhibitory domain (SEQ ID NO:117).

[0125] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a SIGLEC10 inhibitory domain (SEQ ID NO:118).

[0126] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a SIGLEC11inhibitory domain (SEQ ID NO:119).

[0127] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a SIGLEC12inhibitory domain (SEQ ID NO:120).

[0128] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a PECAM1/CD31 inhibitory domain (SEQ ID NO:121).

[0129] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a CD200R1inhibitory domain (SEQ ID NO:122).

[0130] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a FCRL1inhibitory domain (SEQ ID NO:123).

[0131] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a FCRL2inhibitory domain (SEQ ID NO:124).

[0132] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a FCRL3inhibitory domain (SEQ ID NO:125).

[0133] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a FCRL4 inhibitory domain (SEQ ID NO:126).

[0134] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a FCRL5 inhibitory domain (SEQ ID NO:127).

[0135] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a SLAMF1 inhibitory domain (SEQ ID NO:128).

[0136] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a SLAMF5 inhibitory domain (SEQ ID NO:129).

[0137] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a BTLA inhibitory domain (SEQ ID NO:130).

[0138] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a LAG3 inhibitory domain (SEQ ID NO:131).

[0139] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a 2B4 inhibitory domain (SEQ ID NO:132).

[0140] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a CD160 inhibitory domain (SEQ ID NO:133).

[0141] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a CEACAM1 inhibitory domain (SEQ ID NO:134).

[0142] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a TIM3 inhibitory domain (SEQ ID NO:135).

[0143] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a VISTA inhibitory domain (SEQ ID NO:136).

[0144] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a TIGIT inhibitory domain (SEQ ID NO:137).

[0145] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a SIRPalpha inhibitory domain (SEQ ID NO:138).

[0146] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a FcγRIIB inhibitory domain (SEQ ID NO:139).

[0147] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a CD5 inhibitory domain (SEQ ID NO:140).

[0148] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a CD300a inhibitory domain (SEQ ID NO:141).

[0149] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a CD300f inhibitory domain (SEQ ID NO:142).

[0150] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a LIR1 inhibitory domain (SEQ ID NO:143).

[0151] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is SN66E3.2 of SEQ ID NO:285, the iCAR hinge domain component comprises a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component comprises a LIR1 TM domain (SEQ ID NO:98), and the iCAR inhibitory domain component comprises a LIR1 inhibitory domain (SEQ ID NO:143).

[0152] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is SN66E3.2 of SEQ ID NO:285, the iCAR hinge domain component comprises a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98), and the iCAR inhibitory domain component comprises a LIR1 inhibitory domain (SEQ ID NO:143).

[0153] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is SN66E3.2 of SEQ ID NO:285, the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98), and the iCAR inhibitory domain component is a LIR1 inhibitory domain (SEQ ID NO:143).

[0154] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen comprises HLA-A2, the iCAR scFv comprises Hz BB7.2.1 of SEQ ID NO:287, the iCAR hinge domain component comprises a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component comprises a LIR1 TM domain (SEQ ID NO:98), and the iCAR inhibitory domain component comprises a LIR1 inhibitory domain (SEQ ID NO:143).

[0155] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is Hz BB7.2.1 of SEQ ID NO:287, the iCAR hinge domain component comprises a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98), and the iCAR inhibitory domain component comprises a LIR1 inhibitory domain (SEQ ID NO:143).

[0156] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is Hz BB7.2.1 of SEQ ID NO:287, the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98), and the iCAR inhibitory domain component is a LIR1 inhibitory domain (SEQ ID NO:143).

[0157] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a LIR2 inhibitory domain (SEQ ID NO:144).

[0158] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a LIR3 inhibitory domain (SEQ ID NO:145).

[0159] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a LIR5 inhibitory domain (SEQ ID NO:146).

[0160] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a LIR8 inhibitory domain (SEQ ID NO:147).

[0161] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a Ly9 inhibitory domain (SEQ ID NO:148).

[0162] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149).

[0163] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150).

[0164] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a PVRIg inhibitory domain (SEQ ID NO:151).

[0165] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR inhibitory domain component is a AA2AR inhibitory domain (SEQ ID NO:152).

[0166] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR single chain variable fragment (scFv) component targets Her2.

[0167] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen comprises HLA-A2, the iCAR scFv comprises SN66E3.2 of SEQ ID NO:285, the iCAR hinge domain component comprises a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component comprises a LIR1 TM domain (SEQ ID NO:98), the iCAR inhibitory domain component comprises a LIR1 inhibitory domain (SEQ ID NO:143), and the aCAR single chain variable fragment (scFv) component targets Her2.

[0168] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is SN66E3.2 of SEQ ID NO:285, the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98), the iCAR inhibitory domain component is

a LIR1 inhibitory domain (SEQ ID NO:143), and the aCAR single chain variable fragment (scFv) component targets Her2.

[0169] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen comprises HLA-A2, the iCAR scFv comprises Hz BB7.2.1 of SEQ ID NO:287, the iCAR hinge domain component comprises a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component comprises a LIR1TM domain (SEQ ID NO:98), the iCAR inhibitory domain component comprises a LIR1 inhibitory domain (SEQ ID NO:143), and the aCAR single chain variable fragment (scFv) component targets Her2.

[0170] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is Hz BB7.2.1 of SEQ ID NO:287, the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98), the iCAR inhibitory domain component is a LIR1 inhibitory domain (SEQ ID NO:143), and the aCAR single chain variable fragment (scFv) component targets Her2.

[0171] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from trastuzumab (SEQ ID NOs:170 and 171, respectively).

[0172] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen comprises HLA-A2, the iCAR scFv comprises SN66E3.2 of SEQ ID NO:285, the iCAR hinge domain component comprises a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component comprises a LIR1 TM domain (SEQ ID NO:98), the iCAR inhibitory domain component comprises a LIR1 inhibitory domain (SEQ ID NO:143), and the aCAR single chain variable fragment (scFv) component targets Her2, and the aCAR scFv comprises the Vh and Vl from trastuzumab (SEQ ID NOs:170 and 171, respectively).

[0173] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is SN66E3.2 of SEQ ID NO:285, the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98), the iCAR inhibitory domain component is a LIR1 inhibitory domain (SEQ ID NO:143), the aCAR single chain variable fragment (scFv) component targets Her2, and the aCAR single chain variable fragment (scFv) component

targets Her2, and the aCAR scFv comprises the Vh and Vl from trastuzumab (SEQ ID NOs:170 and 171, respectively).

[0174] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen comprises HLA-A2, the iCAR scFv comprises Hz BB7.2.1 of SEQ ID NO:287, the iCAR hinge domain component comprises a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component comprises a LIR1TM domain (SEQ ID NO:98), the iCAR inhibitory domain component comprises a LIR1 inhibitory domain (SEQ ID NO:143), the aCAR single chain variable fragment (scFv) component targets Her2, and the aCAR single chain variable fragment (scFv) component targets Her2, and the aCAR scFv comprises the Vh and Vl from trastuzumab (SEQ ID NOs:170 and 171, respectively).

[0175] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is Hz BB7.2.1 of SEQ ID NO:287, the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98), the iCAR inhibitory domain component is a LIR1 inhibitory domain (SEQ ID NO:143), the aCAR single chain variable fragment (scFv) component targets Her2, and the aCAR scFv comprises the Vh and Vl from trastuzumab (SEQ ID NOs:170 and 171, respectively).

[0176] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is SN66E3.2 of SEQ ID NO:285, the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98), the iCAR inhibitory domain component is a LIR1 inhibitory domain (SEQ ID NO:143), the aCAR single chain variable fragment (scFv) component targets Her2, the aCAR scFv comprises the Vh and Vl from trastuzumab (SEQ ID NOs:170 and 171, respectively), and the aCAR scFv comprises or consists of SEQ ID NO: 451.

[0177] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is SN66E3.2 of SEQ ID NO:285, the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98), the iCAR inhibitory domain component is a LIR1 inhibitory domain (SEQ ID NO:143), the aCAR single chain variable fragment (scFv)

component targets Her2, the aCAR scFv comprises the Vh and Vl from trastuzumab (SEQ ID NOs:170 and 171, respectively), and the aCAR scFv comprises or consists of SEQ ID NO: 452.

[0178] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is Hz BB7.2.1 of SEQ ID NO:287, the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98), the iCAR inhibitory domain component is a LIR1 inhibitory domain (SEQ ID NO:143), the aCAR single chain variable fragment (scFv) component targets Her2, the aCAR scFv comprises the Vh and Vl from trastuzumab (SEQ ID NOs:170 and 171, respectively), and the aCAR scFv comprises or consists of SEQ ID NO: 451.

[0179] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is Hz BB7.2.1 of SEQ ID NO:287, the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98), the iCAR inhibitory domain component is a LIR1 inhibitory domain (SEQ ID NO:143), the aCAR single chain variable fragment (scFv) component targets Her2, the aCAR scFv comprises the Vh and Vl from trastuzumab (SEQ ID NOs:170 and 171, respectively), and the aCAR scFv comprises or consists of SEQ ID NO: 452.

[0180] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv is SEQ ID NO:172.

[0181] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is Hz BB7.2.1 of SEQ ID NO:287, the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98), the iCAR inhibitory domain component is a LIR1 inhibitory domain (SEQ ID NO:143), the aCAR single chain variable fragment (scFv) component targets Her2, the aCAR scFv comprises the Vh and Vl from trastuzumab (SEQ ID NOs:170 and 171, respectively), and the aCAR scFv comprises or consists of SEQ ID NO:172.

[0182] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is Hz BB7.2.1 of SEQ ID NO:287, the

iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98), the iCAR inhibitory domain component is a LIR1 inhibitory domain (SEQ ID NO:143), the aCAR single chain variable fragment (scFv) component targets Her2, the aCAR scFv comprises the Vh and Vl from trastuzumab (SEQ ID NOs:170 and 171, respectively), and the aCAR scFv consists essentially of or is SEQ ID NO:172.

[0183] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is SN66E3.2 of SEQ ID NO:285, the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98), the iCAR inhibitory domain component is a LIR1 inhibitory domain (SEQ ID NO:143), the aCAR single chain variable fragment (scFv) component targets Her2, the aCAR scFv comprises the Vh and Vl from trastuzumab (SEQ ID NOs:170 and 171, respectively), and the aCAR scFv comprises or consists of SEQ ID NO:172.

[0184] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2, the iCAR scFv is SN66E3.2 of SEQ ID NO:285, the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89), the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98), the iCAR inhibitory domain component is a LIR1 inhibitory domain (SEQ ID NO:143), the aCAR single chain variable fragment (scFv) component targets Her2, the aCAR scFv comprises the Vh and Vl from trastuzumab (SEQ ID NOs:170 and 171, respectively), and the aCAR scFv consists essentially of or is SEQ ID NO:172.

[0185] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from trastuzumab F9G (SEQ ID NOs: 307 and 308).

[0186] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from pertuzumab (SEQ ID NOs:173 and 174, respectively).

[0187] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv is SEQ ID NO:175.

[0188] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from FRP5 (SEQ ID NOs:176 and 177, respectively).

[0189] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from A21 (SEQ ID NOs:178 and 179, respectively).

[0190] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from XMT1517 (SEQ ID NOs:180 and 181, respectively).

[0191] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from XMT1518 (SEQ ID NOs:182 and 183, respectively).

[0192] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from XMT1519 (SEQ ID NOs:184 and 185, respectively).

[0193] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from FWP51 (SEQ ID NOs:186 and 187, respectively).

[0194] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises SEQ ID NOs: 188.

[0195] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR single chain variable fragment (scFv) component targets EGFR.

[0196] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from cetuximab (SEQ ID NOs:189 and 190, respectively).

[0197] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv is SEQ ID NO:191.

[0198] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from panitumumab (SEQ ID NOs:192 and 193, respectively).

[0199] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv is SEQ ID NO:194.

[0200] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from Imgatuzumab (SEQ ID NOs:195 and 196, respectively).

[0201] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from Nimotuzumab (SEQ ID NOs:197 and 198, respectively).

[0202] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from Nimotuzumab (K5) (SEQ ID NOs:310 and 311, respectively).

[0203] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from Necitumumab (SEQ ID NOs:199 and 200, respectively).

[0204] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from ICR62 (SEQ ID NOs:201 and 202, respectively).

[0205] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from Matuzumab (SEQ ID NOs:204 and 205, respectively).

[0206] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from C10 (SEQ ID NOs:206 and 207, respectively).

[0207] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from Zalutumumab (SEQ ID NOs:208 and 209, respectively).

[0208] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from P1X (SEQ ID NOs:210 and 211, respectively).

[0209] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from P2X (SEQ ID NOs:212 and 213, respectively).

[0210] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the Vh and Vl from P3X (SEQ ID NOs:214 and 215, respectively).

[0211] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the VH from EGFR-la1-VHH (SEQ ID NO:216).

[0212] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprises the VH from EGFR-VHH (SEQ ID NO:312).

[0213] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR single chain variable fragment (scFv) component targets Mesothelin.

[0214] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprise the Vh and Vl from Amatuximab (SEQ ID NOs:217 and 218, respectively).

[0215] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprise the Vh and Vl from P4 (SEQ ID NOs:219 and 220, respectively).

[0216] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprise the Vh and Vl from SS1 (SEQ ID NOs:222 and 223, respectively).

[0217] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprise the VHH from SD1 (SEQ ID NO:225).

[0218] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprise the VHH from SD2 (SEQ ID NO:226).

[0219] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprise the Vh and Vl from 1H7 (SEQ ID NOs:227 and 228, respectively).

[0220] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the aCAR scFv comprise the Vh and Vl from 3C02 (SEQ ID NOs:230 and 231, respectively).

[0221] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the hinge TM domain component is selected from the group consisting of a CD28 hinge and a CD8 hinge (including a CD8a hinge domain).

[0222] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the hinge TM domain component is a CD28 hinge domain (SEQ ID NO: 85).

[0223] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the hinge TM domain component comprises a CD8 alpha hinge domain (SEQ ID NO: 84).

[0224] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the hinge TM domain component is a CD8 alpha hinge domain (SEQ ID NO: 84).

[0225] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the co-stimulatory domain component is selected from the group consisting of a CD137 (4-1BB) co-stimulatory domain, a CD28 co-stimulatory domain, a 28BB co-stimulatory domain, and a CD3z co-stimulatory domain.

[0226] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the co-stimulatory domain component is a CD137 (4-1BB) co-stimulatory domain (SEQ ID NO:233).

[0227] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the co-stimulatory domain component is a CD28 co-stimulatory domain (SEQ ID NO:234).

[0228] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the co-stimulatory domain component a CD3z activation signaling domain (SEQ ID NO:235).

[0229] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the ITAM comprises a CD3 zeta domain.

[0230] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the ITAM consists of or consists essentially of a CD3 zeta domain.

[0231] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the ITAM is a CD3 zeta domain.

[0232] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the ITAM comprises a CD3 zeta domain (SEQ ID NO:236).

[0233] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the ITAM consists of or consists essentially of a CD3 zeta domain (SEQ ID NO:236).

[0234] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the ITAM is a CD3 zeta domain (SEQ ID NO:236).

[0235] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the ITAM is a CD3 zeta 3F domain (SEQ ID NO:237).

[0236] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the ITAM is a CD3 zeta 4F domain (SEQ ID NO:238).

[0237] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the ITAM is a CD3 zeta 4OF domain (SEQ ID NO:239).

[0238] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the linker connecting the iCAR portion and the aCAR portion comprises one or more linker selected from the group consisting of T2A (SEQ ID NO:155), F2A (SEQ ID NO:156), P2A (SEQ ID NO:157), E2A (SEQ ID NO:158), and an IRES sequence (SEQ ID NO:159 or 160).

[0239] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the linker connecting the iCAR portion and the aCAR portion comprises SEQ ID NO:159.

[0240] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the linker connecting the iCAR portion and the aCAR portion consists of or consists essentially of SEQ ID NO:159.

[0241] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the linker connecting the iCAR portion and the aCAR portion comprises SEQ ID NO:160.

[0242] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the linker connecting the iCAR portion and the aCAR portion consists of or consists essentially of SEQ ID NO:160.

[0243] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the linker connecting the iCAR portion and the aCAR portion is GSG T2A (SEQ ID NO:155).

[0244] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the bicistronic iCAR/aCAR construct comprises an amino acid sequence encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID

NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, SEQ ID NO:325, SEQ ID NO:335, SEQ ID NO:336, SEQ ID NO:337, SEQ ID NO:338, SEQ ID NO:339, SEQ ID NO:340, and SEQ ID NO: 341.

[0245] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the bicistronic iCAR/aCAR construct comprises an amino acid sequence encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0246] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the bicistronic iCAR/aCAR construct comprises an amino acid sequence encoded by the nucleic acid sequence of SEQ ID NO:277.

[0247] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the bicistronic iCAR/aCAR construct consists of or consists essentially of an amino acid sequence encoded by the nucleic acid sequence of SEQ ID NO:277.

[0248] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the nucleic acid sequence that encodes said bicistronic iCAR/aCAR has at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the nucleic acid sequence of SEQ ID NO:277.

[0249] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the nucleic acid sequence that encodes said bicistronic iCAR/aCAR has at least 95% identity to the nucleic acid sequence of SEQ ID NO:277.

[0250] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the nucleic acid sequence that encodes said bicistronic iCAR/aCAR has at least 96% identity to the nucleic acid sequence of SEQ ID NO:277.

[0251] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the nucleic acid sequence that encodes said bicistronic iCAR/aCAR has at least 97% identity to the nucleic acid sequence of SEQ ID NO:277.

[0252] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the nucleic acid sequence that encodes said

bicistronic iCAR/aCAR has at least 98% identity to the nucleic acid sequence of SEQ ID NO:277.

[0253] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the nucleic acid sequence that encodes said bicistronic iCAR/aCAR has at least 99% identity to the nucleic acid sequence of SEQ ID NO:277.

[0254] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the bicistronic iCAR/aCAR construct comprises an amino acid sequence encoded by the nucleic acid sequence of SEQ ID NO:279.

[0255] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the bicistronic iCAR/aCAR construct consists of or consists essentially of an amino acid sequence encoded by the nucleic acid sequence of SEQ ID NO:279.

[0256] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the nucleic acid sequence that encodes said bicistronic iCAR/aCAR has at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the nucleic acid sequence of SEQ ID NO:279.

[0257] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the nucleic acid sequence that encodes said bicistronic iCAR/aCAR has at least 95% identity to the nucleic acid sequence of SEQ ID NO:279.

[0258] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the nucleic acid sequence that encodes said bicistronic iCAR/aCAR has at least 96% identity to the nucleic acid sequence of SEQ ID NO:279.

[0259] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the nucleic acid sequence that encodes said bicistronic iCAR/aCAR has at least 97% identity to the nucleic acid sequence of SEQ ID NO:279.

[0260] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the nucleic acid sequence that encodes said bicistronic iCAR/aCAR has at least 98% identity to the nucleic acid sequence of SEQ ID NO:279.

[0261] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the nucleic acid sequence that encodes said bicistronic iCAR/aCAR has at least 99% identity to the nucleic acid sequence of SEQ ID NO:279.

[0262] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the bicistronic iCAR/aCAR construct comprises an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:276, SEQ ID NO:278, SEQ ID NO:280, SEQ ID NO:282, SEQ ID NO:322, SEQ ID NO:324, and SEQ ID NO:326.

[0263] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the bicistronic iCAR/aCAR construct comprises an amino acid sequence selected from the group consisting of SEQ ID NO:276, SEQ ID NO:278, SEQ ID NO:280, SEQ ID NO:282, SEQ ID NO:322, SEQ ID NO:324, and SEQ ID NO:326.

[0264] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the bicistronic iCAR/aCAR construct comprises or consists of a nucleic acid that encodes SEQ ID NO:278.

[0265] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the bicistronic iCAR/aCAR comprises SEQ ID NO:278.

[0266] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the bicistronic iCAR/aCAR consists of or consists essentially of SEQ ID NO:278.

[0267] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the amino acid sequence of the bicistronic iCAR/aCAR is at least 96% identical to SEQ ID NO:278.

[0268] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the amino acid sequence of the bicistronic iCAR/aCAR is at least 97% identical to SEQ ID NO:278.

[0269] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the amino acid sequence of the bicistronic iCAR/aCAR is at least 98% identical to SEQ ID NO:278.

[0270] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the amino acid sequence of the bicistronic iCAR/aCAR is at least 99% identical to SEQ ID NO:278.

[0271] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the bicistronic iCAR/aCAR construct comprises a nucleic acid that encodes SEQ ID NO:280.

[0272] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the bicistronic iCAR/aCAR construct consists of a nucleic acid that encodes SEQ ID NO:280.

[0273] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the bicistronic iCAR/aCAR comprises SEQ ID NO:280.

[0274] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the bicistronic iCAR/aCAR consists of or consists essentially of SEQ ID NO:280.

[0275] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the amino acid sequence of the bicistronic iCAR/aCAR is at least 96% identical to SEQ ID NO:280.

[0276] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the amino acid sequence of the bicistronic iCAR/aCAR is at least 97% identical to SEQ ID NO:280.

[0277] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the amino acid sequence of the bicistronic iCAR/aCAR is at least 98% identical to SEQ ID NO:280.

[0278] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the amino acid sequence of the bicistronic iCAR/aCAR is at least 99% identical to SEQ ID NO:280.

[0279] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, the bicistronic iCAR/aCAR construct further comprises a short hairpin RNA (shRNA).

[0280] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as described herein comprise an iCAR that comprises a synthetic PD-1 or LIR1 sequence as shown in Table 8, including one selected from the group consisting of SEQ ID NO:243, SEQ ID NO:244, SEQ ID NO:245, SEQ ID NO:246, SEQ ID

NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:296, SEQ ID NO:297, SEQ ID NO:298, SEQ ID NO:299, SEQ ID NO:300, SEQ ID NO:301, SEQ ID NO:302, and SEQ ID NO:304.

[0281] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as described herein comprise a nucleic acid sequence as described in Table 1, including SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0282] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as described herein comprise an amino acid sequence as described in Table 1, including SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:276, SEQ ID NO:278, SEQ ID NO:280, SEQ ID NO:282, SEQ ID NO:322, SEQ ID NO:324, and SEQ ID NO:326.

[0283] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as described herein comprise an iCAR comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:305, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:327, SEQ ID NO:328, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:331, SEQ ID NO:332, SEQ ID NO:333, and SEQ ID NO:334.

[0284] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as described herein comprise a construct as described in Table 1, Table 11 and/or Table 12.

[0285] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as described herein comprise a construct or portion thereof as described in any one of Tables 1 to 22.

[0286] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as described herein comprise a construct as described in any one of Tables 15, 16, 17, and/or 21.

[0287] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as described herein comprise a construct as described in any one of Tables 1, 2, 4, 9, 10, 11 and/or 12.

[0288] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as described herein comprise:

i. an iCAR portion, wherein the iCAR portion comprises:

   a. a CD8a Leader Sequence having the sequence of MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);

   b. an iCAR single chain variable fragment (scFv) component having the sequence of SN66E3.2 scFv: DIVMTQSPDSLAVSLGERATISCKSSQSVLYSSNNKNYLAW YQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISS LQAEDVAVYYCQQYYGTPFTFGGGTKVEIKGGGGSGGGGS GGGGSQVQLVQSGAEVKKPGASVKVSCKASGYTFTDYYLH WVRQAPGQGLEWMGWINPYTGGTNYAQKFQGRVTMTRD TSISTAYMELSGLTSDDTAVYYCARAGASYYDFWSGWVFD YWGQGTLVTVSS (SEQ ID NO: 285);

   c. an iCAR hinge domain component having the sequence of LIR1 Hinge (30): GPTSTSGPEDQPLTPTGSDPQSGLGRHLGV (SEQ ID NO: 91);

   d. an iCAR transmembrane (TM) domain component having the sequence of LIR1 TM: VIGILVAVILLLLLLLLLFLI (SEQ ID NO: 98);

   e. an iCAR inhibitory domain component having the sequence of LIR1 Inhibitory domain: LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRS SPAADAQEENLYAAVKHTQPEDGVEMDTRSPHDEDPQAVT YAEVKHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTE

AAASEAPQDVTYAQLHSLTLRREATEPPPSQEGPSPAVPSIY ATLAIH (SEQ ID NO: 143); and

ii. an aCAR portion, wherein the aCAR portion comprises:

a. a CD8a Leader Sequence: MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);

b. an aCAR scFv component having the sequence of Trastuzumab scFv : VL_whitlow linker_VH: DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKP GKAPKLLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDF ATYYCQQHYTTPPTFGQGTKVEIKGSTSGSGKPGSGEGSTK GEVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQA PGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKNTAYL QMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVS (SEQ ID NO: 451);

c. an aCAR hinge domain component having the sequence of CD8a: Hinge: TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDF ACD (SEQ ID NO: 84);

d. CD8a: TM: IYIWAPLAGTCGVLLLSLVITLYC (SEQ ID NO: 95);

e. an aCAR co-stimulatory domain component having the sequence of 41BB costim: KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCE L (SEQ ID NO: 233);

f. an aCAR activation signaling domain having the sequence of CD3 zeta: RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRG RDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGE RRRGKGHDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID NO: 236); and

iii. an IRES long sequence that connects the iCAR portion in (i) and the aCAR portion in (ii), wherein the IRES has the sequence of SEQ ID NO: 159.

[0289] In some embodiments, the iCAR has the sequence of SEQ ID NO: 258.

[0290] In some embodiments, the iCAR/aCAR construct has the sequence of SEQ ID NO: 280.

[0291] In some embodiments of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as described herein comprise:

i. an iCAR portion, wherein the iCAR portion comprises:

a. a CD8a Leader Sequence having the sequence of MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);

b. an iCAR single chain variable fragment (scFv) component having the sequence of SN66E3.3 scFv: VK(G4S)X3 Linker_VH: DIVMTQSPDSLAVSLGERATISCKSSQSVLYSSNNKNYLAW YQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISS LQAEDVAVYYCQQYYGTPFTFGGGTKVEIKGGGGSGGGGS GGGGSQVQLVQSGAEVKKPGASVKVSCKASGYTFTDYYLH WVRQAPGQGLEWMGWINPYTGGTNYAQKFQGRVTMTRD TSISTAYMELSRLRSEDTAVYYCARAGASYYDFWSGWVFD YWGQGTLVTVSS (SEQ ID NO: 286);

c. an iCAR hinge domain component having the sequence of LIR1 Hinge (26): TSGPEDQPLTPTGSDPQSGLGRHLGV (SEQ ID NO: 289);

d. an iCAR transmembrane (TM) domain component having the sequence of LIR1 TM: VIGILVAVILLLLLLLLLFLI (SEQ ID NO: 98);

e. an iCAR inhibitory domain component having the sequence of LIR1 Inhibitory domain: LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRS SPAADAQEENLYAAVKHTQPEDGVEMDTRSPHDEDPQAVT YAEVKHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTE AAASEAPQDVTYAQLHSLTLRREATEPPPSQEGPSPAVPSIY ATLAIH (SEQ ID NO: 143); and

ii. an aCAR portion, wherein the aCAR portion comprises:

a. a CD8a Leader Sequence: MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);

b. an aCAR scFv component having the sequence of Trastuzumab scFv : VL_whitlow linker_VH: DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKP GKAPKLLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDF ATYYCQQHYTTPPTFGQGTKVEIKGSTSGSGKPGSGEGSTK GEVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQA PGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKNTAYL QMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVS S (SEQ ID NO: 452);

c. an aCAR hinge domain component having the sequence of CD8a: Hinge: TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDF ACD (SEQ ID NO: 84);

d. CD8a: TM: IYIWAPLAGTCGVLLLSLVITLYC (SEQ ID NO: 95);

e. an aCAR co-stimulatory domain component having the sequence of 41BB costim: KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCE L (SEQ ID NO: 233);

f. an aCAR activation signaling domain having the sequence of CD3 zeta: RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRG RDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGE RRRGKGHDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID NO: 236); and

iii. an IRES long sequence that connects the iCAR portion in (i) and the aCAR portion in (ii), wherein the IRES has the sequence of SEQ ID NO:159.

[0292] In some embodiments, the iCAR has the sequence of SEQ ID NO: 305.

[0293] In some embodiments, the iCAR/aCAR construct has the sequence of SEQ ID NO: 282.

[0294] In some embodiments, the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as described herein comprise:

1. an iCAR portion, wherein the iCAR portion comprises:
    a. a CD8a Leader Sequence having the sequence of MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);
    b. an iCAR single chain variable fragment (scFv) component having the sequence of SN66E3.2 scFv: DIVMTQSPDSLAVSLGERATISCKSSQSVLYSSNNKNYLAWYQQKPGQPP KLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYGTP FTFGGGTKVEIKGGGGSGGGGSGGGGSQVQLVQSGAEVKKPGASVKVSC KASGYTFTDYYLHWVRQAPGQGLEWMGWINPYTGGTNYAQKFQGRVT MTRDTSISTAYMELSGLTSDDTAVYYCARAGASYYDFWSGWVFDYWGQ GTLVTVSS (SEQ ID NO: 285);
    c. an iCAR hinge domain component having the sequence of LIR1 Hinge (52): PSDPLELVVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGV (SEQ ID NO: 89);
    d. an iCAR transmembrane (TM) domain component having the sequence of LIR1 TM: VIGILVAVILLLLLLLLLFLI (SEQ ID NO: 98);
    e. an iCAR inhibitory domain component having the sequence of LIR1 Inhibitory domain: LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEE NLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPRREMASPPS PLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYAQLHSLTLRREATEP PPSQEGPSPAVPSIYATLAIH (SEQ ID NO: 143); and

ii. an aCAR portion, wherein the aCAR portion comprises:
    a. a CD8a Leader Sequence: MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);
    b. an aCAR scFv component having the sequence of Trastuzumab scFv : VL_whitlow linker_VH: DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYS ASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGT KVEIKGSTSGSGKPGSGEGSTKGEVQLVESGGGLVQPGGSLRLSCAASGF NIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKN

TAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSS (SEQ ID NO: 452);

c. an aCAR hinge domain component having the sequence of CD8a: Hinge: TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO: 84);

d. CD8a: TM: IYIWAPLAGTCGVLLLSLVITLYC (SEQ ID NO: 95);

e. an aCAR co-stimulatory domain component having the sequence of 41BB costim: KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL (SEQ ID NO: 233);

f. an aCAR activation signaling domain having the sequence of CD3 zeta: RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGK PRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTA TKDTYDALHMQALPPR (SEQ ID NO: 236); and

iii. an IRES long sequence that connects the iCAR portion in (i) and the aCAR portion in (ii), wherein the IRES has the sequence of SEQ ID NO: 159.

[0295] In some embodiments, the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as described herein consist of:

i. an iCAR portion, wherein the iCAR portion consists of:

a. a CD8a Leader Sequence having the sequence of MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);

b. an iCAR single chain variable fragment (scFv) component having the sequence of SN66E3.2 scFv: DIVMTQSPDSLAVSLGERATISCKSSQSVLYSSNNKNYLAWYQQKPGQPP KLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYGTP FTFGGGTKVEIKGGGGSGGGGSGGGGSQVQLVQSGAEVKKPGASVKVSC KASGYTFTDYYLHWVRQAPGQGLEWMGWINPYTGGTNYAQKFQGRVT MTRDTSISTAYMELSGLTSDDTAVYYCARAGASYYDFWSGWVFDYWGQ GTLVTVSS (SEQ ID NO: 285);

c. an iCAR hinge domain component having the sequence of LIR1 Hinge (52): HPSDPLELVVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGV (SEQ ID NO: 89);

d. an iCAR transmembrane (TM) domain component having the sequence of LIR1 TM: VIGILVAVILLLLLLLLLFLI (SEQ ID NO: 98);

e. an iCAR inhibitory domain component having the sequence of LIR1 Inhibitory domain:
LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEE NLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPRREMASPPS PLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYAQLHSLTLRREATEP PPSQEGPSPAVPSIYATLAIH (SEQ ID NO: 143); and

ii. an aCAR portion, wherein the aCAR portion consists of:

a. a CD8a Leader Sequence: MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);

b. an aCAR scFv component having the sequence of Trastuzumab scFv :
VL_whitlow linker_VH:
DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYS ASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGT KVEIKGSTSGSGKPGSGEGSTKGEVQLVESGGGLVQPGGSLRLSCAASGF NIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKN TAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSS (SEQ ID NO: 452);

c. an aCAR hinge domain component having the sequence of CD8a: Hinge:
TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO: 84);

d. CD8a: TM: IYIWAPLAGTCGVLLLSLVITLYC (SEQ ID NO: 95);

e. an aCAR co-stimulatory domain component having the sequence of 41BB costim:
KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL (SEQ ID NO: 233);

f. an aCAR activation signaling domain having the sequence of CD3 zeta:
RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGK PRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTA TKDTYDALHMQALPPR (SEQ ID NO: 236); and

iii. an IRES long sequence that connects the iCAR portion in (i) and the aCAR portion in (ii), wherein the IRES has the sequence of SEQ ID NO: 159.

[0296] In some embodiments, the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as described herein comprise:

i. an iCAR portion, wherein the iCAR portion comprises:

a. a CD8a Leader Sequence having the sequence of MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);

b. an iCAR single chain variable fragment (scFv) component having the sequence of Hz BB7.2.1 scFv:
QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYHIQWVRQAPGQGLEWM
GWIYPGDGSTQYNEKFKGRTTITADKSTSTAYMELSSLRSEDTAVYYCAR
EGTYYAMDYWGQGTLVTVSSGGGGSGGGGSGGGGSDVVMTQTPLSLSV
TPGQPASISCRSSQSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGVP
DRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVPRTFGGGTKVEIK
(SEQ ID NO: 287);
c. an iCAR hinge domain component having the sequence of LIR1 Hinge (52):
HPSDPLELVVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGV
(SEQ ID NO: 89);
d. an iCAR transmembrane (TM) domain component having the sequence of LIR1 TM: VIGILVAVILLLLLLLLLFLI (SEQ ID NO: 98);
e. an iCAR inhibitory domain component having the sequence of LIR1 Inhibitory domain:
LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEE
NLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPRREMASPPS
PLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYAQLHSLTLRREATEP
PPSQEGPSPAVPSIYATLAIH (SEQ ID NO: 143); and

ii. an aCAR portion, wherein the aCAR portion comprises:
a. a CD8a Leader Sequence: MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);
b. an aCAR scFv component having the sequence of Trastuzumab scFv :
VL_whitlow linker_VH:
DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYS
ASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGT
KVEIKGSTSGSGKPGSGEGSTKGEVQLVESGGGLVQPGGSLRLSCAASGF
NIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKN
TAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSS (SEQ ID NO: 452);
c. an aCAR hinge domain component having the sequence of CD8a: Hinge:
TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO: 84);
d. CD8a: TM: IYIWAPLAGTCGVLLLSLVITLYC (SEQ ID NO: 95);

e. an aCAR co-stimulatory domain component having the sequence of 41BB costim: KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL (SEQ ID NO: 233);

f. an aCAR activation signaling domain having the sequence of CD3 zeta: RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGK PRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTA TKDTYDALHMQALPPR (SEQ ID NO: 236); and

iii. an IRES long sequence that connects the iCAR portion in (i) and the aCAR portion in (ii), wherein the IRES has the sequence of SEQ ID NO: 159.

[0297] In some embodiments, the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as described herein consist of:

i. an iCAR portion, wherein the iCAR portion consists of:

a. a CD8a Leader Sequence having the sequence of MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);

b. an iCAR single chain variable fragment (scFv) component having the sequence of Hz BB7.2.1 scFv: QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYHIQWVRQAPGQGLEWM GWIYPGDGSTQYNEKFKGRTTITADKSTSTAYMELSSLRSEDTAVYYCAR EGTYYAMDYWGQGTLVTVSSGGGGSGGGGSGGGGSDVVMTQTPLSLSV TPGQPASISCRSSQSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGVP DRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVPRTFGGGTKVEIK (SEQ ID NO: 287);

c. an iCAR hinge domain component having the sequence of LIR1 Hinge (52): HPSDPLELVVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGV (SEQ ID NO: 89);

d. an iCAR transmembrane (TM) domain component having the sequence of LIR1 TM: VIGILVAVILLLLLLLLLFLI (SEQ ID NO: 98);

e. an iCAR inhibitory domain component having the sequence of LIR1 Inhibitory domain: LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEE NLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPRREMASPPS

PLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYAQLHSLTLRREATEP PPSQEGPSPAVPSIYATLAIH (SEQ ID NO: 143); and

ii. an aCAR portion, wherein the aCAR portion consists of:
   a. a CD8a Leader Sequence: MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);
   b. an aCAR scFv component having the sequence of Trastuzumab scFv : VL_whitlow linker_VH: DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYS ASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGT KVEIKGSTSGSGKPGSGEGSTKGEVQLVESGGGLVQPGGSLRLSCAASGF NIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKN TAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSS (SEQ ID NO: 452);
   c. an aCAR hinge domain component having the sequence of CD8a: Hinge: TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO: 84);
   d. CD8a: TM: IYIWAPLAGTCGVLLLSLVITLYC (SEQ ID NO: 95);
   e. an aCAR co-stimulatory domain component having the sequence of 41BB costim: KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL (SEQ ID NO: 233);
   f. an aCAR activation signaling domain having the sequence of CD3 zeta: RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGK PRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTA TKDTYDALHMQALPPR (SEQ ID NO: 236); and

iii. an IRES long sequence that connects the iCAR portion in (i) and the aCAR portion in (ii), wherein the IRES has the sequence of SEQ ID NO: 159.

[0298] The present invention also provides for a nucleic acid composition comprising a nucleic acid that encodes a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to any one of the preceding claims.

[0299] The present invention also provides for a nucleic acid composition comprising a nucleic acid that encodes a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, wherein the bicistronic iCAR/aCAR construct comprises or consists of a nucleic acid sequence that encodes SEQ ID NO:278.

[0300] The present invention also provides for a nucleic acid composition comprising a nucleic acid that encodes a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, wherein the bicistronic iCAR/aCAR construct comprises or consists of a nucleic acid sequence that encodes SEQ ID NO:280.

[0301] The present invention also provides for a nucleic acid composition comprising a nucleic acid that encodes a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, as described in any one of paragraphs [0294], [0295], [0296] or [0297] above.

[0302] The present invention also provides for a nucleic acid composition comprising a nucleic acid that encodes a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to any one of the preceding embodiments.

[0303] The present invention also provides for a vector comprising a nucleic acid sequence encoding for a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to any one of the preceding claims.

[0304] The present invention also provides for a vector comprising a nucleic acid sequence encoding for a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to any one of the preceding embodiments.

[0305] The present invention also provides for a vector comprising a nucleic acid sequence encoding for a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as described in any one of paragraphs paragraphs [0294], [0295], [0296] or [0297] above.

[0306] The present invention also provides for a vector comprising a nucleic acid sequence encoding for a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to any one of claims 48, 49, 50, 51, 52, or 53.

[0307] In some embodiments, the iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction comprises a signal peptide upstream of the iCAR and/or aCAR portions. In some embodiments, the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0308] The present invention also provides for a vector composition comprising the nucleic acid composition of claim 60.

[0309] The present invention also provides for a vector composition comprising the nucleic acid composition of claim 61.

[0310] The present invention also provides for a safe effector cell comprising a nucleic acid or nucleic acid sequence composition as described herein.

[0311] The present invention also provides for a safe effector cell comprising a nucleic acid or nucleic acid sequence composition according to claim 56.

[0312] The present invention also provides for a safe effector cell comprising a nucleic acid or nucleic acid sequence composition according to claim 58.

[0313] The present invention also provides for a safe effector cell comprising a vector or vector composition as described herein.

[0314] The present invention also provides for a safe effector immune cell expressing a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as described herein.

[0315] The present invention also provides for a method for treating cancer in a patient having a tumor characterized by LOH, comprising administering to the patient a safe effector immune cell as described herein.

[0316] The present invention also provides for a method for treating cancer in a patient having a tumor characterized by LOH, comprising administering to the patient a safe effector immune cell according to claim 64.

[0317] The present invention also provides for a method for treating cancer in a patient having a tumor characterized by LOH, comprising administering to the patient a safe effector immune cell according to claim 65.

[0318] The present invention also provides for a method for treating cancer in a patient having a tumor characterized by a genetic mutation resulting in a complete loss of expression of a target gene or target extracellular polymorphic epitope gene, comprising administering to the patient a safe effector immune cell as described herein.

[0319] The present invention also provides for a method for treating cancer in a patient having a tumor characterized by loss of heterozygosity (LOH), or other genetic loss or allelic imbalance phenotypes including, without limitation, loss of function or expression, resulting from mutations affecting one or more nucleotides, comprising administering to the patient a safe effector immune cell according to any one of claim 66 or claim 67.

[0320] A method for treating cancer in a patient having a tumor characterized by loss of heterozygosity (LOH), or other genetic loss or allelic imbalance phenotypes including, without limitation, loss of function or expression, resulting from mutations affecting one or more nucleotides, comprising administering to the patient a safe effector immune cell according to claim 67.

[0321] In some embodiments, the cancer is selected from the group consisting of Acute Myeloid Leukemia [LAML], Adrenocortical carcinoma [ACC], Bladder Urothelial Carcinoma [BLCA], Brain Lower Grade Glioma [LGG], Breast invasive carcinoma [BRCA], Cervical squamous cell carcinoma and endocervical adenocarcinoma [CESC], Cholangiocarcinoma [CHOL], Colon adenocarcinoma [COAD], Esophageal carcinoma [ESCA], Glioblastoma multiforme [GBM], Head and Neck squamous cell carcinoma [HNSC], Kidney Chromophobe [KICH], Kidney renal clear cell carcinoma [KIRC], Kidney renal papillary cell carcinoma [KIRP], Liver hepatocellular carcinoma [LIHC], Lung adenocarcinoma [LUAD], Lung squamous cell carcinoma [LUSC], Lymphoid Neoplasm Diffuse Large B-cell Lymphoma [DLBC], Mesothelioma [MESO], Ovarian serous cystadenocarcinoma [OV], Pancreatic adenocarcinoma [PAAD], Pheochromocytoma and Paraganglioma [PCPG], Prostate adenocarcinoma [PRAD], Rectum adenocarcinoma [READ], Sarcoma [SARC], Skin Cutaneous Melanoma [SKCM], Stomach adenocarcinoma [STAD], Testicular Germ Cell Tumors [TGCT], Thymoma [THYM], Thyroid carcinoma [THCA], Uterine Carcinosarcoma [UCS], Uterine Corpus Endometrial Carcinoma [UCEC], Uveal Melanoma [UVM], Non-small cell lung carcinoma [NSCLC], and Small cell lung cancer [SCLC].

[0322] In some embodiments, provided herein is an anti-idiotypic antibody comprising an anti-HLA-A2 antibody that comprises FW1, CDRH1, FW2, CDRH2, FX3, CDRH3, and FW4 sequences selected from:

a. SEQ ID NOs: 359, 360, 361, 362, 363, 364, and 365, respectively;

b. SEQ ID NOs: 366, 367, 368, 369, 370, 372, and 372, respectively;

c. SEQ ID NOs: 373, 374, 375, 376, 377, 378, and 379, respectively;

d. SEQ ID NOs: 380, 381, 382, 383, 384, 385, and 386, respectively;

e. SEQ ID NOs: 387, 388, 389, 390, 391, 392, and 393, respectively;

f. SEQ ID NOs: 394, 395, 396, 397, 398, 399, and 400, respectively;

g. SEQ ID NOs: 401, 402, 403, 404, 405, 406, and 407, respectively;

h. SEQ ID NOs: 408, 409, 410, 411, 412, 413, and 414, respectively;

i. SEQ ID NOs: 415, 416, 417, 418, 419, 420, and 421, respectively; and

j. SEQ ID NOs: 422, 423, 424, 425, 426, 427, and 428, respectively.

[0323] In some embodiments, the antibody comprises H and L sequence selected from:

a. the H and L sequences of SEQ ID NOs: 429-432;

b. the H and L sequences of SEQ ID NOs: 433-436;

c. the H and L sequences of SEQ ID NOs: 437-440;

d. the H and L sequences of SEQ ID NOs: 441-444; and

e. the H and L sequences of SEQ ID NOs: 445-448.

[0324] In some embodiments, provided herein is a method for producing a population of cells comprising the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to any one of claims 1-196 as filed in U.S. Provisional Application No 63/318353 (filed on March 9, 2022) the method comprising:

i. obtaining a population of effector immune cells directed to a tumor-associated antigen;

ii. transfecting the effector immune cells with a nucleic acid molecule or a vector comprising a nucleotide sequence encoding the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction; and

iii. enriching the effector immune cells for expression of an anti-HLA-A2 scFv using the anti-idiotypic antibody of claim 210 or 211 as filed in U.S. Provisional Application No. 63/318353 (filed on March 9, 2022).

[0325] In some embodiments, provided herein is a method for producing a population of cells comprising the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to any one of claims 1-196, the method comprising:

i. obtaining a population of naïve effector immune cells;

ii. transfecting the naïve effector immune cells with a nucleic acid molecule or a vector comprising a nucleotide sequence encoding the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction; and

iii. enriching the naïve effector immune cells for expression of an anti-HLA-A2 scFv using the anti-idiotypic antibody of claim 210 or 211.

[0326] In some embodiments, the bicistronic iCAR/aCAR construct is encoded a single vector.

[0327] In some embodiments, the bicistronic iCAR and aCAR constructs are encoded on different/separate vectors.

[0328] In some embodiments, the monocistronic aCAR and iCAR constructs for co-transduction are encoded on a single vector.

[0329] In some embodiments, the monocistronic aCAR and iCAR constructs for co-transduction are encoded on different/separate vectors.

[0330] In some embodiments, the immune cells are T-cells, natural killer cells, or cytokine-induced killer cells.

[0331] In some embodiments, the immune cells are Jurkat T-cells, Jurkat-NFAT T-cells, and/or peripheral blood mononuclear cells (PBMCs).

BRIEF DESCRIPTION OF THE DRAWINGS

[0332] Fig. 1 shows bicistronic construct design overview and component table.

[0333] Fig. 2A-2H show bicistronic survey - constructs MC0280-MC0300, MC0428, MC0447, MC0449, HLA-A2 shRNA.

[0334] Fig. 3A-B shows bicistronic constructs VR033, VR492, VR428, VR442, VR443, VR515, VR447, VR516, VR449, VR517, VR421, VR506, VR507, and VR508.

[0335] Fig. 4A-B shows results of killing (efficacy) and protection analysis of bicistronic candidates VR033, VR428, VR443, VR447, and VR449. The results demonstrated that constructs comprising an SN66E3 iCAR scFv performed better than constructs comprising an HzBB7.2 iCAR scFv.

[0336] Fig. 5A-B shows results of killing (efficacy) and protection analysis of bicistronic candidates comprising an IRES linker (VR443, VR447, and VR449) compared to those comprising a T2A linker (VR515, VR516, and VR517). The results demonstrate that VR447 (IRES) and VR516 (T2A) performed similarly, VR449 (IRES) and VR517 (T2A) performed similarly, and VR443(IRES) protected better than VR515 (T2A), where efficacy was similar.

[0337] Fig. 6 shows IncuCyte images obtained form analysis of bicistronic candidates VR492, VR443, and VR515. The results show that VR443 demonstrated protection in the presence of two separate spheres, no protection was observed in the admix sphere, and VR492 with a mutated iDomain showed no protection indicating protection is driven by the iDomain.

[0338] Fig. 7 shows IncuCyte spheroid analysis of killing (efficacy) of bicistronic candidates VR492, VR443, VR515, VR516, VR517, VR515 (CD4+ enriched), and VR443 (thawed). The results demonstrate that thawed VR443 did not kill the spheres very well; VR515 (CD4+ enriched) had lower efficacy compared to VR515 that was untouched; and that the efficacy was lower in spheroid mix as compared to the admix.

[0339] Fig. 8 shows IncuCyte spheroid analysis of protection of bicistronic candidates VR492, VR443, VR515, VR516, VR517, VR515 (CD4+ enriched), and VR443 (thawed). The results

demonstrate that killing was observed for all bicistronic constructs in the admix; protection of IRES 443 was similar to that of T2A VR515 (CD4+ enriched) in the spheroid mix. The protection ranking was as follows for WT only: VR492< VR515< VR443, VR516, VR517 < VR515 CD4+. The protection ranking was as follows for the admix: VR492, VR515, VR516, VR517, VR443 < VR515 CD4+ < VR443 thawed. The protection ranking was as follows for the spheroid mix: VR492< VR515< VR516, VR517< VR443 < VR515 CD4+ , VR443.

[0340] Fig. 9A-B shows results of killing (efficacy) and protection analysis of bicistronic candidates comprising different hinge transmembrane (HTM) domains (VR33, VR421, VR518, VR506, VR507, and VR508). The results demonstrated that constructs comprising the IgG4(22) hinge performed slightly better than those comprising the LIR1(52) hinge; the performance ranking was as follows for IgG4 hinge lengths: 22>28>18; and the VR518 (tagged VR428) construct did not protect.

[0341] Fig. 10A-B shows results of downregulation of iCAR/aCAR constructs VR033, VR421, VR506, VR507, VR508, and VR518. The results demonstrate that there was strong iCAR downregulation in all samples, and weak aCAR downregulation.

[0342] Fig. 11 shows IncuCyte Annexin analysis of killing (efficacy) of bicistronic candidates VR33, VR421 (LIR1(52)), VR506 (IgG4(28)), VR507 (IgG4(22)), VR508 (IgG4(18)), and VR518 (VR428 cMyc). The results demonstrate that alloreactivity was not seen in IncuCyte; IgG4(22 or 28) hinge was similar to LIR1(52); IgG4(18) did not protect; and VR518 (tagged VR428) protected to background.

[0343] Fig. 12A-B shows results of killing (efficacy) and protection analysis of an in vivo animal study comparing HzBB7.2 vs. fully human SN66E3.2 and SN66E3.3 iCAR scFv at two different doses

[0344] Fig. 13 shows SDS-PAGE analysis of Ni-NTA column purified HzBB7 scFv protein.

[0345] Fig. 14 shows binding specificity of purified anti-HzBB7 anti idiotype antibody to surface of Jurkat cells expressing murine and humanized BB7.2 Chimeric antigen receptor vs trastuzumab CAR (NC VR33).

[0346] Fig. 15 shows binding of purified anti-HzBB7 anti idiotype antibody to BB7.2 derived iCAR expressed on primary T cells.

[0347] Fig. 16A-B shows a schematic for IMPT001: A dual CART system designed to kill based on tumor specific loss-of-HLA-A2 gene expression.

[0348] Fig. 17 show iCAR Engagement Regulates CAR-T Activation. Singular aCAR engagement by iTarget NEG cells induces T-cell activation. Dual aCAR + iCAR engagement inhibits CAR-T activation with iTarget POS cells.

[0349] Fig. 18 show iCAR target POS cancer cells inhibit dual CAR T cells.

[0350] Fig. 19 show iCAR targeted killing of cancer cell lines.

[0351] Fig. 20 show scheme of the in-vivo study design.

[0352] Fig. 21 show scheme of the in-vivo process.

[0353] Fig. 22A-22B shows lentiviral vector constructs. The HLA-A*02 iCAR consists of an scFv that binds a polymorphic sequence in the extracellular domain of a cell-surface target joined by an HTM (hinge transmembrane region to cytoplasmic signaling domain (iDomain) designed to inhibit T-cell activation and killing. The HLA-A*02 iCAR is paired with a potent second generation aCAR targeting the HER2 receptor tyrosine kinase. The iCAR is positioned upstream of the aCAR linked by a T2A or IRES linker in a bicistronic lentiviral vector. A bicistronic lentiviral screen using cytoplasmic regions of a diverse immunoregulatory genes identified the LIR1 iDomain as one effective negative regulator of aCAR activation and killing (AACR Abstract 2848). A high-potency HER2 aCAR with single input clinical data (22A, bottom diagram). A LIR1 iDomain offers greatest tumor selectivity. High iCAR/aCAR expression ratio enhances protection.

[0354] Fig. 23 shows HLA-A and HER2 (target) expression profiles. (a) The expression level (median, 25% percentile, 75% percentile) of HLA-A and HER2 in Normal (GTEX), tumor (TGCA) and cancer cell lines (CCLE) as determined RNAseq were analyzed to identify an aCAR target partner for the HLA-A2 iCAR. The expression of HLA-A*02 and HER2 was found to overlap at a relatively consist ratio in the majority of cell lines and tissue types except blood. (b) Quantitative FACS analysis of selected cancer cell lines using Quantum beads.

[0355] Fig. 24A-24B shows aCAR engagement alone activates and kills and dual aCAR + iCAR engagement inhibits activation & killingIn Vitro validation of the iCAR platform. CRISPR editing was used to delete HLA-A*02 in the H1703 lung cancer cell-line to create in isogenic cell line model representing HLA-A*02 LOH in lung cancer cells. The cells express firefly luciferase to monitor growth and viability. (a) HLA-A*02 NEG HER2 POS. Dual iCAR aCAR T-cells are equally effective at activating T-cells (INFg production) and killing luciferase expressing, HLA-A*02 NEG H1703 lung cancer cells after 24 h treatment. (b) HLA-A*02 POS HER2 POS. iCAR and aCAR dual engagement prevents CAR-T cell activation and killing, whereas a HER2 single input CAR-T cells activates and kills efficiently.

[0356] Fig. 25A-25B shows IncuCyte killing and T cell proliferation. Functional Image Based Killing Assay. Efficacy of VR0518 Dual CAR-T and VR033 in the isogenic NCI-H1650.A*02- and NCI-H1650.A*02+ model. (A-D) NucGFP-labelled cells were treated with CAR-T cells (E:T 4:1) and imaged every 2h for 48h using an IncuCyte S3. Apoptosis was detected using

Annexin-V Red and percent killing was calculated as dead target cell count (high red and high green)/total target cell count (high green). T cell count represents live (low red) T cells (low green).

[0357] Fig. 26 shows HER2 aCAR potency in lung tumor models. The potency of a single input HER2 CAR-T cells was evaluated in an NSG mouse model with three different lung xenograft tumors. Receptor levels were determined by quantitative FACS. PBS, Vehicle Only; NTD, Non-Transduced T-Cells; MC003 Single input HER2 CAR.

[0358] Fig. 27 shows a scheme of the in-vivo process.

[0359] Fig. 28 shows data supporting the iCAR programs HLA-A2 NEG Specific Killing.

[0360] Fig. 29 shows data supporting the dual engagement suppresses T-cell proliferation.

[0361] Fig. 30 shows data supporting the aCAR only engagement results in T-cell expansion and tumor killing.

[0362] Fig. 31 shows data supporting the iCAR Programs HLA-A2 NEG Specific Killing. iCAR Specificity Analysis In Vivo. The ability of the iCAR to distinguish HLA-A2 POS and HLA-A2 NEG was evaluated in NSG mice with established H1703 tumors with or without CRSPR editing of HLA-A2. (a) Scheme of the animal studies run in parallel (b) Study design including implantation, dosing and endpoints (c) Combined Tumor growth curves for HLA-A2 POS and HLA-A2 NEG mice. (d, e) Individual analysis of tumor growth and CD3+ CAR+ T- cells obtained by orbital bleed. PBS, Vehicle Only; NTD, Non-Transduced T-Cells ($5x\ 10^6$); MC0033 Single input HER2 CAR ($1.5\ x\ 10^6$); VR0428 ($5x10^6$). Mice with established tumors were dosed on Day 10 (HLA-A2 POS) or Day 11 (HLA-A2 NEG) post implantation. N= 5 animals per group except the HLA-A2 POS HER2 POS group treated with MC0033 where an outlier was removed.

[0363] Fig. 32 shows more data supporting specific killing.

[0364] Fig. 33 shows more data supporting specific killing.

[0365] Fig. 34 shows more data supporting specific killing.

[0366] Fig. 35 shows the iCARPlatform enables effective and specific targeting of solid tumors. Loss of chromosomal material is characteristic of all cancers and creates a unique antigen repertoire on the cell surface. ImmPACT'sCAR-T cells incorporate an iCARreceptor targeting an antigen lost due to LOH together with an aCAR. Cancer cells that underwent LOH are susceptible to killing due to the loss of the iCARantigen. Normal cells are protected against CAR-T cell killing by iCARantigen engagement.

[0367] Fig. 36 shows iDomain screen. A representative screen of human immune response genes encoding ITIM motifs was conducted to identify iDomainsthat can inhibit CAR-T

activation and killing in the context of a DualCAR. (A) The screen utilized a biscistroniclentiviral construct consisting of an iCARwith an scFvderived from a well-characterized HLA-A*02 specific murine monoclonal antibody10, a PD1 hinge transmembrane motif (HTM) and cytoplasmic regions selected from ITIM containing genes. The aCARtarget specificity and activity was generated with an anti-HER2 scFvjoined with a CD8 HTM to a 41BB costimulatory region and CD3z. (B) List of screened inhibitory domains (C) The absolute level of iCARand aCARexpression in the CAR-T cells that advance to functional assays was determined by quantitative FACS.

[0368] Fig. 37 shows characterization of iDomain Leads-Expression Profile. The expression profiles and functional assays results obtained with Dual CAR-T cells prepared from the same human T-cell donor for the top three performing iDomainconstructs are presented. (A) Diagram of bicistronicKIR2DL1, LIR1, and CD33 constructs and a single input HER2 aCAR control. (B) FACS profiles in which the iCARand aCARwere detected via n-terminal cMycand Flag tags, respectively. (C) The absolute expression level (geometric mean per cell) was determined by quantitative FACS (Quantum beads) for three iDomainconstructs. (D) The ratio of iCARover aCARexpression was calculated using the absolute expression data described in (C).

[0369] Fig. 38 shows Characterization of iDomainLeads – Functional Killing and Cytokine Assay. (A-B) Single aCARengagement induces activation & killing. Firefly luciferase (Luc) labeled HLA-A*02-FaDucancer cell line was treated overnight with increasing Dual CAR-T cells normalized to aCARinput.A sample of culture media was removed for IFNgassay by Cytometric Bead Array (CBA)before determining tumor viability with relative Luc luminescence. Viability was normalized according to maximum Luc reading for a given effector and cytokine results were normalized to secretion mediated by the single input HER2 aCARcontrol. Luc killing assay show viability at E:T of 5:1. (C-D) DualCARengagement inhibits activation and killing.The assays described in (A-B) were run in parallel with the same CAR-T preparation using HLA-A*02+NCI-H1703 lung cancer cells. Luc killing assay show viability at E:T of 1:1 (E-F) Histograms summarizingmultiple determinations of Dual CAR-T cell killing activity against isogenic NCI-H1703.HLA-A*02+and NCI-H1703.HLA-A*02-lung cancer cell lines labeled with firefly Luc. Both EC85and EC50 were estimated using GraphPad Prism Sigmoidal 4PL curve fitting of effector to tumor (E:T) titration versus relative viability data.Protection index was calculated as EC50, HLA-A*02+/ EC50, HLA-A*02. Potency is the EC50determined in NCI-H1703.A*02-cell lines. (G) Target expression (Antibody Binding Capacity (ABC) = sites/cell) levels NCI-H1703.A*02+ and NCI-

H1703.A*02-lung cancer cell lines. The NCI-H1703.A*02-cell line was generated by CRISPR-Cas9 editing with HLA-A specific sgRNA.

[0370] Fig. 39 shows characterization of iDomainLeads-Functional Image Based Killing Assay. Efficacy of VR0354 Dual CAR-T and VR033 in the isogenic NCI-H1650.A*02-and NCI-H1650.A*02+model. (A) Scheme of constructs. (B1-4) NucGFP-labelled cells were treated with CAR-T cells (E:T 4:1) and imaged every 2h for 48h using an IncuCyteS3. (C-D) Apoptosis was detected using Annexin-V Red and %killing was calculated as dead target cell count (high red and high green)/total target cell count (high green).

[0371] Fig. 40 shows in-vivo PoC. Determine the efficacy of VR051 and VR354 Dual CAR-T and VR033 single input HER2 CAR-T in the isogenic NCI-H1703.A*02+ and NCI-H1703.A*02-tumor model in female NSG mice. The structure of VR354 was identical to VR051 except the PD1 HTM was replaced with a LIR1 HTM. Test articles were enriched by iCARcapture and stored frozen in Liquid N2 until thawed for subcutaneous injection into mice (A) The iCAR(myc-tagged) and aCAR(flag-tagged) surface expression of test articles was characterized 3 hrafter thawing by FACS. (B-D) The functional activity of test articles was quantitatively evaluated separately in the isogenic NCI-H1703.A*02+ and NCI-H1703.A*02-Luc viability assays. (E) Parameters of test articles obtained from in-vitro Luc killing assay presented in B-C. (F) The effect of Dual CAR and single input HER2 aCART-cells on tumor growth. NSG mice (n= 5 per group) bearing ~ 150 mm3 NCI-H1703.A*02+ (G) or NCI-H1703.A*02-(H) subcutaneous tumors were injected with 1.5 x E6 CAR-T cells at day 10 or day 11 respectively. Tumor burden was measured using calipers.

DETAILED DESCRIPTION OF THE INVENTION

I. INTRODUCTION

[0372] The present invention provides bicistronic and co-administered monocistronic constructs specifically targeting tumor cells while keeping the normal cells protected. The constructs provided herein provide iCAR/aCAR constructs that target single allelic variants of polymorphic cell surface epitopes, which are lost from tumor cells due to loss of heterozygosity (LOH) of the chromosomal region they reside in, while remaining expressed on normal tissue. Because of the polymorphic variation, the iCAR/aCAR pair is able to distinguish the two alleles and target only the tumor cells missing the target allele due to LOH.

II. SELECT DEFINITIONS

[0373] The term "nucleic acid molecule" as used herein refers to a DNA or RNA molecule.

[0374] The term "encoding" refers to the inherent property of specific sequences of nucleotides in a polynucleotide, such as a gene, a cDNA, or an mRNA, to serve as templates for synthesis of other polymers and macromolecules in biological processes having either a defined sequence of nucleotides (*e.g.*, rRNA, tRNA and mRNA) or a defined sequence of amino acids and the biological properties resulting therefrom. Thus, a gene encodes a protein if transcription and translation of mRNA corresponding to that gene produces the protein in a cell or other biological system. Both the coding strand, the nucleotide sequence of which is identical to the mRNA sequence and is usually provided in sequence listings, and the non-coding strand, used as the template for transcription of a gene or cDNA, can be referred to as encoding the protein or other product of that gene or cDNA.

[0375] Unless otherwise specified, a "nucleotide sequence encoding an amino acid sequence" includes all nucleotide sequences that are degenerate versions of each other and that encode the same amino acid sequence. Nucleotide sequences that encode proteins and RNA may include introns.

[0376] The term "endogenous" refers to any material from or produced inside an organism, cell, tissue or system.

[0377] The term "exogenous" refers to any material introduced from or produced outside an organism, cell, tissue or system.

[0378] The term "expression" as used herein is defined as the transcription and/or translation of a particular nucleotide sequence driven by its promoter.

[0379] "Expression vector" refers to a vector comprising a recombinant polynucleotide comprising expression control sequences operatively linked to a nucleotide sequence to be expressed. An expression vector comprises sufficient cis-acting elements for expression; other elements for expression can be supplied by the host cell or in an in vitro expression system. Expression vectors include all those known in the art, such as cosmids, plasmids (*e.g.*, naked or contained in liposomes) and viruses (*e.g.*, lentiviruses, retroviruses, adenoviruses, and adeno-associated viruses) that incorporate the recombinant polynucleotide.

[0380] The term "genomic variant" as used herein refers to a change of at least one nucleotide at the genomic level in a sequenced sample compared to the reference or consensus sequence at the same genomic position.

[0381] The term "corresponding reference allele" as used herein with reference to a variant means the reference or consensus sequence or nucleotide at the same genomic position as the variant.

[0382] The term "extracellular domain" as used herein with reference to a protein means a region of the protein which is outside of the cell membrane.

[0383] The term "loss of heterozygosity" or "LOH" as used herein means the loss of chromosomal materials such as a complete chromosome or a part thereof, in one copy of the two chromosomes in a somatic cell.

[0384] The term "sequence region" as used herein with reference to a variant or a reference allele means a sequence starting upstream and ending downstream from the position of the variant, which can be translated into an "epitope peptide" that can be recognized by an antibody.

[0385] The term "CAR", as that term is used herein, refers to a chimeric polypeptide that shares structural and functional properties with a cell immune-function receptor or adaptor molecule, from *e.g.*, a T cell or a NK cell. CARs include TCARs and NKR-CARs. Upon binding to cognate antigen, a CAR can activate or inactivate the cytotoxic cell in which it is disposed, or modulate the cell's antitumor activity or otherwise modulate the cells immune response.

[0386] The term "specific binding" as used herein in the context of an extracellular domain, such as an scFv, that specifically binds to a single allelic variant of a polymorphic cell surface epitope, refers to the relative binding of the scFv to one allelic variant and its failure to bind to the corresponding different allelic variant of the same polymorphic cell surface epitope. Since this depends on the avidity (number of CAR copies on the T cell, number of antigen molecules on the surface of target cells (or cells to be protected) and the affinity of the specific CARs used, a functional definition would be that the specific scFv would provide a significant signal in an ELISA against the single allelic variant of a polymorphic cell surface epitope to which it is specific or cells transfected with a CAR displaying the scFv would be clearly labeled with the single allelic variant of a polymorphic cell surface epitope in a FACS assay, while the same assays using the corresponding different allelic variant of the same polymorphic cell surface epitope would not give any detectable signal.

[0387] The term "treating" as used herein refers to means of obtaining a desired physiological effect. The effect may be therapeutic in terms of partially or completely curing a disease and/or symptoms attributed to the disease. The term refers to inhibiting the disease, *e.g.*, arresting its development; or ameliorating the disease, *e.g.*, causing regression of the disease.

[0388] As used herein, the terms "subject" or "individual" or "animal" or "patient" or "mammal," refers to any subject, particularly a mammalian subject, for whom diagnosis, prognosis, or therapy is desired, for example, a human.

[0389] The phrase "safe effector immune cell" or "safe effector cell" includes those cells described by the invention that express at least one bicistronic iCAR/aCAR construct, or portion thereof, as described herein, or exhibit co-expression of monocistronic aCAR and iCAR constructs. In some embodiments, the "safe effector immune cell" or "safe effector cell" is capable of administration to a subject. In some embodiments, the "safe effector immune cell" or "safe effector cell" further expresses at least one bicistronic iCAR/aCAR construct, or portion thereof, or exhibit co-expression of monocistronic aCAR and iCAR constructs, as described herein.

[0390] Pharmaceutical compositions for use in accordance with the present invention may be formulated in conventional manner using one or more physiologically acceptable carriers or excipients. The carrier(s) must be "acceptable" in the sense of being compatible with the other ingredients of the composition and not deleterious to the recipient thereof.

[0391] The phrase "effective amount" or "therapeutically effective amount" are used interchangeably herein, and refer to an amount of a compound, formulation, material, or composition, as described herein effective to achieve a particular biological result.

[0392] The term "peripheral blood mononuclear cell (PBMC)" as used herein refers to any blood cell having a round nucleus, such as a lymphocyte, or a monocyte. Methods for isolating PBMCs from blood are readily apparent to those skilled in the art. A non-limiting example is the extraction of these cells from whole blood using ficoll, a hydrophilic polysaccharide that separates layers of blood, with monocytes and lymphocytes forming a buffy coat under a layer of plasma or by leukapheresis, the preparation of leukocyte concentrates with the return of red cells and leukocyte-poor plasma to the donor.

[0393] The term "cancer" as used herein is defined as disease characterized by the rapid and uncontrolled growth of aberrant cells. Cancer cells can spread locally or through the bloodstream and lymphatic system to other parts of the body. Examples of various cancers include but are not limited to, breast cancer, prostate cancer, ovarian cancer, cervical cancer, skin cancer, pancreatic cancer, colorectal cancer, renal cancer, liver cancer, brain cancer, lymphoma, leukemia, lung cancer, glioma, and the like.

III. CAR-T SYSTEM: iCARs and aCARs

[0394] LOH, being a genomic event, results in a total loss of a specific variant from the tumor with a very rare probability of gaining back the lost allele. If the LOH event occurs very early in the development of tumors, it ensures a uniform target signature in all tumor cells derived from the initial pre-malignant tissue including metastatic tumors. Additionally, LOH occurs in almost all types of cancer and this concept can therefore be relied upon as a universal tool for

developing markers relevant to all these cancer types. Since the LOH events are to some extent random, the present invention further provides for selection of personalized tumor markers for each individual cancer patient, based on the specific LOH events which took place in that patient. The tools relied upon to execute this concept, the aCARs and the iCARs, are well-known and can be easily prepared using methods well-known in the art as taught for example, in WO 2015/142314 and in US 9,745,368, both incorporated by reference as if fully disclosed herein.

[0395] According to one strategy, the two CARs in every given pair specifically recognize the product of a different allelic variant of the same target gene for which the patient is heterozygous. The basic principle is as follows: the aCAR targets an allelic variant of a selected cell surface protein that is expressed by the given tumor cells and is not affected by LOH while the iCAR targets the product encoded by the allelic variant of the same gene that has been lost from these tumor cells due to LOH. In other normal tissues of that individual patient that express the said gene, both alleles are present and are known to be equally functional, that is, expression is biallelic in all tissues (in contrast to other genes which may exhibit random monoallelic expression (Chess, 2012; Savova et al., 2016). In one scenario, the two CARs target two related epitopes residing at the same location on the protein product, which differ by one, or only few amino acids. In another scenario, the aCAR targets a non-polymorphic epitope on the same protein while the iCAR is allele-specific. In these embodiments, the density of the aCAR epitope on normal cells would generally be two-fold higher than that of the iCAR one. In some embodiments, a single nucleic acid vector encodes both the aCAR and iCAR, as exemplified with the bicistronic constructs described herein. In some embodiments, the aCAR and iCAR are encoded by separate nucleic acid vectors and co-expressed.

[0396] Care must be taken to ensure that the inhibitory signal transmitted by the iCAR is dominant over the aCAR signal and that cross-recognition between the iCAR and the aCAR is limited and/or negligible. Dominance of the iCAR guarantees that activation of the killer cell upon encounter with normal cells expressing both alleles would be prevented. This default brake would not operate upon engagement with tumor cells: in the absence of its target antigen the iCAR would not deliver inhibitory signals, thus unleashing the anticipated aCAR-mediated cellular activation and subsequent tumor cell lysis. Dominance of the iCARs over their aCARs counterparts is a significant portion of how the system functions. The present invention provides novel bicistronic iCAR/aCAR constructs that function in this manner, as well as methods for co-transduction of monocistronic aCAR and iCAR constructs.

[0397] The bicistronic constructs of the present invention comprise the following components: an iCAR and aCAR connected via a linker domain. In some embodiments, the iCAR (protective) portion comprises an iCAR scFv, a hinge transmembrane (TM) domain, and inhibitory domain. In some embodiments, the aCAR (efficacy) portion comprises an aCAR scFv, a hinge transmembrane (TM) domain, a co-stimulatory domain, and a CD3 zeta domain.

i. BICISTRONIC SEQUENCES

[0398] In some embodiments, the bicistronic iCAR/aCAR comprises an amino acid sequence encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, SEQ ID NO:325, SEQ ID NO:335, SEQ ID NO:336, SEQ ID NO:337, SEQ ID NO:338, SEQ ID NO:339, SEQ ID NO:340, and SEQ ID NO: 341, as provided in Table 1 below. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:1. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:3. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:5. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:7. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:9. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:11. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:13. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:15. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:17. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:19. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:21. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:23. In some

embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:25. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:27. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:29. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:31. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:33. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:35. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:275. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:277. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:279. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:281. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:321. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:323. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:325. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:335. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:336. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:337. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:338. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:339. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:340. In some embodiments, the bicistronic iCAR/aCAR comprise an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:341.

[0399] In some embodiments, the bicistronic iCAR/aCAR comprises an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:276, SEQ ID NO:278, SEQ ID NO:280, SEQ ID NO:282, SEQ ID NO:322, SEQ ID NO:324, SEQ ID NO:326, SEQ ID NO:342, SEQ ID NO:343, SEQ ID NO:344, SEQ ID NO:345, SEQ ID NO:346, SEQ ID NO:347, and SEQ ID NO: 348, as provided in Table 1 below. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:2. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:4. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:6. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:8. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:10. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:12. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:14. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:16. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:18. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:20. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:22. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:24. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:26. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:28. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:30. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:32, SEQ ID NO:34. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:36. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:276. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:278. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:280. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:282. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:322. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:324. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:326. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:342. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:343. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:344. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:345. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:346. In some embodiments,

the bicistronic iCAR/aCAR comprises SEQ ID NO:347. In some embodiments, the bicistronic iCAR/aCAR comprises SEQ ID NO:348.

Table 1: Bicistonic iCAR/aCARs: nucleic acid and amino acid sequences

Sequence name	SEQ ID NO:	Polynucleotide or polypeptide sequences
MC0280-BB7.2_28_PD1_HER2 Nucleotide sequence (VR280)	SEQ ID NO:1	ATGGCACTGCCAGTGACCGCCCTGCTGCTGCCTCTGGCCC TGCTGCTGCACGCAGCCAGACCCCAGGTGCAGCTGCAGC AGTCTGGACCTGAGCTGGTGAAGCCAGGAGCCTCCGTGA AGATGTCTTGCAAGGCCAGCGGCTACACCTTCACATCTTA TCACATCCAGTGGGTGAAGCAGCGGCCCGGACAGGGCCT GGAGTGGATCGGATGGATCTACCCAGGCGACGGCTCCAC ACAGTATAACGAGAAGTTCAAGGGCAAGACCACACTGAC CGCCGATAAGAGCAGCAGCACCGCCTACATGCTGCTGAG CAGCCTGACCAGCGAGGACAGCGCCATCTACTTTTGCGC CAGGGAGGGCACATACTATGCTATGGACTATTGGGGCCA GGGCACCAGCGTGACAGTGTCTAGCGGAGGAGGAGGCTC CGGAGGAGGAGGCTCTGGCGGCGGCGGCAGCGACGTGC TGATGACCCAGACACCACTGAGCCTGCCCGTGAGCCTGG GCGATCAGGTGAGCATCTCCTGTAGATCCTCTCAGAGCA TCGTGCACTCCAACGGCAATACCTACCTGGAGTGGTATCT GCAGAAGCCAGGCCAGTCCCCCAAGCTGCTGATCTATAA GGTGTCTAATCGGTTCAGCGGCGTGCCTGACAGATTTTCT GGCAGCGGCTCCGGCACCGACTTCACCCTGAAGATCAGC CGGGTGGAGGCAGAGGATCTGGGCGTGTACTATTGTTTC CAGGGCTCCCACGTGCCACGCACCTTTGGCGGCGGTACC AAGCTGGAGATCAAGATTGAAGTTATGTATCCTCCTCCTT ACCTAGACAATGAGAAGAGCAATGGAACCATTATCCATG TGAAAGGGAAACACCTTTGTCCAAGTCCCCTATTTCCCGG GCCTTCGAAGCCCTTTTGGGTGCTGGTGGTGGTTGGTGGA GTCCTGGCTTGCTATAGCTTGCTAGTAACAGTAGCGTTTA TTATTTTCTGGGTGTGCAGCAGGGCCGCCCGCGGCACCAT CGGCGCCAGGCGCACAGGCCAGCCTCTGAAGGAGGACCC TTCCGCCGTGCCAGTGTTCTCTGTGGACTACGGCGAGCTG GATTTTCAGTGGCGGGAGAAAACCCCAGAGCCACCTGTG CCCTGCGTGCCTGAGCAGACCGAGTATGCCACAATCGTG TTTCCATCCGGAATGGGCACAAGCTCCCCTGCAAGGAGA GGCAGCGCCGACGGACCACGGTCCGCCCAGCCACTGCGG CCCGAGGATGGCCACTGTTCTTGGCCCCTGCGGAGAAAG CGTGGATCCGGGGAAGGCCGAGGCTCCCTTCTAACATGT GGAGATGTCGAGGAAAACCCTGGCCCTATGGCGCTGCCA GTCACTGCATTGTTATTGCCTCTGGCCCTGCTTCTCCATG CGGCGCGCCCAGAAGTGCAGCTGGTCGAGAGCGGAGGC GGACTGGTTCAACCCGGAGGCAGCTTGAGACTGTCCTGC GCGGCCAGCGGCTTCAACATCAAGGATACCTATATCCAC TGGGTGAGGCAGGCTCCAGGAAAGGGCCTGGAGTGGGT GGCAAGGATTTACCCTACTAATGGATATACACGCTACGC TGATTCCGTGAAGGGACGCTTTACAATCTCAGCAGATAC ATCCAAAAACACGGCCTATTTACAGATGAATAGTTTGCG

		GGCCGAAGACACGGCTGTATACTATTGTTCTCGGTGGGG GGGCGATGGATTTTATGCGATGGATTACTGGGGCCAGGG CACCCTGGTAACCGTGTCAAGCGGCTCAACATCCGGGTC CGGTAAGCCGGGCTCCGGCGAGGGGTCTACAAAGGGAG ATATACAGATGACACAGTCCCCCAGTTCCCTGTCCGCCTC AGTGGGAGACCGAGTGACGATTACCTGTCGTGCCAGCCA GGACGTCAATACCGCCGTCGCTTGGTATCAGCAAAAACC AGGCAAGGCCCCGAAACTATTGATCTACAGTGCCTCTTTT CTGTACTCCGGGGTGCCGAGCAGATTTAGTGGCTCCAGG AGCGGAACCGATTTCACCCTAACCATTTCCAGTTTGCAGC CAGAGGATTTCGCGACCTATTACTGCCAGCAACACTACA CCACACCGCCAACTTTCGGACAAGGAACCAAGGTTGAAA TCAAAACTACGACCCCAGCACCTAGACCTCCCACCCCAG CTCCAACTATAGCTTCCCAGCCATTGTCTCTCCGGCCAGA GGCGTGTCGACCAGCCGCTGGAGGGGCCGTTCATACAAG AGGACTCGATTTCGCTTGCGATATCTACATATGGGCCCCT CTTGCCGGGACATGCGGTGTCCTGCTTCTAAGCTTGGTTA TTACCCTCTATTGCAAACGCGGCCGCAAGAAACTGCTCT ACATCTTTAAACAGCCGTTCATGAGGCCTGTGCAGACAA CGCAGGAAGAGGATGGCTGTAGTTGTCGGTTTCCGGAAG AGGAAGAGGGGGGCTGCGAGTTGCGTGTCAAATTTTCTC GGTCTGCCGACGCCCCCGCGTACCAGCAAGGGCAGAACC AGCTTTATAATGAGCTGAATCTTGGACGACGGGAGGAAT ATGACGTGCTTGACAAGAGGCGAGGTAGGGACCCTGAGA TGGGGGGAAAACCTCGGAGGAAAAACCCACAGGAAGGC CTGTATAACGAACTGCAGAAGGACAAGATGGCTGAAGCC TACTCTGAGATTGGAATGAAAGGGGAACGCAGACGCGGC AAGGGCCATGATGGCCTCTACCAAGGTCTAAGCACTGCC ACCAAGGACACCTATGACGCACTCCACATGCAAGCTCTA CCTCCCCGTTGATAA
MC0280-BB7.2_28_PD1_HER2 Protein sequence (VR280)	SEQ ID NO:2	MALPVTALLLPLALLLHAARPQVQLQQSGPELVKPGASVK MSCKASGYTFTSYHIQWVKQRPGQGLEWIGWIYPGDGSTQ YNEKFKGKTTLTADKSSSTAYMLLSSLTSEDSAIYFCAREGT YYAMDYWGQGTSVTVSSGGGGSGGGGSGGGGSDVLMTQ TPLSLPVSLGDQVSISCRSSQSIVHSNGNTYLEWYLQKPGQS PKLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGV YYCFQGSHVPRTFGGGTKLEIKIEVMYPPPYLDNEKSNGTII HVKGKHLCPSPLFPGPSKPFWVLVVVGGVLACYSLLVTVAF IIFWVCSRAARGTIGARRTGQPLKEDPSAVPVFSVDYGELDF QWREKTPEPPVPCVPEQTEYATIVFPSGMGTSSPARRGSAD GPRSAQPLRPEDGHCSWPLRRKRGSGEGRGSLLTCGDVEEN PGPMALPVTALLLPLALLLHAARPEVQLVESGGGLVQPGGS LRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYT RYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSR WGGDGFYAMDYWGQGTLVTVSSGSTSGSGKPGSGEGSTK GDIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQK PGKAPKLLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDF ATYYCQQHYTTPPTFGQGTKVEIKTTTPAPRPPTPAPTIASQP LSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL LSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFP

		EEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREE YDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEA YSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQAL PPR
MC0281- BB7.2_28_ PD1_EGFR nucleotide Sequence (VR281)	SEQ ID NO:3	ATGGCACTGCCAGTGACCGCCCTGCTGCTGCCTCTGGCCC TGCTGCTGCACGCAGCCAGACCCCAGGTGCAGCTGCAGC AGTCTGGACCTGAGCTGGTGAAGCCAGGAGCCTCCGTGA AGATGTCTTGCAAGGCCAGCGGCTACACCTTCACATCTTA TCACATCCAGTGGGTGAAGCAGCGGCCCGGACAGGGCCT GGAGTGGATCGGATGGATCTACCCAGGCGACGGCTCCAC ACAGTATAACGAGAAGTTCAAGGGCAAGACCACACTGAC CGCCGATAAGAGCAGCAGCACCGCCTACATGCTGCTGAG CAGCCTGACCAGCGAGGACAGCGCCATCTACTTTTGCGC CAGGGAGGGCACATACTATGCTATGGACTATTGGGGCCA GGGCACCAGCGTGACAGTGTCTAGCGGAGGAGGAGGCTC CGGAGGAGGAGGCTCTGGCGGCGGCGGCAGCGACGTGC TGATGACCCAGACACCACTGAGCCTGCCCGTGAGCCTGG GCGATCAGGTGAGCATCTCCTGTAGATCCTCTCAGAGCA TCGTGCACTCCAACGGCAATACCTACCTGGAGTGGTATCT GCAGAAGCCAGGCCAGTCCCCCAAGCTGCTGATCTATAA GGTGTCTAATCGGTTCAGCGGCGTGCCTGACAGATTTTCT GGCAGCGGCTCCGGCACCGACTTCACCCTGAAGATCAGC CGGGTGGAGGCAGAGGATCTGGGCGTGTACTATTGTTTC CAGGGCTCCCACGTGCCACGCACCTTTGGCGGCGGTACC AAGCTGGAGATCAAGATTGAAGTTATGTATCCTCCTCCTT ACCTAGACAATGAGAAGAGCAATGGAACCATTATCCATG TGAAAGGGAAACACCTTTGTCCAAGTCCCCTATTTCCCGG GCCTTCGAAGCCCTTTTGGGTGCTGGTGGTGGTTGGTGGA GTCCTGGCTTGCTATAGCTTGCTAGTAACAGTAGCGTTTA TTATTTTCTGGGTGTGCAGCAGGGCCGCCCGCGGCACCAT CGGCGCCAGGCGCACAGGCCAGCCTCTGAAGGAGGACCC TTCCGCCGTGCCAGTGTTCTCTGTGGACTACGGCGAGCTG GATTTTCAGTGGCGGGAGAAAACCCCAGAGCCACCTGTG CCCTGCGTGCCTGAGCAGACCGAGTATGCCACAATCGTG TTTCCATCCGGAATGGGCACAAGCTCCCCTGCAAGGAGA GGCAGCGCCGACGGACCACGGTCCGCCCAGCCACTGCGG CCCGAGGATGGCCACTGTTCTTGGCCCCTGCGGAGAAAG CGTGGATCCGGGGAAGGCCGAGGCTCCCTTCTAACATGT GGAGATGTCGAGGAAAACCCTGGCCCTATGGCGCTGCCA GTCACTGCATTGTTATTGCCTCTGGCCCTGCTTCTCCATG CGGCGCGCCCACAAGTGCAGCTGAAACAGAGCGGACCA GGACTGGTTCAACCCAGCCAGAGCTTGAGCATCACGTGC ACGGTTAGCGGCTTCAGTCTGACCAATTATGGTGTGCACT GGGTGAGGCAGTCTCCAGGAAAGGGCCTGGAGTGGCTTG GAGTCATTTGGAGCGGTGGGAATACAGATTACAATACAC CTTTTACGTCACGTCTCTCCATTAACAAGGACAACTCCAA ATCCCAAGTATTTTTCAAAATGAATAGCCTGCAGAGTAA TGATACCGCCATCTATTACTGTGCACGAGCTTTGACATAT TACGACTATGAATTTGCCTATTGGGGTCAAGGCACGCTG GTGACCGTATCAGGCTCAACATCCGGGTCCGGTAAGCCG

		GGCTCCGGCGAGGGGTCTACAAAGGGAGACATCCTTCTG ACACAGAGCCCCGTGATCCTGTCCGTGTCCCCCGGCGAG AGAGTATCATTTTCCTGTAGGGCTTCTCAGAGCATCGGAA CAAATATCCACTGGTATCAGCAACGGACTAACGGATCAC CTCGCCTGCTCATAAAGTACGCCAGTGAATCTATTAGTGG CATACCGAGCCGCTTCAGCGGGAGTGGCTCCGGCACAGA CTTTACTCTGAGTATAAATTCCGTGGAATCTGAGGACATC GCGGACTATTACTGCCAGCAAAACAATAACTGGCCCACC ACGTTCGGCGCGGGAACTAAACTAGAACTAAAGACTACG ACCCCAGCACCTAGACCTCCCACCCCAGCTCCAACTATA GCTTCCCAGCCATTGTCTCTCCGGCCAGAGGCGTGTCGAC CAGCCGCTGGAGGGGCCGTTCATACAAGAGGACTCGATT TCGCTTGCGATATCTACATATGGGCCCCTCTTGCCGGGAC ATGCGGTGTCCTGCTTCTAAGCTTGGTTATTACCCTCTAT TGCAAACGCGGCCGCAAGAAACTGCTCTACATCTTTAAA CAGCCGTTCATGAGGCCTGTGCAGACAACGCAGGAAGAG GATGGCTGTAGTTGTCGGTTTCCGGAAGAGGAAGAGGGG GGCTGCGAGTTGCGTGTCAAATTTTCTCGGTCTGCCGACG CCCCCGCGTACCAGCAAGGGCAGAACCAGCTTTATAATG AGCTGAATCTTGGACGACGGGAGGAATATGACGTGCTTG ACAAGAGGCGAGGTAGGGACCCTGAGATGGGGGGAAAA CCTCGGAGGAAAAACCCACAGGAAGGCCTGTATAACGA ACTGCAGAAGGACAAGATGGCTGAAGCCTACTCTGAGAT TGGAATGAAAGGGGAACGCAGACGCGGCAAGGGCCATG ATGGCCTCTACCAAGGTCTAAGCACTGCCACCAAGGACA CCTATGACGCACTCCACATGCAAGCTCTACCTCCCCGTTG ATAA
MC0281-BB7.2_28_PD1_EGFR Protein Sequence (VR281)	SEQ ID NO:4	MALPVTALLLPLALLLHAARPQVQLQQSGPELVKPGASVK MSCKASGYTFTSYHIQWVKQRPGQGLEWIGWIYPGDGSTQ YNEKFKGKTTLTADKSSSTAYMLLSSLTSEDSAIYFCAREGT YYAMDYWGQGTSVTVSSGGGGSGGGGSGGGGSDVLMTQ TPLSLPVSLGDQVSISCRSSQSIVHSNGNTYLEWYLQKPGQS PKLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGV YYCFQGSHVPRTFGGGTKLEIKIEVMYPPPYLDNEKSNGTII HVKGKHLCPSPLFPGPSKPFWVLVVVGGVLACYSLLVTVAF IIFWVCSRAARGTIGARRTGQPLKEDPSAVPVFSVDYGELDF QWREKTPEPPVPCVPEQTEYATIVFPSGMGTSSPARRGSAD GPRSAQPLRPEDGHCSWPLRRKRGSGEGRGSLLTCGDVEEN PGPMALPVTALLLPLALLLHAARPQVQLKQSGPGLVQPSQS LSITCTVSGFSLTNYGVHWVRQSPGKGLEWLGVIWSGGNT DYNTPFTSRLSINKDNSKSQVFFKMNSLQSNDTAIYYCARA LTYYDYEFAYWGQGTLVTVSGSTSGSGKPGSGEGSTKGDIL LTQSPVILSVSPGERVSFSCRASQSIGTNIHWYQQRTNGSPRL LIKYASESISGIPSRFSGSGSGTDFTLSINSVESEDIADYYCQQ NNNWPTTFGAGTKLELKTTTPAPRPPTPAPTIASQPLSLRPE ACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVIT LYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEG GCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLD KRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIG MKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR

MC0282-3PF12_28_PD1_HER2 Nucleotide Sequence (VR282)	SEQ ID NO:5	ATGGCACTGCCAGTGACCGCCCTGCTGCTGCCTCTGGCCC TGCTGCTGCACGCAGCCAGACCCCAAGTGCAACTAGTCC AATCAGGTGGAGGCGTCGTGCAACCTGGAGGGTCCCTCC GCGTTAGCTGCGCCGCATCAGGCGTTACCTTGTCAGACTA CGGCATGCATTGGGTTAGGCAAGCCCCCGGCAAGGGGCT CGAATGGATGGCTTTCATTCGGAATGACGGGAGCGATAA ATATTACGCGGATTCAGTTAAAGGGCGGTTCACCATCAG CCGCGACAATAGCAAAAAGACGGTCTCCTTACAGATGTC CAGCTTGCGGGCCGAAGACACGGCTGTATACTATTGTGC TAAAAATGGCGAGAGCGGCCCCCTGGATTACTGGTACTT TGACCTGTGGGGCAGAGGCACCCTGGTCACGGTGTCCTC TGGAGGAGGAGGCTCCGGAGGAGGAGGCTCTGGCGGCG GCGGCAGCGACATTGTAATGACCCAGTCACCCTCCTTCCT TAGTGCCTCAGTCGGAGACCGCGTGACTATCACTTGTCGT GCCTCACACGGAATTAATAACTACCTCGCTTGGTATCAGC AAAAACCAGGCAAGGCCCCGAAACTATTGATCTACGCCG CATCTACTCTGCAGAGCGGAGTACCGAGCAGATTTAGTG GTTCCGGCAGCGGAACCGAGTTCACCCTAACCATTTCCA GTTTGCAGCCAGAGGATTTCGCGACCTATTACTGCCAGC AATACGATTCATACCCGCCAACTTTCGGAAGAGGTACCA AGGTTGAAATCAAGATTGAAGTTATGTATCCTCCTCCTTA CCTAGACAATGAGAAGAGCAATGGAACCATTATCCATGT GAAAGGGAAACACCTTTGTCCAAGTCCCCTATTTCCCGG GCCTTCGAAGCCCTTTTGGGTGCTGGTGGTGGTTGGTGGA GTCCTGGCTTGCTATAGCTTGCTAGTAACAGTAGCGTTTA TTATTTTCTGGGTGTGCAGCAGGGCCGCCCGCGGCACCAT CGGCGCCAGGCGCACAGGCCAGCCTCTGAAGGAGGACCC TTCCGCCGTGCCAGTGTTCTCTGTGGACTACGGCGAGCTG GATTTTCAGTGGCGGGAGAAAACCCCAGAGCCACCTGTG CCCTGCGTGCCTGAGCAGACCGAGTATGCCACAATCGTG TTTCCATCCGGAATGGGCACAAGCTCCCCTGCAAGGAGA GGCAGCGCCGACGGACCACGGTCCGCCCAGCCACTGCGG CCCGAGGATGGCCACTGTTCTTGGCCCCTGCGGAGAAAG CGTGGATCCGGGGAAGGCCGAGGCTCCCTTCTAACATGT GGAGATGTCGAGGAAAACCCTGGCCCTATGGCGCTGCCA GTCACTGCATTGTTATTGCCTCTGGCCCTGCTTCTCCATG CGGCGCGCCCAGAAGTGCAGCTGGTCGAGAGCGGAGGC GGACTGGTTCAACCCGGAGGCAGCTTGAGACTGTCCTGC GCGGCCAGCGGCTTCAACATCAAGGATACCTATATCCAC TGGGTGAGGCAGGCTCCAGGAAAGGGCCTGGAGTGGGT GGCAAGGATTTACCCTACTAATGGATATACACGCTACGC TGATTCCGTGAAGGGACGCTTTACAATCTCAGCAGATAC ATCCAAAAACACGGCCTATTTACAGATGAATAGTTTGCG GGCCGAAGACACGGCTGTATACTATTGTTCTCGGTGGGG GGGCGATGGATTTTATGCGATGGATTACTGGGGCCAGGG CACCCTGGTAACCGTGTCAAGCGGCTCAACATCCGGGTC CGGTAAGCCGGGCTCCGGCGAGGGGTCTACAAAGGGAG ATATACAGATGACACAGTCCCCCAGTTCCCTGTCCGCCTC AGTGGGAGACCGAGTGACGATTACCTGTCGTGCCAGCCA GGACGTCAATACCGCCGTCGCTTGGTATCAGCAAAAACC

		AGGCAAGGCCCCGAAACTATTGATCTACAGTGCCTCTTTT CTGTACTCCGGGGTGCCGAGCAGATTTAGTGGCTCCAGG AGCGGAACCGATTTCACCCTAACCATTTCCAGTTTGCAGC CAGAGGATTTCGCGACCTATTACTGCCAGCAACACTACA CCACACCGCCAACTTTCGGACAAGGAACCAAGGTTGAAA TCAAAACTACGACCCCAGCACCTAGACCTCCCACCCCAG CTCCAACTATAGCTTCCCAGCCATTGTCTCTCCGGCCAGA GGCGTGTCGACCAGCCGCTGGAGGGGCCGTTCATACAAG AGGACTCGATTTCGCTTGCGATATCTACATATGGGCCCCT CTTGCCGGGACATGCGGTGTCCTGCTTCTAAGCTTGGTTA TTACCCTCTATTGCAAACGCGGCCGCAAGAAACTGCTCT ACATCTTTAAACAGCCGTTCATGAGGCCTGTGCAGACAA CGCAGGAAGAGGATGGCTGTAGTTGTCGGTTTCCGGAAG AGGAAGAGGGGGGCTGCGAGTTGCGTGTCAAATTTTCTC GGTCTGCCGACGCCCCCGCGTACCAGCAAGGGCAGAACC AGCTTTATAATGAGCTGAATCTTGGACGACGGGAGGAAT ATGACGTGCTTGACAAGAGGCGAGGTAGGGACCCTGAGA TGGGGGGAAAACCTCGGAGGAAAAACCCACAGGAAGGC CTGTATAACGAACTGCAGAAGGACAAGATGGCTGAAGCC TACTCTGAGATTGGAATGAAAGGGGAACGCAGACGCGGC AAGGGCCATGATGGCCTCTACCAAGGTCTAAGCACTGCC ACCAAGGACACCTATGACGCACTCCACATGCAAGCTCTA CCTCCCCGTTGATAA
MC0282-3PF12_28_PD1_HER2 Protein Sequence (VR282)	SEQ ID NO:6	MALPVTALLLPLALLLHAARPQVQLVQSGGGVVQPGGSLR VSCAASGVTLSDYGMHWVRQAPGKGLEWMAFIRNDGSDK YYADSVKGRFTISRDNSKKTVSLQMSSLRAEDTAVYYCAK NGESGPLDYWYFDLWGRGTLVTVSSGGGGSGGGGSGGGG SDIVMTQSPSFLSASVGDRVTITCRASHGINNYLAWYQQKP GKAPKLLIYAASTLQSGVPSRFSGSGSGTEFTLTISSLQPEDF ATYYCQQYDSYPPTFGRGTKVEIKIEVMYPPPYLDNEKSNG TIIHVKGKHLCPSPLFPGPSKPFWVLVVVGGVLACYSLLVTV AFIIFWVCSRAARGTIGARRTGQPLKEDPSAVPVFSVDYGEL DFQWREKTPEPPVPCVPEQTEYATIVFPSGMGTSSPARRGSA DGPRSAQPLRPEDGHCSWPLRRKRGSGEGRGSLLTCGDVEE NPGPMALPVTALLLPLALLLHAARPEVQLVESGGGLVQPGG SLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGY TRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCS RWGGDGFYAMDYWGQGTLVTVSSGSTSGSGKPGSGEGST KGDIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQ KPGKAPKLLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQPE DFATYYCQQHYTTPPTFGQGTKVEIKTTTPAPRPPTPAPTIAS QPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGV LLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCR FPEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRRE EYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAE AYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
MC0283-3PF12_28_PD1_EGFR	SEQ ID NO:7	ATGGCACTGCCAGTGACCGCCCTGCTGCTGCCTCTGGCCC TGCTGCTGCACGCAGCCAGACCCCAAGTGCAACTAGTCC AATCAGGTGGAGGCGTCGTGCAACCTGGAGGGTCCCTCC

Nucleotide Sequence (VR283)		GCGTTAGCTGCGCCGCATCAGGCGTTACCTTGTCAGACTA CGGCATGCATTGGGTTAGGCAAGCCCCCGGCAAGGGGCT CGAATGGATGGCTTTCATTCGGAATGACGGGAGCGATAA ATATTACGCGGATTCAGTTAAAGGGCGGTTCACCATCAG CCGCGACAATAGCAAAAAGACGGTCTCCTTACAGATGTC CAGCTTGCGGGCCGAAGACACGGCTGTATACTATTGTGC TAAAAATGGCGAGAGCGGCCCCCTGGATTACTGGTACTT TGACCTGTGGGGCAGAGGCACCCTGGTCACGGTGTCCTC TGGAGGAGGAGGCTCCGGAGGAGGAGGCTCTGGCGGCG GCGGCAGCGACATTGTAATGACCCAGTCACCCTCCTTCCT TAGTGCCTCAGTCGGAGACCGCGTGACTATCACTTGTCGT GCCTCACACGGAATTAATAACTACCTCGCTTGGTATCAGC AAAAACCAGGCAAGGCCCCGAAACTATTGATCTACGCCG CATCTACTCTGCAGAGCGGAGTACCGAGCAGATTTAGTG GTTCCGGCAGCGGAACCGAGTTCACCCTAACCATTTCCA GTTTGCAGCCAGAGGATTTCGCGACCTATTACTGCCAGC AATACGATTCATACCCGCCAACTTTCGGAAGAGGTACCA AGGTTGAAATCAAGATTGAAGTTATGTATCCTCCTCCTTA CCTAGACAATGAGAAGAGCAATGGAACCATTATCCATGT GAAAGGGAAACACCTTTGTCCAAGTCCCCTATTTCCCGG GCCTTCGAAGCCCTTTTGGGTGCTGGTGGTGGTTGGTGGA GTCCTGGCTTGCTATAGCTTGCTAGTAACAGTAGCGTTTA TTATTTTCTGGGTGTGCAGCAGGGCCGCCCGCGGCACCAT CGGCGCCAGGCGCACAGGCCAGCCTCTGAAGGAGGACCC TTCCGCCGTGCCAGTGTTCTCTGTGGACTACGGCGAGCTG GATTTTCAGTGGCGGGAGAAAACCCCAGAGCCACCTGTG CCCTGCGTGCCTGAGCAGACCGAGTATGCCACAATCGTG TTTCCATCCGGAATGGGCACAAGCTCCCCTGCAAGGAGA GGCAGCGCCGACGGACCACGGTCCGCCCAGCCACTGCGG CCCGAGGATGGCCACTGTTCTTGGCCCCTGCGGAGAAAG CGTGGATCCGGGGAAGGCCGAGGCTCCCTTCTAACATGT GGAGATGTCGAGGAAAACCCTGGCCCTATGGCGCTGCCA GTCACTGCATTGTTATTGCCTCTGGCCCTGCTTCTCCATG CGGCGCGCCCACAAGTGCAGCTGAAACAGAGCGGACCA GGACTGGTTCAACCCAGCCAGAGCTTGAGCATCACGTGC ACGGTTAGCGGCTTCAGTCTGACCAATTATGGTGTGCACT GGGTGAGGCAGTCTCCAGGAAAGGGCCTGGAGTGGCTTG GAGTCATTTGGAGCGGTGGGAATACAGATTACAATACAC CTTTTACGTCACGTCTCTCCATTAACAAGGACAACTCCAA ATCCCAAGTATTTTTCAAAATGAATAGCCTGCAGAGTAA TGATACCGCCATCTATTACTGTGCACGAGCTTTGACATAT TACGACTATGAATTTGCCTATTGGGGTCAAGGCACGCTG GTGACCGTATCAGGCTCAACATCCGGGTCCGGTAAGCCG GGCTCCGGCGAGGGGTCTACAAAGGGAGACATCCTTCTG ACACAGAGCCCCGTGATCCTGTCCGTGTCCCCCGGCGAG AGAGTATCATTTTCCTGTAGGGCTTCTCAGAGCATCGGAA CAAATATCCACTGGTATCAGCAACGGACTAACGGATCAC CTCGCCTGCTCATAAAGTACGCCAGTGAATCTATTAGTGG CATACCGAGCCGCTTCAGCGGGAGTGGCTCCGGCACAGA CTTTACTCTGAGTATAAATTCCGTGGAATCTGAGGACATC

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MC0283-3PF12_28_PD1_EGFR Protein Sequence (VR283)	SEQ ID NO:8	MALPVTALLLPLALLLHAARPQVQLVQSGGGVVQPGGSLR VSCAASGVTLSDYGMHWVRQAPGKGLEWMAFIRNDGSDK YYADSVKGRFTISRDNSKKTVSLQMSSLRAEDTAVYYCAK NGESGPLDYWYFDLWGRGTLVTVSSGGGGSGGGGSGGGG SDIVMTQSPSFLSASVGDRVTITCRASHGINNYLAWYQQKP GKAPKLLIYAASTLQSGVPSRFSGSGSGTEFTLTISSLQPEDF ATYYCQQYDSYPPTFGRGTKVEIKIEVMYPPPYLDNEKSNG TIIHVKGKHLCPSPLFPGPSKPFWVLVVVGGVLACYSLLVTV AFIIFWVCSRAARGTIGARRTGQPLKEDPSAVPVFSVDYGEL DFQWREKTPEPPVPCVPEQTEYATIVFPSGMGTSSPARRGSA DGPRSAQPLRPEDGHCSWPLRRKRGSGEGRGSLLTCGDVEE NPGPMALPVTALLLPLALLLHAARPQVQLKQSGPGLVQPSQ SLSITCTVSGFSLTNYGVHWVRQSPGKGLEWLGVIWSGGNT DYNTPFTSRLSINKDNSKSQVFFKMNSLQSNDTAIYYCARA LTYYDYEFAYWGQGTLVTVSGSTSGSGKPGSGEGSTKGDIL LTQSPVILSVSPGERVSFSCRASQSIGTNIHWYQQRTNGSPRL LIKYASESISGIPSRFSGSGSGTDFTLSINSVESEDIADYYCQQ NNNWPTTFGAGTKLELKTTTPAPRPPTPAPTIASQPLSLRPE ACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVIT LYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEG GCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLD KRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIG MKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
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		GAAAGGGAAACACCTTTGTCCAAGTCCCCTATTTCCCGG GCCTTCGAAGCCCTTTTGGGTGCTGGTGGTGGTTGGTGGA GTCCTGGCTTGCTATAGCTTGCTAGTAACAGTAGCGTTTA TTATTTTCTGGGTGAAACGCGGCCGCAAGAAACTGCTCT ACATCTTTAAACAGCCGTTCATGAGGCCTGTGCAGACAA CGCAGGAAGAGGATGGCTGTAGTTGTCGGTTTCCGGAAG AGGAAGAGGGGGGCTGCGAGTTGCGTGTCAAATTTTCTC GGTCTGCCGACGCCCCCGCGTACCAGCAAGGGCAGAACC AGCTTTATAATGAGCTGAATCTTGGACGACGGGAGGAAT ATGACGTGCTTGACAAGAGGCGAGGTAGGGACCCTGAGA TGGGGGGAAAACCTCGGAGGAAAAACCCACAGGAAGGC CTGTATAACGAACTGCAGAAGGACAAGATGGCTGAAGCC TACTCTGAGATTGGAATGAAAGGGGAACGCAGACGCGGC AAGGGCCATGATGGCCTCTACCAAGGTCTAAGCACTGCC ACCAAGGACACCTATGACGCACTCCACATGCAAGCTCTA CCTCCCCGTTGATAA
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		TGACCTGTGGGGCAGAGGCACCCTGGTCACGGTGTCCTC TGGAGGAGGAGGCTCCGGAGGAGGAGGCTCTGGCGGCG GCGGCAGCGACATTGTAATGACCCAGTCACCCTCCTTCCT TAGTGCCTCAGTCGGAGACCGCGTGACTATCACTTGTCGT GCCTCACACGGAATTAATAACTACCTCGCTTGGTATCAGC AAAAACCAGGCAAGGCCCCGAAACTATTGATCTACGCCG CATCTACTCTGCAGAGCGGAGTACCGAGCAGATTTAGTG GTTCCGGCAGCGGAACCGAGTTCACCCTAACCATTTCCA GTTTGCAGCCAGAGGATTTCGCGACCTATTACTGCCAGC AATACGATTCATACCCGCCAACTTTCGGAAGAGGTACCA AGGTTGAAATCAAGACTACGACCCCAGCACCTAGACCTC CCACCCCAGCTCCAACTATAGCTTCCCAGCCATTGTCTCT CCGGCCAGAGGCGTGTCGACCAGCCGCTGGAGGGGCCGT TCATACAAGAGGACTCGATTTCGCTTGCGATATCTACATA TGGGCCCCTCTTGCCGGGACATGCGGTGTCCTGCTTCTAA GCTTGGTTATTACCCTCTATTGCTGCAGCAGGGCCGCCCG CGGCACCATCGGCGCCAGGCGCACAGGCCAGCCTCTGAA GGAGGACCCTTCCGCCGTGCCAGTGTTCTCTGTGGACTAC GGCGAGCTGGATTTTCAGTGGCGGGAGAAAACCCCAGAG CCACCTGTGCCCTGCGTGCCTGAGCAGACCGAGTATGCC ACAATCGTGTTTCCATCCGGAATGGGCACAAGCTCCCCT GCAAGGAGAGGCAGCGCCGACGGACCACGGTCCGCCCA GCCACTGCGGCCCGAGGATGGCCACTGTTCTTGGCCCCT GCGGAGAAAGCGTGGATCCGGGGAAGGCCGAGGCTCCC TTCTAACATGTGGAGATGTCGAGGAAAACCCTGGCCCTA TGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCCT GCTTCTCCATGCGGCGCGCCCAGAAGTGCAGCTGGTCGA GAGCGGAGGCGGACTGGTTCAACCCGGAGGCAGCTTGAG ACTGTCCTGCGCGGCCAGCGGCTTCAACATCAAGGATAC CTATATCCACTGGGTGAGGCAGGCTCCAGGAAAGGGCCT GGAGTGGGTGGCAAGGATTTACCCTACTAATGGATATAC ACGCTACGCTGATTCCGTGAAGGGACGCTTTACAATCTC AGCAGATACATCCAAAAACACGGCCTATTTACAGATGAA TAGTTTGCGGGCCGAAGACACGGCTGTATACTATTGTTCT CGGTGGGGGGGCGATGGATTTTATGCGATGGATTACTGG GGCCAGGGCACCCTGGTAACCGTGTCAAGCGGCTCAACA TCCGGGTCCGGTAAGCCGGGCTCCGGCGAGGGGTCTACA AAGGGAGATATACAGATGACACAGTCCCCCAGTTCCCTG TCCGCCTCAGTGGGAGACCGAGTGACGATTACCTGTCGT GCCAGCCAGGACGTCAATACCGCCGTCGCTTGGTATCAG CAAAAACCAGGCAAGGCCCCGAAACTATTGATCTACAGT GCCTCTTTTCTGTACTCCGGGGTGCCGAGCAGATTTAGTG GCTCCAGGAGCGGAACCGATTTCACCCTAACCATTTCCA GTTTGCAGCCAGAGGATTTCGCGACCTATTACTGCCAGC AACACTACACCACACCGCCAACTTTCGGACAAGGAACCA AGGTTGAAATCAAAATTGAAGTTATGTATCCTCCTCCTTA CCTAGACAATGAGAAGAGCAATGGAACCATTATCCATGT GAAAGGGAAACACCTTTGTCCAAGTCCCCTATTTCCCGG GCCTTCGAAGCCCTTTTGGGTGCTGGTGGTGGTTGGTGGA GTCCTGGCTTGCTATAGCTTGCTAGTAACAGTAGCGTTTA

		TTATTTTCTGGGTGAAACGCGGCCGCAAGAAACTGCTCT ACATCTTTAAACAGCCGTTCATGAGGCCTGTGCAGACAA CGCAGGAAGAGGATGGCTGTAGTTGTCGGTTTCCGGAAG AGGAAGAGGGGGGCTGCGAGTTGCGTGTCAAATTTTCTC GGTCTGCCGACGCCCCCGCGTACCAGCAAGGGCAGAACC AGCTTTATAATGAGCTGAATCTTGGACGACGGGAGGAAT ATGACGTGCTTGACAAGAGGCGAGGTAGGGACCCTGAGA TGGGGGGAAAACCTCGGAGGAAAAACCCACAGGAAGGC CTGTATAACGAACTGCAGAAGGACAAGATGGCTGAAGCC TACTCTGAGATTGGAATGAAAGGGGAACGCAGACGCGGC AAGGGCCATGATGGCCTCTACCAAGGTCTAAGCACTGCC ACCAAGGACACCTATGACGCACTCCACATGCAAGCTCTA CCTCCCCGTTGATAAMC
MC0285-3PF12_8_PD1_HER2 Protein Sequence (VR285)	SEQ ID NO:12	MALPVTALLLPLALLLHAARPQVQLVQSGGGVVQPGGSLR VSCAASGVTLSDYGMHWVRQAPGKGLEWMAFIRNDGSDK YYADSVKGRFTISRDNSKKTVSLQMSSLRAEDTAVYYCAK NGESGPLDYWYFDLWGRGTLVTVSSGGGGSGGGGSGGGG SDIVMTQSPSFLSASVGDRVTITCRASHGINNYLAWYQQKP GKAPKLLIYAASTLQSGVPSRFSGSGSGTEFTLTISSLQPEDF ATYYCQQYDSYPPTFGRGTKVEIKTTTPAPRPPTPAPTIASQP LSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL LSLVITLYCCSRAARGTIGARRTGQPLKEDPSAVPVFSVDYG ELDFQWREKTPEPPVPCVPEQTEYATIVFPSGMGTSSPARRG SADGPRSAQPLRPEDGHCSWPLRRKRGSGEGRGSLLTCGDV EENPGPMALPVTALLLPLALLLHAARPEVQLVESGGGLVQP GGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTN GYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYY CSRWGGDGFYAMDYWGQGTLVTVSSGSTSGSGKPGSGEG STKGDIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQ QKPGKAPKLLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQP EDFATYYCQQHYTTPPTFGQGTKVEIKIEVMYPPPYLDNEK SNGTIIHVKGKHLCPSPLFPGPSKPFWVLVVVGGVLACYSLL VTVAFIIFWVKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRF PEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRRE EYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAE AYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR
MC0286-BB7.2_8_PD1_EGFR nucleotide Sequence (VR286)	SEQ ID NO:13	ATGGCACTGCCAGTGACCGCCCTGCTGCTGCCTCTGGCCC TGCTGCTGCACGCAGCCAGACCCCAGGTGCAGCTGCAGC AGTCTGGACCTGAGCTGGTGAAGCCAGGAGCCTCCGTGA AGATGTCTTGCAAGGCCAGCGGCTACACCTTCACATCTTA TCACATCCAGTGGGTGAAGCAGCGGCCCGGACAGGGCCT GGAGTGGATCGGATGGATCTACCCAGGCGACGGCTCCAC ACAGTATAACGAGAAGTTCAAGGGCAAGACCACACTGAC CGCCGATAAGAGCAGCAGCACCGCCTACATGCTGCTGAG CAGCCTGACCAGCGAGGACAGCGCCATCTACTTTTGCGC CAGGGAGGGCACATACTATGCTATGGACTATTGGGGCCA GGGCACCAGCGTGACAGTGTCTAGCGGAGGAGGAGGCTC CGGAGGAGGAGGCTCTGGCGGCGGCGGCAGCGACGTGC TGATGACCCAGACACCACTGAGCCTGCCCGTGAGCCTGG

		GCGATCAGGTGAGCATCTCCTGTAGATCCTCTCAGAGCA TCGTGCACTCCAACGGCAATACCTACCTGGAGTGGTATCT GCAGAAGCCAGGCCAGTCCCCCAAGCTGCTGATCTATAA GGTGTCTAATCGGTTCAGCGGCGTGCCTGACAGATTTTCT GGCAGCGGCTCCGGCACCGACTTCACCCTGAAGATCAGC CGGGTGGAGGCAGAGGATCTGGGCGTGTACTATTGTTTC CAGGGCTCCCACGTGCCACGCACCTTTGGCGGCGGTACC AAGCTGGAGATCAAGACTACGACCCCAGCACCTAGACCT CCCACCCCAGCTCCAACTATAGCTTCCCAGCCATTGTCTC TCCGGCCAGAGGCGTGTCGACCAGCCGCTGGAGGGGCCG TTCATACAAGAGGACTCGATTTCGCTTGCGATATCTACAT ATGGGCCCCTCTTGCCGGGACATGCGGTGTCCTGCTTCTA AGCTTGGTTATTACCCTCTATTGCTGCAGCAGGGCCGCCC GCGGCACCATCGGCGCCAGGCGCACAGGCCAGCCTCTGA AGGAGGACCCTTCCGCCGTGCCAGTGTTCTCTGTGGACTA CGGCGAGCTGGATTTTCAGTGGCGGGAGAAAACCCCAGA GCCACCTGTGCCCTGCGTGCCTGAGCAGACCGAGTATGC CACAATCGTGTTTCCATCCGGAATGGGCACAAGCTCCCCT GCAAGGAGAGGCAGCGCCGACGGACCACGGTCCGCCCA GCCACTGCGGCCCGAGGATGGCCACTGTTCTTGGCCCCT GCGGAGAAAGCGTGGATCCGGGGAAGGCCGAGGCTCCC TTCTAACATGTGGAGATGTCGAGGAAAACCCTGGCCCTA TGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCCT GCTTCTCCATGCGGCGCGCCCACAAGTGCAGCTGAAACA GAGCGGACCAGGACTGGTTCAACCCAGCCAGAGCTTGAG CATCACGTGCACGGTTAGCGGCTTCAGTCTGACCAATTAT GGTGTGCACTGGGTGAGGCAGTCTCCAGGAAAGGGCCTG GAGTGGCTTGGAGTCATTTGGAGCGGTGGGAATACAGAT TACAATACACCTTTTACGTCACGTCTCTCCATTAACAAGG ACAACTCCAAATCCCAAGTATTTTTCAAAATGAATAGCCT GCAGAGTAATGATACCGCCATCTATTACTGTGCACGAGC TTTGACATATTACGACTATGAATTTGCCTATTGGGGTCAA GGCACGCTGGTGACCGTATCAGGCTCAACATCCGGGTCC GGTAAGCCGGGCTCCGGCGAGGGGTCTACAAAGGGAGA CATCCTTCTGACACAGAGCCCCGTGATCCTGTCCGTGTCC CCCGGCGAGAGAGTATCATTTTCCTGTAGGGCTTCTCAGA GCATCGGAACAAATATCCACTGGTATCAGCAACGGACTA ACGGATCACCTCGCCTGCTCATAAAGTACGCCAGTGAAT CTATTAGTGGCATACCGAGCCGCTTCAGCGGGAGTGGCT CCGGCACAGACTTTACTCTGAGTATAAATTCCGTGGAATC TGAGGACATCGCGGACTATTACTGCCAGCAAAACAATAA CTGGCCCACCACGTTCGGCGCGGGAACTAAACTAGAACT AAAGATTGAAGTTATGTATCCTCCTCCTTACCTAGACAAT GAGAAGAGCAATGGAACCATTATCCATGTGAAAGGGAA ACACCTTTGTCCAAGTCCCCTATTTCCCGGGCCTTCGAAG CCCTTTTGGGTGCTGGTGGTGGTTGGTGGAGTCCTGGCTT GCTATAGCTTGCTAGTAACAGTAGCGTTTATTATTTTCTG GGTGAAACGCGGCCGCAAGAAACTGCTCTACATCTTTAA ACAGCCGTTCATGAGGCCTGTGCAGACAACGCAGGAAGA GGATGGCTGTAGTTGTCGGTTTCCGGAAGAGGAAGAGGG

		GGGCTGCGAGTTGCGTGTCAAATTTTCTCGGTCTGCCGAC GCCCCCGCGTACCAGCAAGGGCAGAACCAGCTTTATAAT GAGCTGAATCTTGGACGACGGGAGGAATATGACGTGCTT GACAAGAGGCGAGGTAGGGACCCTGAGATGGGGGGAAA ACCTCGGAGGAAAAACCCACAGGAAGGCCTGTATAACG AACTGCAGAAGGACAAGATGGCTGAAGCCTACTCTGAGA TTGGAATGAAAGGGGAACGCAGACGCGGCAAGGGCCAT GATGGCCTCTACCAAGGTCTAAGCACTGCCACCAAGGAC ACCTATGACGCACTCCACATGCAAGCTCTACCTCCCCGTT GATAA
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MC0287-3PF12_8_PD1_EGFR Nucleotide Sequence (VR287)	SEQ ID NO:15	ATGGCACTGCCAGTGACCGCCCTGCTGCTGCCTCTGGCCC TGCTGCTGCACGCAGCCAGACCCCAAGTGCAACTAGTCC AATCAGGTGGAGGCGTCGTGCAACCTGGAGGGTCCCTCC GCGTTAGCTGCGCCGCATCAGGCGTTACCTTGTCAGACTA CGGCATGCATTGGGTTAGGCAAGCCCCCGGCAAGGGGCT CGAATGGATGGCTTTCATTCGGAATGACGGGAGCGATAA ATATTACGCGGATTCAGTTAAAGGGCGGTTCACCATCAG CCGCGACAATAGCAAAAAGACGGTCTCCTTACAGATGTC CAGCTTGCGGGCCGAAGACACGGCTGTATACTATTGTGC TAAAAATGGCGAGAGCGGCCCCCTGGATTACTGGTACTT TGACCTGTGGGGCAGAGGCACCCTGGTCACGGTGTCCTC TGGAGGAGGAGGCTCCGGAGGAGGAGGCTCTGGCGGCG GCGGCAGCGACATTGTAATGACCCAGTCACCCTCCTTCCT TAGTGCCTCAGTCGGAGACCGCGTGACTATCACTTGTCGT GCCTCACACGGAATTAATAACTACCTCGCTTGGTATCAGC AAAAACCAGGCAAGGCCCCGAAACTATTGATCTACGCCG CATCTACTCTGCAGAGCGGAGTACCGAGCAGATTTAGTG

		GTTCCGGCAGCGGAACCGAGTTCACCCTAACCATTTCCA GTTTGCAGCCAGAGGATTTCGCGACCTATTACTGCCAGC AATACGATTCATACCCGCCAACTTTCGGAAGAGGTACCA AGGTTGAAATCAAGACTACGACCCCAGCACCTAGACCTC CCACCCCAGCTCCAACTATAGCTTCCCAGCCATTGTCTCT CCGGCCAGAGGCGTGTCGACCAGCCGCTGGAGGGGCCGT TCATACAAGAGGACTCGATTTCGCTTGCGATATCTACATA TGGGCCCCTCTTGCCGGGACATGCGGTGTCCTGCTTCTAA GCTTGGTTATTACCCTCTATTGCTGCAGCAGGGCCGCCCG CGGCACCATCGGCGCCAGGCGCACAGGCCAGCCTCTGAA GGAGGACCCTTCCGCCGTGCCAGTGTTCTCTGTGGACTAC GGCGAGCTGGATTTTCAGTGGCGGGAGAAAACCCCAGAG CCACCTGTGCCCTGCGTGCCTGAGCAGACCGAGTATGCC ACAATCGTGTTTCCATCCGGAATGGGCACAAGCTCCCCT GCAAGGAGAGGCAGCGCCGACGGACCACGGTCCGCCCA GCCACTGCGGCCCGAGGATGGCCACTGTTCTTGGCCCCT GCGGAGAAAGCGTGGATCCGGGGAAGGCCGAGGCTCCC TTCTAACATGTGGAGATGTCGAGGAAAACCCTGGCCCTA TGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCCT GCTTCTCCATGCGGCGCGCCCACAAGTGCAGCTGAAACA GAGCGGACCAGGACTGGTTCAACCCAGCCAGAGCTTGAG CATCACGTGCACGGTTAGCGGCTTCAGTCTGACCAATTAT GGTGTGCACTGGGTGAGGCAGTCTCCAGGAAAGGGCCTG GAGTGGCTTGGAGTCATTTGGAGCGGTGGGAATACAGAT TACAATACACCTTTTACGTCACGTCTCTCCATTAACAAGG ACAACTCCAAATCCCAAGTATTTTTCAAAATGAATAGCCT GCAGAGTAATGATACCGCCATCTATTACTGTGCACGAGC TTTGACATATTACGACTATGAATTTGCCTATTGGGGTCAA GGCACGCTGGTGACCGTATCAGGCTCAACATCCGGGTCC GGTAAGCCGGGCTCCGGCGAGGGGTCTACAAAGGGAGA CATCCTTCTGACACAGAGCCCCGTGATCCTGTCCGTGTCC CCCGGCGAGAGAGTATCATTTTCCTGTAGGGCTTCTCAGA GCATCGGAACAAATATCCACTGGTATCAGCAACGGACTA ACGGATCACCTCGCCTGCTCATAAAGTACGCCAGTGAAT CTATTAGTGGCATACCGAGCCGCTTCAGCGGGAGTGGCT CCGGCACAGACTTTACTCTGAGTATAAATTCCGTGGAATC TGAGGACATCGCGGACTATTACTGCCAGCAAAACAATAA CTGGCCCACCACGTTCGGCGCGGGAACTAAACTAGAACT AAAGATTGAAGTTATGTATCCTCCTCCTTACCTAGACAAT GAGAAGAGCAATGGAACCATTATCCATGTGAAAGGGAA ACACCTTTGTCCAAGTCCCCTATTTCCCGGGCCTTCGAAG CCCTTTTGGGTGCTGGTGGTGGTTGGTGGAGTCCTGGCTT GCTATAGCTTGCTAGTAACAGTAGCGTTTATTATTTTCTG GGTGAAACGCGGCCGCAAGAAACTGCTCTACATCTTTAA ACAGCCGTTCATGAGGCCTGTGCAGACAACGCAGGAAGA GGATGGCTGTAGTTGTCGGTTTCCGGAAGAGGAAGAGGG GGGCTGCGAGTTGCGTGTCAAATTTTCTCGGTCTGCCGAC GCCCCCGCGTACCAGCAAGGGCAGAACCAGCTTTATAAT GAGCTGAATCTTGGACGACGGGAGGAATATGACGTGCTT GACAAGAGGCGAGGTAGGGACCCTGAGATGGGGGGAAA

		ACCTCGGAGGAAAAACCCACAGGAAGGCCTGTATAACG AACTGCAGAAGGACAAGATGGCTGAAGCCTACTCTGAGA TTGGAATGAAAGGGGAACGCAGACGCGGCAAGGGCCAT GATGGCCTCTACCAAGGTCTAAGCACTGCCACCAAGGAC ACCTATGACGCACTCCACATGCAAGCTCTACCTCCCCGTT GATAA
MC0287-3PF12_8_PD1_EGFR Protein Sequence (VR287)	SEQ ID NO:16	MALPVTALLLPLALLLHAARPQVQLVQSGGGVVQPGGSLR VSCAASGVTLSDYGMHWVRQAPGKGLEWMAFIRNDGSDK YYADSVKGRFTISRDNSKKTVSLQMSSLRAEDTAVYYCAK NGESGPLDYWYFDLWGRGTLVTVSSGGGGSGGGGSGGGG SDIVMTQSPSFLSASVGDRVTITCRASHGINNYLAWYQQKP GKAPKLLIYAASTLQSGVPSRFSGSGSGTEFTLTISSLQPEDF ATYYCQQYDSYPPTFGRGTKVEIKTTTPAPRPPTPAPTIASQP LSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL LSLVITLYCCSRAARGTIGARRTGQPLKEDPSAVPVFSVDYG ELDFQWREKTPEPPVPCVPEQTEYATIVFPSGMGTSSPARRG SADGPRSAQPLRPEDGHCSWPLRRKRGSGEGRGSLLTCGDV EENPGPMALPVTALLLPLALLLHAARPQVQLKQSGPGLVQP SQSLSITCTVSGFSLTNYGVHWVRQSPGKGLEWLGVIWSGG NTDYNTPFTSRLSINKDNSKSQVFFKMNSLQSNDTAIYYCA RALTYYDYEFAYWGQGTLVTVSGSTSGSGKPGSGEGSTKG DILLTQSPVILSVSPGERVSFSCRASQSIGTNIHWYQQRTNGS PRLLIKYASESISGIPSRFSGSGSGTDFTLSINSVESEDIADYY CQQNNNWPTTFGAGTKLELKIEVMYPPPYLDNEKSNGTIIH VKGKHLCPSPLFPGPSKPFWVLVVVGGVLACYSLLVTVAFII FWVKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEG GCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLD KRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIG MKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
MC0288-BB7.2_28_Pdel_HER2 Nucleotide Sequence (VR288)	SEQ ID NO:17	ATGGCACTGCCAGTGACCGCCCTGCTGCTGCCTCTGGCCC TGCTGCTGCACGCAGCCAGACCCCAGGTGCAGCTGCAGC AGTCTGGACCTGAGCTGGTGAAGCCAGGAGCCTCCGTGA AGATGTCTTGCAAGGCCAGCGGCTACACCTTCACATCTTA TCACATCCAGTGGGTGAAGCAGCGGCCCGGACAGGGCCT GGAGTGGATCGGATGGATCTACCCAGGCGACGGCTCCAC ACAGTATAACGAGAAGTTCAAGGGCAAGACCACACTGAC CGCCGATAAGAGCAGCAGCACCGCCTACATGCTGCTGAG CAGCCTGACCAGCGAGGACAGCGCCATCTACTTTTGCGC CAGGGAGGGCACATACTATGCTATGGACTATTGGGGCCA GGGCACCAGCGTGACAGTGTCTAGCGGAGGAGGAGGCTC CGGAGGAGGAGGCTCTGGCGGCGGCGGCAGCGACGTGC TGATGACCCAGACACCACTGAGCCTGCCCGTGAGCCTGG GCGATCAGGTGAGCATCTCCTGTAGATCCTCTCAGAGCA TCGTGCACTCCAACGGCAATACCTACCTGGAGTGGTATCT GCAGAAGCCAGGCCAGTCCCCCAAGCTGCTGATCTATAA GGTGTCTAATCGGTTCAGCGGCGTGCCTGACAGATTTTCT GGCAGCGGCTCCGGCACCGACTTCACCCTGAAGATCAGC CGGGTGGAGGCAGAGGATCTGGGCGTGTACTATTGTTTC CAGGGCTCCCACGTGCCACGCACCTTTGGCGGCGGTACC AAGCTGGAGATCAAGATTGAAGTTATGTATCCTCCTCCTT

		ACCTAGACAATGAGAAGAGCAATGGAACCATTATCCATG TGAAAGGGAAACACCTTTGTCCAAGTCCCCTATTTCCCGG GCCTTCGAAGCCCTTTTGGGTGCTGGTGGTGGTTGGTGGA GTCCTGGCTTGCTATAGCTTGCTAGTAACAGTAGCGTTTA TTATTTTCTGGGTGCGGAGAAAGCGTGGATCCGGGGAAG GCCGAGGCTCCCTTCTAACATGTGGAGATGTCGAGGAAA ACCCTGGCCCTATGGCGCTGCCAGTCACTGCATTGTTATT GCCTCTGGCCCTGCTTCTCCATGCGGCGCGCCCAGAAGTG CAGCTGGTCGAGAGCGGAGGCGGACTGGTTCAACCCGGA GGCAGCTTGAGACTGTCCTGCGCGGCCAGCGGCTTCAAC ATCAAGGATACCTATATCCACTGGGTGAGGCAGGCTCCA GGAAAGGGCCTGGAGTGGGTGGCAAGGATTTACCCTACT AATGGATATACACGCTACGCTGATTCCGTGAAGGGACGC TTTACAATCTCAGCAGATACATCCAAAAACACGGCCTAT TTACAGATGAATAGTTTGCGGGCCGAAGACACGGCTGTA TACTATTGTTCTCGGTGGGGGGGCGATGGATTTTATGCGA TGGATTACTGGGGCCAGGGCACCCTGGTAACCGTGTCAA GCGGCTCAACATCCGGGTCCGGTAAGCCGGGCTCCGGCG AGGGGTCTACAAAGGGAGATATACAGATGACACAGTCCC CCAGTTCCCTGTCCGCCTCAGTGGGAGACCGAGTGACGA TTACCTGTCGTGCCAGCCAGGACGTCAATACCGCCGTCG CTTGGTATCAGCAAAAACCAGGCAAGGCCCCGAAACTAT TGATCTACAGTGCCTCTTTTCTGTACTCCGGGGTGCCGAG CAGATTTAGTGGCTCCAGGAGCGGAACCGATTTCACCCT AACCATTTCCAGTTTGCAGCCAGAGGATTTCGCGACCTAT TACTGCCAGCAACACTACACCACACCGCCAACTTTCGGA CAAGGAACCAAGGTTGAAATCAAAACTACGACCCCAGCA CCTAGACCTCCCACCCCAGCTCCAACTATAGCTTCCCAGC CATTGTCTCTCCGGCCAGAGGCGTGTCGACCAGCCGCTG GAGGGGCCGTTCATACAAGAGGACTCGATTTCGCTTGCG ATATCTACATATGGGCCCCTCTTGCCGGGACATGCGGTGT CCTGCTTCTAAGCTTGGTTATTACCCTCTATTGCAAACGC GGCCGCAAGAAACTGCTCTACATCTTTAAACAGCCGTTC ATGAGGCCTGTGCAGACAACGCAGGAAGAGGATGGCTGT AGTTGTCGGTTTCCGGAAGAGGAAGAGGGGGGCTGCGAG TTGCGTGTCAAATTTTCTCGGTCTGCCGACGCCCCCGCGT ACCAGCAAGGGCAGAACCAGCTTTATAATGAGCTGAATC TTGGACGACGGGAGGAATATGACGTGCTTGACAAGAGGC GAGGTAGGGACCCTGAGATGGGGGGAAAACCTCGGAGG AAAAACCCACAGGAAGGCCTGTATAACGAACTGCAGAA GGACAAGATGGCTGAAGCCTACTCTGAGATTGGAATGAA AGGGGAACGCAGACGCGGCAAGGGCCATGATGGCCTCT ACCAAGGTCTAAGCACTGCCACCAAGGACACCTATGACG CACTCCACATGCAAGCTCTACCTCCCCGTTGATAA
MC0288-BB7.2_28_Pdel_HER2 Protein Sequence (VR288)	SEQ ID NO:18	MALPVTALLLPLALLLHAARPQVQLQQSGPELVKPGASVK MSCKASGYTFTSYHIQWVKQRPGQGLEWIGWIYPGDGSTQ YNEKFKGKTTLTADKSSSTAYMLLSSLTSEDSAIYFCAREGT YYAMDYWGQGTSVTVSSGGGGSGGGGSGGGGSDVLMTQ TPLSLPVSLGDQVSISCRSSQSIVHSNGNTYLEWYLQKPGQS PKLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGV

		YYCFQGSHVPRTFGGGTKLEIKIEVMYPPPYLDNEKSNGTII HVKGKHLCPSPLFPGPSKPFWVLVVVGGVLACYSLLVTVAF IIFWVRRKRGSGEGRGSLLTCGDVEENPGPMALPVTALLLP LALLLHAARPEVQLVESGGGLVQPGGSLRLSCAASGFNIKD TYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKGRFTIS ADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDY WGQGTLVTVSSGSTSGSGKPGSGEGSTKGDIQMTQSPSSLS ASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSAS FLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTP PTFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAA GGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRG RKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRV KFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRD PEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERR RGKGHDGLYQGLSTATKDTYDALHMQALPPR
MC0289-3PF12_28_Pdel_HER2 Nucleotide Sequence (VR289)	SEQ ID NO:19	ATGGCACTGCCAGTGACCGCCCTGCTGCTGCCTCTGGCCC TGCTGCTGCACGCAGCCAGACCCCAAGTGCAACTAGTCC AATCAGGTGGAGGCGTCGTGCAACCTGGAGGGTCCCTCC GCGTTAGCTGCGCCGCATCAGGCGTTACCTTGTCAGACTA CGGCATGCATTGGGTTAGGCAAGCCCCCGGCAAGGGGCT CGAATGGATGGCTTTCATTCGGAATGACGGGAGCGATAA ATATTACGCGGATTCAGTTAAAGGGCGGTTCACCATCAG CCGCGACAATAGCAAAAAGACGGTCTCCTTACAGATGTC CAGCTTGCGGGCCGAAGACACGGCTGTATACTATTGTGC TAAAAATGGCGAGAGCGGCCCCCTGGATTACTGGTACTT TGACCTGTGGGGCAGAGGCACCCTGGTCACGGTGTCCTC TGGAGGAGGAGGCTCCGGAGGAGGAGGCTCTGGCGGCG GCGGCAGCGACATTGTAATGACCCAGTCACCCTCCTTCCT TAGTGCCTCAGTCGGAGACCGCGTGACTATCACTTGTCGT GCCTCACACGGAATTAATAACTACCTCGCTTGGTATCAGC AAAAACCAGGCAAGGCCCCGAAACTATTGATCTACGCCG CATCTACTCTGCAGAGCGGAGTACCGAGCAGATTTAGTG GTTCCGGCAGCGGAACCGAGTTCACCCTAACCATTTCCA GTTTGCAGCCAGAGGATTTCGCGACCTATTACTGCCAGC AATACGATTCATACCCGCCAACTTTCGGAAGAGGTACCA AGGTTGAAATCAAGATTGAAGTTATGTATCCTCCTCCTTA CCTAGACAATGAGAAGAGCAATGGAACCATTATCCATGT GAAAGGGAAACACCTTTGTCCAAGTCCCCTATTTCCCGG GCCTTCGAAGCCCTTTTGGGTGCTGGTGGTGGTTGGTGGA GTCCTGGCTTGCTATAGCTTGCTAGTAACAGTAGCGTTTA TTATTTTCTGGGTGCGGAGAAAGCGTGGATCCGGGGAAG GCCGAGGCTCCCTTCTAACATGTGGAGATGTCGAGGAAA ACCCTGGCCCTATGGCGCTGCCAGTCACTGCATTGTTATT GCCTCTGGCCCTGCTTCTCCATGCGGCGCGCCCAGAAGTG CAGCTGGTCGAGAGCGGAGGCGGACTGGTTCAACCCGGA GGCAGCTTGAGACTGTCCTGCGCGGCCAGCGGCTTCAAC ATCAAGGATACCTATATCCACTGGGTGAGGCAGGCTCCA GGAAAGGGCCTGGAGTGGGTGGCAAGGATTTACCCTACT AATGGATATACACGCTACGCTGATTCCGTGAAGGGACGC TTTACAATCTCAGCAGATACATCCAAAAACACGGCCTAT

		TTACAGATGAATAGTTTGCGGGCCGAAGACACGGCTGTA TACTATTGTTCTCGGTGGGGGGGCGATGGATTTTATGCGA TGGATTACTGGGGCCAGGGCACCCTGGTAACCGTGTCAA GCGGCTCAACATCCGGGTCCGGTAAGCCGGGCTCCGGCG AGGGGTCTACAAAGGGAGATATACAGATGACACAGTCCC CCAGTTCCCTGTCCGCCTCAGTGGGAGACCGAGTGACGA TTACCTGTCGTGCCAGCCAGGACGTCAATACCGCCGTCG CTTGGTATCAGCAAAAACCAGGCAAGGCCCCGAAACTAT TGATCTACAGTGCCTCTTTTCTGTACTCCGGGGTGCCGAG CAGATTTAGTGGCTCCAGGAGCGGAACCGATTTCACCCT AACCATTTCCAGTTTGCAGCCAGAGGATTTCGCGACCTAT TACTGCCAGCAACACTACACCACACCGCCAACTTTCGGA CAAGGAACCAAGGTTGAAATCAAAACTACGACCCCAGCA CCTAGACCTCCCACCCCAGCTCCAACTATAGCTTCCCAGC CATTGTCTCTCCGGCCAGAGGCGTGTCGACCAGCCGCTG GAGGGGCCGTTCATACAAGAGGACTCGATTTCGCTTGCG ATATCTACATATGGGCCCCTCTTGCCGGGACATGCGGTGT CCTGCTTCTAAGCTTGGTTATTACCCTCTATTGCAAACGC GGCCGCAAGAAACTGCTCTACATCTTTAAACAGCCGTTC ATGAGGCCTGTGCAGACAACGCAGGAAGAGGATGGCTGT AGTTGTCGGTTTCCGGAAGAGGAAGAGGGGGGCTGCGAG TTGCGTGTCAAATTTTCTCGGTCTGCCGACGCCCCCGCGT ACCAGCAAGGGCAGAACCAGCTTTATAATGAGCTGAATC TTGGACGACGGGAGGAATATGACGTGCTTGACAAGAGGC GAGGTAGGGACCCTGAGATGGGGGGAAAACCTCGGAGG AAAAACCCACAGGAAGGCCTGTATAACGAACTGCAGAA GGACAAGATGGCTGAAGCCTACTCTGAGATTGGAATGAA AGGGGAACGCAGACGCGGCAAGGGCCATGATGGCCTCT ACCAAGGTCTAAGCACTGCCACCAAGGACACCTATGACG CACTCCACATGCAAGCTCTACCTCCCCGTTGATAA
MC0289-3PF12_28_Pdel_HER2 Protein Sequence (VR289)	SEQ ID NO:20	MALPVTALLLPLALLLHAARPQVQLVQSGGGVVQPGGSLR VSCAASGVTLSDYGMHWVRQAPGKGLEWMAFIRNDGSDK YYADSVKGRFTISRDNSKKTVSLQMSSLRAEDTAVYYCAK NGESGPLDYWYFDLWGRGTLVTVSSGGGGSGGGGSGGGG SDIVMTQSPSFLSASVGDRVTITCRASHGINNYLAWYQQKP GKAPKLLIYAASTLQSGVPSRFSGSGSGTEFTLTISSLQPEDF ATYYCQQYDSYPPTFGRGTKVEIKIEVMYPPPYLDNEKSNG TIIHVKGKHLCPSPLFPGPSKPFWVLVVVGGVLACYSLLVTV AFIIFWVRRKRGSGEGRGSLLTCGDVEENPGPMALPVTALL LPLALLLHAARPEVQLVESGGGLVQPGGSLRLSCAASGFNI KDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKGRFT ISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMD YWGQGTLVTVSSGSTSGSGKPGSGEGSTKGDIQMTQSPSSL SASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSA SFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTT PPTFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPA AGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKR GRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELR VKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGR

		DPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGER RRGKGHDGLYQGLSTATKDTYDALHMQALPPR
MC0290-3PF12_28_LIR1_HER2 Nucleic acid sequence (VR290)	SEQ ID NO:21	ATGGCACTGCCAGTGACCGCCCTGCTGCTGCCTCTGGCCC TGCTGCTGCACGCAGCCAGACCCCAAGTGCAACTAGTCC AATCAGGTGGAGGCGTCGTGCAACCTGGAGGGTCCCTCC GCGTTAGCTGCGCCGCATCAGGCGTTACCTTGTCAGACTA CGGCATGCATTGGGTTAGGCAAGCCCCCGGCAAGGGGCT CGAATGGATGGCTTTCATTCGGAATGACGGGAGCGATAA ATATTACGCGGATTCAGTTAAAGGGCGGTTCACCATCAG CCGCGACAATAGCAAAAAGACGGTCTCCTTACAGATGTC CAGCTTGCGGGCCGAAGACACGGCTGTATACTATTGTGC TAAAAATGGCGAGAGCGGCCCCCTGGATTACTGGTACTT TGACCTGTGGGGCAGAGGCACCCTGGTCACGGTGTCCTC TGGAGGAGGAGGCTCCGGAGGAGGAGGCTCTGGCGGCG GCGGCAGCGACATTGTAATGACCCAGTCACCCTCCTTCCT TAGTGCCTCAGTCGGAGACCGCGTGACTATCACTTGTCGT GCCTCACACGGAATTAATAACTACCTCGCTTGGTATCAGC AAAAACCAGGCAAGGCCCCGAAACTATTGATCTACGCCG CATCTACTCTGCAGAGCGGAGTACCGAGCAGATTTAGTG GTTCCGGCAGCGGAACCGAGTTCACCCTAACCATTTCCA GTTTGCAGCCAGAGGATTTCGCGACCTATTACTGCCAGC AATACGATTCATACCCGCCAACTTTCGGAAGAGGTACCA AGGTTGAAATCAAGATTGAAGTTATGTATCCTCCTCCTTA CCTAGACAATGAGAAGAGCAATGGAACCATTATCCATGT GAAAGGGAAACACCTTTGTCCAAGTCCCCTATTTCCCGG GCCTTCGAAGCCCTTTTGGGTGCTGGTGGTGGTTGGTGGA GTCCTGGCTTGCTATAGCTTGCTAGTAACAGTAGCGTTTA TTATTTTCTGGGTGCTGCGCCACAGGAGACAGGGCAAGC ACTGGACCAGCACCCAGCGGAAGGCCGACTTTCAGCACC CTGCCGGCGCCGTGGGCCCTGAGCCTACCGACAGGGGCC TGCAGTGGAGGAGCTCCCCAGCCGCCGATGCCCAGGAGG AGAATCTGTACGCCGCCGTGAAGCACACCCAGCCAGAGG ACGGCGTGGAGATGGACACCCGCTCCCCACACGACGAGG ATCCACAGGCCGTGACCTACGCCGAGGTGAAGCACAGCC GCCCCAGACGCGAGATGGCCAGCCCACCCAGCCCCCTGT CCGGCGAGTTCCTGGACACCAAGGACAGGCAGGCCGAG GAGGACCGGCAGATGGACACCGAGGCCGCCGCCTCCGA GGCCCCCCAGGACGTGACCTACGCCCAGCTGCACTCCCT GACCCTGCGGAGAGAGGCCACCGAGCCCCCACCCAGCCA GGAGGGCCCCTCCCCCGCCGTGCCTAGCATCTACGCCAC CCTGGCCATCCACCGGAGAAAGCGTGGATCCGGGGAAGG CCGAGGCTCCCTTCTAACATGTGGAGATGTCGAGGAAAA CCCTGGCCCTATGGCGCTGCCAGTCACTGCATTGTTATTG CCTCTGGCCCTGCTTCTCCATGCGGCGCGCCCAGAAGTGC AGCTGGTCGAGAGCGGAGGCGGACTGGTTCAACCCGGAG GCAGCTTGAGACTGTCCTGCGCGGCCAGCGGCTTCAACA TCAAGGATACCTATATCCACTGGGTGAGGCAGGCTCCAG GAAAGGGCCTGGAGTGGGTGGCAAGGATTTACCCTACTA ATGGATATACACGCTACGCTGATTCCGTGAAGGGACGCT TTACAATCTCAGCAGATACATCCAAAAACACGGCCTATT

		TACAGATGAATAGTTTGCGGGCCGAAGACACGGCTGTAT ACTATTGTTCTCGGTGGGGGGGCGATGGATTTTATGCGAT GGATTACTGGGGCCAGGGCACCCTGGTAACCGTGTCAAG CGGCTCAACATCCGGGTCCGGTAAGCCGGGCTCCGGCGA GGGGTCTACAAAGGGAGATATACAGATGACACAGTCCCC CAGTTCCCTGTCCGCCTCAGTGGGAGACCGAGTGACGAT TACCTGTCGTGCCAGCCAGGACGTCAATACCGCCGTCGC TTGGTATCAGCAAAAACCAGGCAAGGCCCCGAAACTATT GATCTACAGTGCCTCTTTTCTGTACTCCGGGGTGCCGAGC AGATTTAGTGGCTCCAGGAGCGGAACCGATTTCACCCTA ACCATTTCCAGTTTGCAGCCAGAGGATTTCGCGACCTATT ACTGCCAGCAACACTACACCACACCGCCAACTTTCGGAC AAGGAACCAAGGTTGAAATCAAAACTACGACCCCAGCAC CTAGACCTCCCACCCCAGCTCCAACTATAGCTTCCCAGCC ATTGTCTCTCCGGCCAGAGGCGTGTCGACCAGCCGCTGG AGGGGCCGTTCATACAAGAGGACTCGATTTCGCTTGCGA TATCTACATATGGGCCCCTCTTGCCGGGACATGCGGTGTC CTGCTTCTAAGCTTGGTTATTACCCTCTATTGCAAACGCG GCCGCAAGAAACTGCTCTACATCTTTAAACAGCCGTTCAT GAGGCCTGTGCAGACAACGCAGGAAGAGGATGGCTGTA GTTGTCGGTTTCCGGAAGAGGAAGAGGGGGGCTGCGAGT TGCGTGTCAAATTTTCTCGGTCTGCCGACGCCCCCGCGTA CCAGCAAGGGCAGAACCAGCTTTATAATGAGCTGAATCT TGGACGACGGGAGGAATATGACGTGCTTGACAAGAGGC GAGGTAGGGACCCTGAGATGGGGGGAAAACCTCGGAGG AAAAACCCACAGGAAGGCCTGTATAACGAACTGCAGAA GGACAAGATGGCTGAAGCCTACTCTGAGATTGGAATGAA AGGGGAACGCAGACGCGGCAAGGGCCATGATGGCCTCT ACCAAGGTCTAAGCACTGCCACCAAGGACACCTATGACG CACTCCACATGCAAGCTCTACCTCCCCGTTGATAA
MC0290-3PF12_28_LIR1_HER2 Protein sequence (VR290)	SEQ ID NO:22	MALPVTALLLPLALLLHAARPQVQLVQSGGGVVQPGGSLR VSCAASGVTLSDYGMHWVRQAPGKGLEWMAFIRNDGSDK YYADSVKGRFTISRDNSKKTVSLQMSSLRAEDTAVYYCAK NGESGPLDYWYFDLWGRGTLVTVSSGGGGSGGGGSGGGG SDIVMTQSPSFLSASVGDRVTITCRASHGINNYLAWYQQKP GKAPKLLIYAASTLQSGVPSRFSGSGSGTEFTLTISSLQPEDF ATYYCQQYDSYPPTFGRGTKVEIKIEVMYPPPYLDNEKSNG TIIHVKGKHLCPSPLFPGPSKPFWVLVVVGGVLACYSLLVTV AFIIFWVLRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDR GLQWRSSPAADAQEENLYAAVKHTQPEDGVEMDTRSPHD EDPQAVTYAEVKHSRPRREMASPPSPLSGEFLDTKDRQAEE DRQMDTEAAASEAPQDVTYAQLHSLTLRREATEPPPSQEGP SPAVPSIYATLAIHRRKRGSGEGRGSLLTCGDVEENPGPMAL PVTALLLPLALLLHAARPEVQLVESGGGLVQPGGSLRLSCA ASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADS VKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDG FYAMDYWGQGTLVTVSSGSTSGSGKPGSGEGSTKGDIQMT QSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPK LLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYC QQHYTTPPTFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRP

		EACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVI TLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEE GGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVL DKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIG MKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
MC0291-3PF12_28_KIR2DL1_HER2 nucleotide Sequence (VR291)	SEQ ID NO:23	ATGGCACTGCCAGTGACCGCCCTGCTGCTGCCTCTGGCCC TGCTGCTGCACGCAGCCAGACCCCAAGTGCAACTAGTCC AATCAGGTGGAGGCGTCGTGCAACCTGGAGGGTCCCTCC GCGTTAGCTGCGCCGCATCAGGCGTTACCTTGTCAGACTA CGGCATGCATTGGGTTAGGCAAGCCCCCGGCAAGGGGCT CGAATGGATGGCTTTCATTCGGAATGACGGGAGCGATAA ATATTACGCGGATTCAGTTAAAGGGCGGTTCACCATCAG CCGCGACAATAGCAAAAAGACGGTCTCCTTACAGATGTC CAGCTTGCGGGCCGAAGACACGGCTGTATACTATTGTGC TAAAAATGGCGAGAGCGGCCCCCTGGATTACTGGTACTT TGACCTGTGGGGCAGAGGCACCCTGGTCACGGTGTCCTC TGGAGGAGGAGGCTCCGGAGGAGGAGGCTCTGGCGGCG GCGGCAGCGACATTGTAATGACCCAGTCACCCTCCTTCCT TAGTGCCTCAGTCGGAGACCGCGTGACTATCACTTGTCGT GCCTCACACGGAATTAATAACTACCTCGCTTGGTATCAGC AAAAACCAGGCAAGGCCCCGAAACTATTGATCTACGCCG CATCTACTCTGCAGAGCGGAGTACCGAGCAGATTTAGTG GTTCCGGCAGCGGAACCGAGTTCACCCTAACCATTTCCA GTTTGCAGCCAGAGGATTTCGCGACCTATTACTGCCAGC AATACGATTCATACCCGCCAACTTTCGGAAGAGGTACCA AGGTTGAAATCAAGATTGAAGTTATGTATCCTCCTCCTTA CCTAGACAATGAGAAGAGCAATGGAACCATTATCCATGT GAAAGGGAAACACCTTTGTCCAAGTCCCCTATTTCCCGG GCCTTCGAAGCCCTTTTGGGTGCTGGTGGTGGTTGGTGGA GTCCTGGCTTGCTATAGCTTGCTAGTAACAGTAGCGTTTA TTATTTTCTGGGTGCATAGGTGGTGCTCAAACAAAAAGA ATGCTGCCGTCATGGACCAGGAGAGCGCGGGCAATCGGA CCGCAAACTCAGAGGACTCAGATGAACAAGATCCACAGG AAGTGACCTACACTCAGCTGAACCATTGTGTGTTTACACA GCGCAAGATTACTCGTCCAAGCCAGCGTCCTAAGACCCC CCCGACCGATATCATTGTGTATACCGAGCTTCCTAATGCC GAATCCCGCAGCAAGGTGGTCTCCTGCCCGCGGAGAAAG CGTGGATCCGGGGAAGGCCGAGGCTCCCTTCTAACATGT GGAGATGTCGAGGAAAACCCTGGCCCTATGGCGCTGCCA GTCACTGCATTGTTATTGCCTCTGGCCCTGCTTCTCCATG CGGCGCGCCCAGAAGTGCAGCTGGTCGAGAGCGGAGGC GGACTGGTTCAACCCGGAGGCAGCTTGAGACTGTCCTGC GCGGCCAGCGGCTTCAACATCAAGGATACCTATATCCAC TGGGTGAGGCAGGCTCCAGGAAAGGGCCTGGAGTGGGT GGCAAGGATTTACCCTACTAATGGATATACACGCTACGC TGATTCCGTGAAGGGACGCTTTACAATCTCAGCAGATAC ATCCAAAAACACGGCCTATTTACAGATGAATAGTTTGCG GGCCGAAGACACGGCTGTATACTATTGTTCTCGGTGGGG GGGCGATGGATTTTATGCGATGGATTACTGGGGCCAGGG CACCCTGGTAACCGTGTCAAGCGGCTCAACATCCGGGTC

		CGGTAAGCCGGGCTCCGGCGAGGGGTCTACAAAGGGAG ATATACAGATGACACAGTCCCCCAGTTCCCTGTCCGCCTC AGTGGGAGACCGAGTGACGATTACCTGTCGTGCCAGCCA GGACGTCAATACCGCCGTCGCTTGGTATCAGCAAAAACC AGGCAAGGCCCCGAAACTATTGATCTACAGTGCCTCTTTT CTGTACTCCGGGGTGCCGAGCAGATTTAGTGGCTCCAGG AGCGGAACCGATTTCACCCTAACCATTTCCAGTTTGCAGC CAGAGGATTTCGCGACCTATTACTGCCAGCAACACTACA CCACACCGCCAACTTTCGGACAAGGAACCAAGGTTGAAA TCAAAACTACGACCCCAGCACCTAGACCTCCCACCCCAG CTCCAACTATAGCTTCCCAGCCATTGTCTCTCCGGCCAGA GGCGTGTCGACCAGCCGCTGGAGGGGCCGTTCATACAAG AGGACTCGATTTCGCTTGCGATATCTACATATGGGCCCCT CTTGCCGGGACATGCGGTGTCCTGCTTCTAAGCTTGGTTA TTACCCTCTATTGCAAACGCGGCCGCAAGAAACTGCTCT ACATCTTTAAACAGCCGTTCATGAGGCCTGTGCAGACAA CGCAGGAAGAGGATGGCTGTAGTTGTCGGTTTCCGGAAG AGGAAGAGGGGGGCTGCGAGTTGCGTGTCAAATTTTCTC GGTCTGCCGACGCCCCCGCGTACCAGCAAGGGCAGAACC AGCTTTATAATGAGCTGAATCTTGGACGACGGGAGGAAT ATGACGTGCTTGACAAGAGGCGAGGTAGGGACCCTGAGA TGGGGGGAAAACCTCGGAGGAAAAACCCACAGGAAGGC CTGTATAACGAACTGCAGAAGGACAAGATGGCTGAAGCC TACTCTGAGATTGGAATGAAAGGGGAACGCAGACGCGGC AAGGGCCATGATGGCCTCTACCAAGGTCTAAGCACTGCC ACCAAGGACACCTATGACGCACTCCACATGCAAGCTCTA CCTCCCCGTTGATAA
MC0291-3PF12_28_KIR2DL1_HER2 Protein Sequence (VR291)	SEQ ID NO:24	MALPVTALLLPLALLLHAARPQVQLVQSGGGVVQPGGSLR VSCAASGVTLSDYGMHWVRQAPGKGLEWMAFIRNDGSDK YYADSVKGRFTISRDNSKKTVSLQMSSLRAEDTAVYYCAK NGESGPLDYWYFDLWGRGTLVTVSSGGGGSGGGGSGGGG SDIVMTQSPSFLSASVGDRVTITCRASHGINNYLAWYQQKP GKAPKLLIYAASTLQSGVPSRFSGSGSGTEFTLTISSLQPEDF ATYYCQQYDSYPPTFGRGTKVEIKIEVMYPPPYLDNEKSNG TIIHVKGKHLCPSPLFPGPSKPFWVLVVVGGVLACYSLLVTV AFIIFWVHRWCSNKKNAAVMDQESAGNRTANSEDSDEQDP QEVTYTQLNHCVFTQRKITRPSQRPKTPPTDIIVYTELPNAES RSKVVSCPRRKRGSGEGRGSLLTCGDVEENPGPMALPVTAL LLPLALLLHAARPEVQLVESGGGLVQPGGSLRLSCAASGFNI KDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKGRFT ISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMD YWGQGTLVTVSSGSTSGSGKPGSGEGSTKGDIQMTQSPSSL SASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSA SFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTT PPTFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPA AGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKR GRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELR VKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGR DPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGER RRGKGHDGLYQGLSTATKDTYDALHMQALPPR

MC0292-BB7.2_28_LIR1_HER2 nucleotide Sequence (VR292)	SEQ ID NO:25	ATGGCACTGCCAGTGACCGCCCTGCTGCTGCCTCTGGCCC TGCTGCTGCACGCAGCCAGACCCCAGGTGCAGCTGCAGC AGTCTGGACCTGAGCTGGTGAAGCCAGGAGCCTCCGTGA AGATGTCTTGCAAGGCCAGCGGCTACACCTTCACATCTTA TCACATCCAGTGGGTGAAGCAGCGGCCCGGACAGGGCCT GGAGTGGATCGGATGGATCTACCCAGGCGACGGCTCCAC ACAGTATAACGAGAAGTTCAAGGGCAAGACCACACTGAC CGCCGATAAGAGCAGCAGCACCGCCTACATGCTGCTGAG CAGCCTGACCAGCGAGGACAGCGCCATCTACTTTTGCGC CAGGGAGGGCACATACTATGCTATGGACTATTGGGGCCA GGGCACCAGCGTGACAGTGTCTAGCGGAGGAGGAGGCTC CGGAGGAGGAGGCTCTGGCGGCGGCGGCAGCGACGTGC TGATGACCCAGACACCACTGAGCCTGCCCGTGAGCCTGG GCGATCAGGTGAGCATCTCCTGTAGATCCTCTCAGAGCA TCGTGCACTCCAACGGCAATACCTACCTGGAGTGGTATCT GCAGAAGCCAGGCCAGTCCCCCAAGCTGCTGATCTATAA GGTGTCTAATCGGTTCAGCGGCGTGCCTGACAGATTTTCT GGCAGCGGCTCCGGCACCGACTTCACCCTGAAGATCAGC CGGGTGGAGGCAGAGGATCTGGGCGTGTACTATTGTTTC CAGGGCTCCCACGTGCCACGCACCTTTGGCGGCGGTACC AAGCTGGAGATCAAGATTGAAGTTATGTATCCTCCTCCTT ACCTAGACAATGAGAAGAGCAATGGAACCATTATCCATG TGAAAGGGAAACACCTTTGTCCAAGTCCCCTATTTCCCGG GCCTTCGAAGCCCTTTTGGGTGCTGGTGGTGGTTGGTGGA GTCCTGGCTTGCTATAGCTTGCTAGTAACAGTAGCGTTTA TTATTTTCTGGGTGCTGCGCCACAGGAGACAGGGCAAGC ACTGGACCAGCACCCAGCGGAAGGCCGACTTTCAGCACC CTGCCGGCGCCGTGGGCCCTGAGCCTACCGACAGGGGCC TGCAGTGGAGGAGCTCCCCAGCCGCCGATGCCCAGGAGG AGAATCTGTACGCCGCCGTGAAGCACACCCAGCCAGAGG ACGGCGTGGAGATGGACACCCGCTCCCCACACGACGAGG ATCCACAGGCCGTGACCTACGCCGAGGTGAAGCACAGCC GCCCCAGACGCGAGATGGCCAGCCCACCCAGCCCCCTGT CCGGCGAGTTCCTGGACACCAAGGACAGGCAGGCCGAG GAGGACCGGCAGATGGACACCGAGGCCGCCGCCTCCGA GGCCCCCCAGGACGTGACCTACGCCCAGCTGCACTCCCT GACCCTGCGGAGAGAGGCCACCGAGCCCCCACCCAGCCA GGAGGGCCCCTCCCCCGCCGTGCCTAGCATCTACGCCAC CCTGGCCATCCACCGGAGAAAGCGTGGATCCGGGGAAGG CCGAGGCTCCCTTCTAACATGTGGAGATGTCGAGGAAAA CCCTGGCCCTATGGCGCTGCCAGTCACTGCATTGTTATTG CCTCTGGCCCTGCTTCTCCATGCGGCGCGCCCAGAAGTGC AGCTGGTCGAGAGCGGAGGCGGACTGGTTCAACCCGGAG GCAGCTTGAGACTGTCCTGCGCGGCCAGCGGCTTCAACA TCAAGGATACCTATATCCACTGGGTGAGGCAGGCTCCAG GAAAGGGCCTGGAGTGGGTGGCAAGGATTTACCCTACTA ATGGATATACACGCTACGCTGATTCCGTGAAGGGACGCT TTACAATCTCAGCAGATACATCCAAAAACACGGCCTATT TACAGATGAATAGTTTGCGGGCCGAAGACACGGCTGTAT ACTATTGTTCTCGGTGGGGGGGCGATGGATTTTATGCGAT

		GGATTACTGGGGCCAGGGCACCCTGGTAACCGTGTCAAG CGGCTCAACATCCGGGTCCGGTAAGCCGGGCTCCGGCGA GGGGTCTACAAAGGGAGATATACAGATGACACAGTCCCC CAGTTCCCTGTCCGCCTCAGTGGGAGACCGAGTGACGAT TACCTGTCGTGCCAGCCAGGACGTCAATACCGCCGTCGC TTGGTATCAGCAAAAACCAGGCAAGGCCCCGAAACTATT GATCTACAGTGCCTCTTTTCTGTACTCCGGGGTGCCGAGC AGATTTAGTGGCTCCAGGAGCGGAACCGATTTCACCCTA ACCATTTCCAGTTTGCAGCCAGAGGATTTCGCGACCTATT ACTGCCAGCAACACTACACCACACCGCCAACTTTCGGAC AAGGAACCAAGGTTGAAATCAAAACTACGACCCCAGCAC CTAGACCTCCCACCCCAGCTCCAACTATAGCTTCCCAGCC ATTGTCTCTCCGGCCAGAGGCGTGTCGACCAGCCGCTGG AGGGGCCGTTCATACAAGAGGACTCGATTTCGCTTGCGA TATCTACATATGGGCCCCTCTTGCCGGGACATGCGGTGTC CTGCTTCTAAGCTTGGTTATTACCCTCTATTGCAAACGCG GCCGCAAGAAACTGCTCTACATCTTTAAACAGCCGTTCAT GAGGCCTGTGCAGACAACGCAGGAAGAGGATGGCTGTA GTTGTCGGTTTCCGGAAGAGGAAGAGGGGGGCTGCGAGT TGCGTGTCAAATTTTCTCGGTCTGCCGACGCCCCCGCGTA CCAGCAAGGGCAGAACCAGCTTTATAATGAGCTGAATCT TGGACGACGGGAGGAATATGACGTGCTTGACAAGAGGC GAGGTAGGGACCCTGAGATGGGGGGAAAACCTCGGAGG AAAAACCCACAGGAAGGCCTGTATAACGAACTGCAGAA GGACAAGATGGCTGAAGCCTACTCTGAGATTGGAATGAA AGGGGAACGCAGACGCGGCAAGGGCCATGATGGCCTCT ACCAAGGTCTAAGCACTGCCACCAAGGACACCTATGACG CACTCCACATGCAAGCTCTACCTCCCCGTTGATAA
MC0292-BB7.2_28_LIR1_HER2 Protein Sequence (VR292)	SEQ ID NO:26	MALPVTALLLPLALLLHAARPQVQLQQSGPELVKPGASVK MSCKASGYTFTSYHIQWVKQRPGQGLEWIGWIYPGDGSTQ YNEKFKGKTTLTADKSSSTAYMLLSSLTSEDSAIYFCAREGT YYAMDYWGQGTSVTVSSGGGGSGGGGSGGGGSDVLMTQ TPLSLPVSLGDQVSISCRSSQSIVHSNGNTYLEWYLQKPGQS PKLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGV YYCFQGSHVPRTFGGGTKLEIKIEVMYPPPYLDNEKSNGTII HVKGKHLCPSPLFPGPSKPFWVLVVVGGVLACYSLLVTVAF IIFWVLRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGL QWRSSPAADAQEENLYAAVKHTQPEDGVEMDTRSPHDEDP QAVTYAEVKHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQ MDTEAAASEAPQDVTYAQLHSLTLRREATEPPPSQEGPSPA VPSIYATLAIHRRKRGSGEGRGSLLTCGDVEENPGPMALPV TALLLPLALLLHAARPEVQLVESGGGLVQPGGSLRLSCAAS GFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVK GRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFY AMDYWGQGTLVTVSSGSTSGSGKPGSGEGSTKGDIQMTQS PSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLI YSASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQH YTTPPTFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEAC RPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLY CKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGC

		ELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKR RGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMK GERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
MC0293-BB7.2_28_KIR2DL1_HER2 nucleotide sequence (VR293)	SEQ ID NO:27	ATGGCACTGCCAGTGACCGCCCTGCTGCTGCCTCTGGCCC TGCTGCTGCACGCAGCCAGACCCCAGGTGCAGCTGCAGC AGTCTGGACCTGAGCTGGTGAAGCCAGGAGCCTCCGTGA AGATGTCTTGCAAGGCCAGCGGCTACACCTTCACATCTTA TCACATCCAGTGGGTGAAGCAGCGGCCCGGACAGGGCCT GGAGTGGATCGGATGGATCTACCCAGGCGACGGCTCCAC ACAGTATAACGAGAAGTTCAAGGGCAAGACCACACTGAC CGCCGATAAGAGCAGCAGCACCGCCTACATGCTGCTGAG CAGCCTGACCAGCGAGGACAGCGCCATCTACTTTTGCGC CAGGGAGGGCACATACTATGCTATGGACTATTGGGGCCA GGGCACCAGCGTGACAGTGTCTAGCGGAGGAGGAGGCTC CGGAGGAGGAGGCTCTGGCGGCGGCGGCAGCGACGTGC TGATGACCCAGACACCACTGAGCCTGCCCGTGAGCCTGG GCGATCAGGTGAGCATCTCCTGTAGATCCTCTCAGAGCA TCGTGCACTCCAACGGCAATACCTACCTGGAGTGGTATCT GCAGAAGCCAGGCCAGTCCCCCAAGCTGCTGATCTATAA GGTGTCTAATCGGTTCAGCGGCGTGCCTGACAGATTTTCT GGCAGCGGCTCCGGCACCGACTTCACCCTGAAGATCAGC CGGGTGGAGGCAGAGGATCTGGGCGTGTACTATTGTTTC CAGGGCTCCCACGTGCCACGCACCTTTGGCGGCGGTACC AAGCTGGAGATCAAGATTGAAGTTATGTATCCTCCTCCTT ACCTAGACAATGAGAAGAGCAATGGAACCATTATCCATG TGAAAGGGAAACACCTTTGTCCAAGTCCCCTATTTCCCGG GCCTTCGAAGCCCTTTTGGGTGCTGGTGGTGGTTGGTGGA GTCCTGGCTTGCTATAGCTTGCTAGTAACAGTAGCGTTTA TTATTTTCTGGGTGCATAGGTGGTGCTCAAACAAAAAGA ATGCTGCCGTCATGGACCAGGAGAGCGCGGGCAATCGGA CCGCAAACTCAGAGGACTCAGATGAACAAGATCCACAGG AAGTGACCTACACTCAGCTGAACCATTGTGTGTTTACACA GCGCAAGATTACTCGTCCAAGCCAGCGTCCTAAGACCCC CCCGACCGATATCATTGTGTATACCGAGCTTCCTAATGCC GAATCCCGCAGCAAGGTGGTCTCCTGCCCGCGGAGAAAG CGTGGATCCGGGGAAGGCCGAGGCTCCCTTCTAACATGT GGAGATGTCGAGGAAAACCCTGGCCCTATGGCGCTGCCA GTCACTGCATTGTTATTGCCTCTGGCCCTGCTTCTCCATG CGGCGCGCCCAGAAGTGCAGCTGGTCGAGAGCGGAGGC GGACTGGTTCAACCCGGAGGCAGCTTGAGACTGTCCTGC GCGGCCAGCGGCTTCAACATCAAGGATACCTATATCCAC TGGGTGAGGCAGGCTCCAGGAAAGGGCCTGGAGTGGGT GGCAAGGATTTACCCTACTAATGGATATACACGCTACGC TGATTCCGTGAAGGGACGCTTTACAATCTCAGCAGATAC ATCCAAAAACACGGCCTATTTACAGATGAATAGTTTGCG GGCCGAAGACACGGCTGTATACTATTGTTCTCGGTGGGG GGGCGATGGATTTTATGCGATGGATTACTGGGGCCAGGG CACCCTGGTAACCGTGTCAAGCGGCTCAACATCCGGGTC CGGTAAGCCGGGCTCCGGCGAGGGGTCTACAAAGGGAG ATATACAGATGACACAGTCCCCCAGTTCCCTGTCCGCCTC

		AGTGGGAGACCGAGTGACGATTACCTGTCGTGCCAGCCA GGACGTCAATACCGCCGTCGCTTGGTATCAGCAAAAACC AGGCAAGGCCCCGAAACTATTGATCTACAGTGCCTCTTTT CTGTACTCCGGGGTGCCGAGCAGATTTAGTGGCTCCAGG AGCGGAACCGATTTCACCCTAACCATTTCCAGTTTGCAGC CAGAGGATTTCGCGACCTATTACTGCCAGCAACACTACA CCACACCGCCAACTTTCGGACAAGGAACCAAGGTTGAAA TCAAAACTACGACCCCAGCACCTAGACCTCCCACCCCAG CTCCAACTATAGCTTCCCAGCCATTGTCTCTCCGGCCAGA GGCGTGTCGACCAGCCGCTGGAGGGGCCGTTCATACAAG AGGACTCGATTTCGCTTGCGATATCTACATATGGGCCCCT CTTGCCGGGACATGCGGTGTCCTGCTTCTAAGCTTGGTTA TTACCCTCTATTGCAAACGCGGCCGCAAGAAACTGCTCT ACATCTTTAAACAGCCGTTCATGAGGCCTGTGCAGACAA CGCAGGAAGAGGATGGCTGTAGTTGTCGGTTTCCGGAAG AGGAAGAGGGGGGCTGCGAGTTGCGTGTCAAATTTTCTC GGTCTGCCGACGCCCCCGCGTACCAGCAAGGGCAGAACC AGCTTTATAATGAGCTGAATCTTGGACGACGGGAGGAAT ATGACGTGCTTGACAAGAGGCGAGGTAGGGACCCTGAGA TGGGGGGAAAACCTCGGAGGAAAAACCCACAGGAAGGC CTGTATAACGAACTGCAGAAGGACAAGATGGCTGAAGCC TACTCTGAGATTGGAATGAAAGGGGAACGCAGACGCGGC AAGGGCCATGATGGCCTCTACCAAGGTCTAAGCACTGCC ACCAAGGACACCTATGACGCACTCCACATGCAAGCTCTA CCTCCCCGTTGATAA
MC0293-BB7.2_28_KIR2DL1_HER2 Protein Sequence (VR293)	SEQ ID NO:28	MALPVTALLLPLALLLHAARPQVQLQQSGPELVKPGASVK MSCKASGYTFTSYHIQWVKQRPGQGLEWIGWIYPGDGSTQ YNEKFKGKTTLTADKSSSTAYMLLSSLTSEDSAIYFCAREGT YYAMDYWGQGTSVTVSSGGGGSGGGGSGGGGSDVLMTQ TPLSLPVSLGDQVSISCRSSQSIVHSNGNTYLEWYLQKPGQS PKLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGV YYCFQGSHVPRTFGGGTKLEIKIEVMYPPPYLDNEKSNGTII HVKGKHLCPSPLFPGPSKPFWVLVVVGGVLACYSLLVTVAF IIFWVHRWCSNKKNAAVMDQESAGNRTANSEDSDEQDPQE VTYTQLNHCVFTQRKITRPSQRPKTPPTDIIVYTELPNAESRS KVVSCPRRKRGSGEGRGSLLTCGDVEENPGPMALPVTALLL PLALLLHAARPEVQLVESGGGLVQPGGSLRLSCAASGFNIK DTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKGRFTI SADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDY WGQGTLVTVSSGSTSGSGKPGSGEGSTKGDIQMTQSPSSLS ASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSAS FLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTP PTFGQGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAA GGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRG RKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRV KFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRD PEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERR RGKGHDGLYQGLSTATKDTYDALHMQALPPR
MC0294-3PF12_CD8	SEQ ID NO:29	ATGGCACTGCCAGTGACCGCCCTGCTGCTGCCTCTGGCCC TGCTGCTGCACGCAGCCAGACCCCAAGTGCAACTAGTCC

_LIR1_HE R2 Nucleotide sequence (VR294)		AATCAGGTGGAGGCGTCGTGCAACCTGGAGGGTCCCTCC GCGTTAGCTGCGCCGCATCAGGCGTTACCTTGTCAGACTA CGGCATGCATTGGGTTAGGCAAGCCCCCGGCAAGGGGCT CGAATGGATGGCTTTCATTCGGAATGACGGGAGCGATAA ATATTACGCGGATTCAGTTAAAGGGCGGTTCACCATCAG CCGCGACAATAGCAAAAAGACGGTCTCCTTACAGATGTC CAGCTTGCGGGCCGAAGACACGGCTGTATACTATTGTGC TAAAAATGGCGAGAGCGGCCCCCTGGATTACTGGTACTT TGACCTGTGGGGCAGAGGCACCCTGGTCACGGTGTCCTC TGGAGGAGGAGGCTCCGGAGGAGGAGGCTCTGGCGGCG GCGGCAGCGACATTGTAATGACCCAGTCACCCTCCTTCCT TAGTGCCTCAGTCGGAGACCGCGTGACTATCACTTGTCGT GCCTCACACGGAATTAATAACTACCTCGCTTGGTATCAGC AAAAACCAGGCAAGGCCCCGAAACTATTGATCTACGCCG CATCTACTCTGCAGAGCGGAGTACCGAGCAGATTTAGTG GTTCCGGCAGCGGAACCGAGTTCACCCTAACCATTTCCA GTTTGCAGCCAGAGGATTTCGCGACCTATTACTGCCAGC AATACGATTCATACCCGCCAACTTTCGGAAGAGGTACCA AGGTTGAAATCAAGACTACGACCCCAGCACCTAGACCTC CCACCCCAGCTCCAACTATAGCTTCCCAGCCATTGTCTCT CCGGCCAGAGGCGTGTCGACCAGCCGCTGGAGGGGCCGT TCATACAAGAGGACTCGATTTCGCTTGCGATATCTACATA TGGGCCCCTCTTGCCGGGACATGCGGTGTCCTGCTTCTAA GCTTGGTTATTACCCTCTATTGCCTGCGCCACAGGAGACA GGGCAAGCACTGGACCAGCACCCAGCGGAAGGCCGACTT TCAGCACCCTGCCGGCGCCGTGGGCCCTGAGCCTACCGA CAGGGGCCTGCAGTGGAGGAGCTCCCCAGCCGCCGATGC CCAGGAGGAGAATCTGTACGCCGCCGTGAAGCACACCCA GCCAGAGGACGGCGTGGAGATGGACACCCGCTCCCCACA CGACGAGGATCCACAGGCCGTGACCTACGCCGAGGTGAA GCACAGCCGCCCCAGACGCGAGATGGCCAGCCCACCCAG CCCCCTGTCCGGCGAGTTCCTGGACACCAAGGACAGGCA GGCCGAGGAGGACCGGCAGATGGACACCGAGGCCGCCG CCTCCGAGGCCCCCCAGGACGTGACCTACGCCCAGCTGC ACTCCCTGACCCTGCGGAGAGAGGCCACCGAGCCCCCAC CCAGCCAGGAGGGCCCCTCCCCCGCCGTGCCTAGCATCT ACGCCACCCTGGCCATCCACCGGAGAAAGCGTGGATCCG GGGAAGGCCGAGGCTCCCTTCTAACATGTGGAGATGTCG AGGAAAACCCTGGCCCTATGGCGCTGCCAGTCACTGCAT TGTTATTGCCTCTGGCCCTGCTTCTCCATGCGGCGCGCCC AGAAGTGCAGCTGGTCGAGAGCGGAGGCGGACTGGTTCA ACCCGGAGGCAGCTTGAGACTGTCCTGCGCGGCCAGCGG CTTCAACATCAAGGATACCTATATCCACTGGGTGAGGCA GGCTCCAGGAAAGGGCCTGGAGTGGGTGGCAAGGATTTA CCCTACTAATGGATATACACGCTACGCTGATTCCGTGAA GGGACGCTTTACAATCTCAGCAGATACATCCAAAAACAC GGCCTATTTACAGATGAATAGTTTGCGGGCCGAAGACAC GGCTGTATACTATTGTTCTCGGTGGGGGGGCGATGGATTT TATGCGATGGATTACTGGGGCCAGGGCACCCTGGTAACC GTGTCAAGCGGCTCAACATCCGGGTCCGGTAAGCCGGGC

		TCCGGCGAGGGGTCTACAAAGGGAGATATACAGATGACA CAGTCCCCCAGTTCCCTGTCCGCCTCAGTGGGAGACCGA GTGACGATTACCTGTCGTGCCAGCCAGGACGTCAATACC GCCGTCGCTTGGTATCAGCAAAAACCAGGCAAGGCCCCG AAACTATTGATCTACAGTGCCTCTTTTCTGTACTCCGGGG TGCCGAGCAGATTTAGTGGCTCCAGGAGCGGAACCGATT TCACCCTAACCATTTCCAGTTTGCAGCCAGAGGATTTCGC GACCTATTACTGCCAGCAACACTACACCACACCGCCAAC TTTCGGACAAGGAACCAAGGTTGAAATCAAAATTGAAGT TATGTATCCTCCTCCTTACCTAGACAATGAGAAGAGCAAT GGAACCATTATCCATGTGAAAGGGAAACACCTTTGTCCA AGTCCCCTATTTCCCGGGCCTTCGAAGCCCTTTTGGGTGC TGGTGGTGGTTGGTGGAGTCCTGGCTTGCTATAGCTTGCT AGTAACAGTAGCGTTTATTATTTTCTGGGTGAAACGCGGC CGCAAGAAACTGCTCTACATCTTTAAACAGCCGTTCATG AGGCCTGTGCAGACAACGCAGGAAGAGGATGGCTGTAGT TGTCGGTTTCCGGAAGAGGAAGAGGGGGGCTGCGAGTTG CGTGTCAAATTTTCTCGGTCTGCCGACGCCCCCGCGTACC AGCAAGGGCAGAACCAGCTTTATAATGAGCTGAATCTTG GACGACGGGAGGAATATGACGTGCTTGACAAGAGGCGA GGTAGGGACCCTGAGATGGGGGGAAAACCTCGGAGGAA AAACCCACAGGAAGGCCTGTATAACGAACTGCAGAAGG ACAAGATGGCTGAAGCCTACTCTGAGATTGGAATGAAAG GGGAACGCAGACGCGGCAAGGGCCATGATGGCCTCTACC AAGGTCTAAGCACTGCCACCAAGGACACCTATGACGCAC TCCACATGCAAGCTCTACCTCCCCGTTGATAA
MC0294-3PF12_CD8_LIR1_HER2 Protein Sequence (VR294)	SEQ ID NO:30	MALPVTALLLPLALLLHAARPQVQLVQSGGGVVQPGGSLR VSCAASGVTLSDYGMHWVRQAPGKGLEWMAFIRNDGSDK YYADSVKGRFTISRDNSKKTVSLQMSSLRAEDTAVYYCAK NGESGPLDYWYFDLWGRGTLVTVSSGGGGSGGGGSGGGG SDIVMTQSPSFLSASVGDRVTITCRASHGINNYLAWYQQKP GKAPKLLIYAASTLQSGVPSRFSGSGSGTEFTLTISSLQPEDF ATYYCQQYDSYPPTFGRGTKVEIKTTTPAPRPPTPAPTIASQP LSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL LSLVITLYCLRHRRQGKHWTSTQRKADFQHPAGAVGPEPT DRGLQWRSSPAADAQEENLYAAVKHTQPEDGVEMDTRSP HDEDPQAVTYAEVKHSRPRREMASPPSPLSGEFLDTKDRQA EEDRQMDTEAAASEAPQDVTYAQLHSLTLRREATEPPPSQE GPSPAVPSIYATLAIHRRKRGSGEGRGSLLTCGDVEENPGPM ALPVTALLLPLALLLHAARPEVQLVESGGGLVQPGGSLRLS CAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYA DSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGG DGFYAMDYWGQGTLVTVSSGSTSGSGKPGSGEGSTKGDIQ MTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKA PKLLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYY CQQHYTTPPTFGQGTKVEIKIEVMYPPPYLDNEKSNGTIIHV KGKHLCPSPLFPGPSKPFWVLVVVGGVLACYSLLVTVAFIIF WVKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGG CELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDK

		RRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGM KGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
MC0295- 3PF12_CD8 _KIR2DL1_ HER2 nucleotide Sequence (VR295)	SEQ ID NO:31	ATGGCACTGCCAGTGACCGCCCTGCTGCTGCCTCTGGCCC TGCTGCTGCACGCAGCCAGACCCCAAGTGCAACTAGTCC AATCAGGTGGAGGCGTCGTGCAACCTGGAGGGTCCCTCC GCGTTAGCTGCGCCGCATCAGGCGTTACCTTGTCAGACTA CGGCATGCATTGGGTTAGGCAAGCCCCCGGCAAGGGGCT CGAATGGATGGCTTTCATTCGGAATGACGGGAGCGATAA ATATTACGCGGATTCAGTTAAAGGGCGGTTCACCATCAG CCGCGACAATAGCAAAAAGACGGTCTCCTTACAGATGTC CAGCTTGCGGGCCGAAGACACGGCTGTATACTATTGTGC TAAAAATGGCGAGAGCGGCCCCCTGGATTACTGGTACTT TGACCTGTGGGGCAGAGGCACCCTGGTCACGGTGTCCTC TGGAGGAGGAGGCTCCGGAGGAGGAGGCTCTGGCGGCG GCGGCAGCGACATTGTAATGACCCAGTCACCCTCCTTCCT TAGTGCCTCAGTCGGAGACCGCGTGACTATCACTTGTCGT GCCTCACACGGAATTAATAACTACCTCGCTTGGTATCAGC AAAAACCAGGCAAGGCCCCGAAACTATTGATCTACGCCG CATCTACTCTGCAGAGCGGAGTACCGAGCAGATTTAGTG GTTCCGGCAGCGGAACCGAGTTCACCCTAACCATTTCCA GTTTGCAGCCAGAGGATTTCGCGACCTATTACTGCCAGC AATACGATTCATACCCGCCAACTTTCGGAAGAGGTACCA AGGTTGAAATCAAGACTACGACCCCAGCACCTAGACCTC CCACCCCAGCTCCAACTATAGCTTCCCAGCCATTGTCTCT CCGGCCAGAGGCGTGTCGACCAGCCGCTGGAGGGGCCGT TCATACAAGAGGACTCGATTTCGCTTGCGATATCTACATA TGGGCCCCTCTTGCCGGGACATGCGGTGTCCTGCTTCTAA GCTTGGTTATTACCCTCTATTGCCATAGGTGGTGCTCAAA CAAAAAGAATGCTGCCGTCATGGACCAGGAGAGCGCGG GCAATCGGACCGCAAACTCAGAGGACTCAGATGAACAA GATCCACAGGAAGTGACCTACACTCAGCTGAACCATTGT GTGTTTACACAGCGCAAGATTACTCGTCCAAGCCAGCGT CCTAAGACCCCCCCGACCGATATCATTGTGTATACCGAG CTTCCTAATGCCGAATCCCGCAGCAAGGTGGTCTCCTGCC CGCGGAGAAAGCGTGGATCCGGGGAAGGCCGAGGCTCC CTTCTAACATGTGGAGATGTCGAGGAAAACCCTGGCCCT ATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCC TGCTTCTCCATGCGGCGCGCCCAGAAGTGCAGCTGGTCG AGAGCGGAGGCGGACTGGTTCAACCCGGAGGCAGCTTGA GACTGTCCTGCGCGGCCAGCGGCTTCAACATCAAGGATA CCTATATCCACTGGGTGAGGCAGGCTCCAGGAAAGGGCC TGGAGTGGGTGGCAAGGATTTACCCTACTAATGGATATA CACGCTACGCTGATTCCGTGAAGGGACGCTTTACAATCTC AGCAGATACATCCAAAAACACGGCCTATTTACAGATGAA TAGTTTGCGGGCCGAAGACACGGCTGTATACTATTGTTCT CGGTGGGGGGGCGATGGATTTTATGCGATGGATTACTGG GGCCAGGGCACCCTGGTAACCGTGTCAAGCGGCTCAACA TCCGGGTCCGGTAAGCCGGGCTCCGGCGAGGGGTCTACA AAGGGAGATATACAGATGACACAGTCCCCCAGTTCCCTG TCCGCCTCAGTGGGAGACCGAGTGACGATTACCTGTCGT

		GCCAGCCAGGACGTCAATACCGCCGTCGCTTGGTATCAG CAAAAACCAGGCAAGGCCCCGAAACTATTGATCTACAGT GCCTCTTTTCTGTACTCCGGGGTGCCGAGCAGATTTAGTG GCTCCAGGAGCGGAACCGATTTCACCCTAACCATTTCCA GTTTGCAGCCAGAGGATTTCGCGACCTATTACTGCCAGC AACACTACACCACACCGCCAACTTTCGGACAAGGAACCA AGGTTGAAATCAAAATTGAAGTTATGTATCCTCCTCCTTA CCTAGACAATGAGAAGAGCAATGGAACCATTATCCATGT GAAAGGGAAACACCTTTGTCCAAGTCCCCTATTTCCCGG GCCTTCGAAGCCCTTTTGGGTGCTGGTGGTGGTTGGTGGA GTCCTGGCTTGCTATAGCTTGCTAGTAACAGTAGCGTTTA TTATTTTCTGGGTGAAACGCGGCCGCAAGAAACTGCTCT ACATCTTTAAACAGCCGTTCATGAGGCCTGTGCAGACAA CGCAGGAAGAGGATGGCTGTAGTTGTCGGTTTCCGGAAG AGGAAGAGGGGGGCTGCGAGTTGCGTGTCAAATTTTCTC GGTCTGCCGACGCCCCCGCGTACCAGCAAGGGCAGAACC AGCTTTATAATGAGCTGAATCTTGGACGACGGGAGGAAT ATGACGTGCTTGACAAGAGGCGAGGTAGGGACCCTGAGA TGGGGGGAAAACCTCGGAGGAAAAACCCACAGGAAGGC CTGTATAACGAACTGCAGAAGGACAAGATGGCTGAAGCC TACTCTGAGATTGGAATGAAAGGGGAACGCAGACGCGGC AAGGGCCATGATGGCCTCTACCAAGGTCTAAGCACTGCC ACCAAGGACACCTATGACGCACTCCACATGCAAGCTCTA CCTCCCCGTTGATAA
MC0295-3PF12_CD8_KIR2DL1_HER2 Protein Sequence (VR295)	SEQ ID NO:32	MALPVTALLLPLALLLHAARPQVQLVQSGGGVVQPGGSLR VSCAASGVTLSDYGMHWVRQAPGKGLEWMAFIRNDGSDK YYADSVKGRFTISRDNSKKTVSLQMSSLRAEDTAVYYCAK NGESGPLDYWYFDLWGRGTLVTVSSGGGGSGGGGSGGGG SDIVMTQSPSFLSASVGDRVTITCRASHGINNYLAWYQQKP GKAPKLLIYAASTLQSGVPSRFSGSGSGTEFTLTISSLQPEDF ATYYCQQYDSYPPTFGRGTKVEIKTTTPAPRPPTPAPTIASQP LSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL LSLVITLYCHRWCSNKKNAAVMDQESAGNRTANSEDSDEQ DPQEVTYTQLNHCVFTQRKITRPSQRPKTPPTDIIVYTELPNA ESRSKVVSCPRRKRGSGEGRGSLLTCGDVEENPGPMALPVT ALLLPLALLLHAARPEVQLVESGGGLVQPGGSLRLSCAASG FNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKG RFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYA MDYWGQGTLVTVSSGSTSGSGKPGSGEGSTKGDIQMTQSP SSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIY SASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHY TTPPTFGQGTKVEIKIEVMYPPPYLDNEKSNGTIIHVKGKHL CPSPLFPGPSKPFWVLVVVGGVLACYSLLVTVAFIIFWVKR GRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELR VKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGR DPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGER RRGKGHDGLYQGLSTATKDTYDALHMQALPPR
MC00296-BB7.2_CD8	SEQ ID NO:33	ATGGCACTGCCAGTGACCGCCCTGCTGCTGCCTCTGGCCC TGCTGCTGCACGCAGCCAGACCCCAGGTGCAGCTGCAGC AGTCTGGACCTGAGCTGGTGAAGCCAGGAGCCTCCGTGA

_LIR1_HE R2 (VR296)		AGATGTCTTGCAAGGCCAGCGGCTACACCTTCACATCTTA TCACATCCAGTGGGTGAAGCAGCGGCCCGGACAGGGCCT GGAGTGGATCGGATGGATCTACCCAGGCGACGGCTCCAC ACAGTATAACGAGAAGTTCAAGGGCAAGACCACACTGAC CGCCGATAAGAGCAGCAGCACCGCCTACATGCTGCTGAG CAGCCTGACCAGCGAGGACAGCGCCATCTACTTTTGCGC CAGGGAGGGCACATACTATGCTATGGACTATTGGGGCCA GGGCACCAGCGTGACAGTGTCTAGCGGAGGAGGAGGCTC CGGAGGAGGAGGCTCTGGCGGCGGCGGCAGCGACGTGC TGATGACCCAGACACCACTGAGCCTGCCCGTGAGCCTGG GCGATCAGGTGAGCATCTCCTGTAGATCCTCTCAGAGCA TCGTGCACTCCAACGGCAATACCTACCTGGAGTGGTATCT GCAGAAGCCAGGCCAGTCCCCCAAGCTGCTGATCTATAA GGTGTCTAATCGGTTCAGCGGCGTGCCTGACAGATTTTCT GGCAGCGGCTCCGGCACCGACTTCACCCTGAAGATCAGC CGGGTGGAGGCAGAGGATCTGGGCGTGTACTATTGTTTC CAGGGCTCCCACGTGCCACGCACCTTTGGCGGCGGTACC AAGCTGGAGATCAAGACTACGACCCCAGCACCTAGACCT CCCACCCCAGCTCCAACTATAGCTTCCCAGCCATTGTCTC TCCGGCCAGAGGCGTGTCGACCAGCCGCTGGAGGGGCCG TTCATACAAGAGGACTCGATTTCGCTTGCGATATCTACAT ATGGGCCCCTCTTGCCGGGACATGCGGTGTCCTGCTTCTA AGCTTGGTTATTACCCTCTATTGCCTGCGCCACAGGAGAC AGGGCAAGCACTGGACCAGCACCCAGCGGAAGGCCGAC TTTCAGCACCCTGCCGGCGCCGTGGGCCCTGAGCCTACC GACAGGGGCCTGCAGTGGAGGAGCTCCCCAGCCGCCGAT GCCCAGGAGGAGAATCTGTACGCCGCCGTGAAGCACACC CAGCCAGAGGACGGCGTGGAGATGGACACCCGCTCCCCA CACGACGAGGATCCACAGGCCGTGACCTACGCCGAGGTG AAGCACAGCCGCCCCAGACGCGAGATGGCCAGCCCACCC AGCCCCCTGTCCGGCGAGTTCCTGGACACCAAGGACAGG CAGGCCGAGGAGGACCGGCAGATGGACACCGAGGCCGC CGCCTCCGAGGCCCCCCAGGACGTGACCTACGCCCAGCT GCACTCCCTGACCCTGCGGAGAGAGGCCACCGAGCCCCC ACCCAGCCAGGAGGGCCCCTCCCCCGCCGTGCCTAGCAT CTACGCCACCCTGGCCATCCACCGGAGAAAGCGTGGATC CGGGGAAGGCCGAGGCTCCCTTCTAACATGTGGAGATGT CGAGGAAAACCCTGGCCCTATGGCGCTGCCAGTCACTGC ATTGTTATTGCCTCTGGCCCTGCTTCTCCATGCGGCGCGC CCAGAAGTGCAGCTGGTCGAGAGCGGAGGCGGACTGGTT CAACCCGGAGGCAGCTTGAGACTGTCCTGCGCGGCCAGC GGCTTCAACATCAAGGATACCTATATCCACTGGGTGAGG CAGGCTCCAGGAAAGGGCCTGGAGTGGGTGGCAAGGATT TACCCTACTAATGGATATACACGCTACGCTGATTCCGTGA AGGGACGCTTTACAATCTCAGCAGATACATCCAAAAACA CGGCCTATTTACAGATGAATAGTTTGCGGGCCGAAGACA CGGCTGTATACTATTGTTCTCGGTGGGGGGGCGATGGATT TTATGCGATGGATTACTGGGGCCAGGGCACCCTGGTAAC CGTGTCAAGCGGCTCAACATCCGGGTCCGGTAAGCCGGG CTCCGGCGAGGGGTCTACAAAGGGAGATATACAGATGAC

		ACAGTCCCCCAGTTCCCTGTCCGCCTCAGTGGGAGACCG AGTGACGATTACCTGTCGTGCCAGCCAGGACGTCAATAC CGCCGTCGCTTGGTATCAGCAAAAACCAGGCAAGGCCCC GAAACTATTGATCTACAGTGCCTCTTTTCTGTACTCCGGG GTGCCGAGCAGATTTAGTGGCTCCAGGAGCGGAACCGAT TTCACCCTAACCATTTCCAGTTTGCAGCCAGAGGATTTCG CGACCTATTACTGCCAGCAACACTACACCACACCGCCAA CTTTCGGACAAGGAACCAAGGTTGAAATCAAAATTGAAG TTATGTATCCTCCTCCTTACCTAGACAATGAGAAGAGCAA TGGAACCATTATCCATGTGAAAGGGAAACACCTTTGTCC AAGTCCCCTATTTCCCGGGCCTTCGAAGCCCTTTTGGGTG CTGGTGGTGGTTGGTGGAGTCCTGGCTTGCTATAGCTTGC TAGTAACAGTAGCGTTTATTATTTTCTGGGTGAAACGCGG CCGCAAGAAACTGCTCTACATCTTTAAACAGCCGTTCATG AGGCCTGTGCAGACAACGCAGGAAGAGGATGGCTGTAGT TGTCGGTTTCCGGAAGAGGAAGAGGGGGGCTGCGAGTTG CGTGTCAAATTTTCTCGGTCTGCCGACGCCCCCGCGTACC AGCAAGGGCAGAACCAGCTTTATAATGAGCTGAATCTTG GACGACGGGAGGAATATGACGTGCTTGACAAGAGGCGA GGTAGGGACCCTGAGATGGGGGGAAAACCTCGGAGGAA AAACCCACAGGAAGGCCTGTATAACGAACTGCAGAAGG ACAAGATGGCTGAAGCCTACTCTGAGATTGGAATGAAAG GGGAACGCAGACGCGGCAAGGGCCATGATGGCCTCTACC AAGGTCTAAGCACTGCCACCAAGGACACCTATGACGCAC TCCACATGCAAGCTCTACCTCCCCGTTGATAA
MC00296-BB7.2_CD8_LIR1_HER2 protein Sequence (VR296)	SEQ ID NO:34	MALPVTALLLPLALLLHAARPQVQLQQSGPELVKPGASVK MSCKASGYTFTSYHIQWVKQRPGQGLEWIGWIYPGDGSTQ YNEKFKGKTTLTADKSSSTAYMLLSSLTSEDSAIYFCAREGT YYAMDYWGQGTSVTVSSGGGGSGGGGSGGGGSDVLMTQ TPLSLPVSLGDQVSISCRSSQSIVHSNGNTYLEWYLQKPGQS PKLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGV YYCFQGSHVPRTFGGGTKLEIKTTTPAPRPPTPAPTIASQPLS LRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLS LVITLYCLRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDR GLQWRSSPAADAQEENLYAAVKHTQPEDGVEMDTRSPHD EDPQAVTYAEVKHSRPRREMASPPSPLSGEFLDTKDRQAEE DRQMDTEAAASEAPQDVTYAQLHSLTLRREATEPPPSQEGP SPAVPSIYATLAIHRRKRGSGEGRGSLLTCGDVEENPGPMAL PVTALLLPLALLLHAARPEVQLVESGGGLVQPGGSLRLSCA ASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADS VKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDG FYAMDYWGQGTLVTVSSGSTSGSGKPGSGEGSTKGDIQMT QSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPK LLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYC QQHYTTPPTFGQGTKVEIKIEVMYPPPYLDNEKSNGTIIHVK GKHLCPSPLFPGPSKPFWVLVVVGGVLACYSLLVTVAFIIFW VKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGC ELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKR RGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMK GERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR

MC00297-BB7.2_CD8_KIR2DL1_HER2-nucleic acid (VR297)	SEQ ID NO:35	ATGGCACTGCCAGTGACCGCCCTGCTGCTGCCTCTGGCCC TGCTGCTGCACGCAGCCAGACCCCAGGTGCAGCTGCAGC AGTCTGGACCTGAGCTGGTGAAGCCAGGAGCCTCCGTGA AGATGTCTTGCAAGGCCAGCGGCTACACCTTCACATCTTA TCACATCCAGTGGGTGAAGCAGCGGCCCGGACAGGGCCT GGAGTGGATCGGATGGATCTACCCAGGCGACGGCTCCAC ACAGTATAACGAGAAGTTCAAGGGCAAGACCACACTGAC CGCCGATAAGAGCAGCAGCACCGCCTACATGCTGCTGAG CAGCCTGACCAGCGAGGACAGCGCCATCTACTTTTGCGC CAGGGAGGGCACATACTATGCTATGGACTATTGGGGCCA GGGCACCAGCGTGACAGTGTCTAGCGGAGGAGGAGGCTC CGGAGGAGGAGGCTCTGGCGGCGGCGGCAGCGACGTGC TGATGACCCAGACACCACTGAGCCTGCCCGTGAGCCTGG GCGATCAGGTGAGCATCTCCTGTAGATCCTCTCAGAGCA TCGTGCACTCCAACGGCAATACCTACCTGGAGTGGTATCT GCAGAAGCCAGGCCAGTCCCCCAAGCTGCTGATCTATAA GGTGTCTAATCGGTTCAGCGGCGTGCCTGACAGATTTTCT GGCAGCGGCTCCGGCACCGACTTCACCCTGAAGATCAGC CGGGTGGAGGCAGAGGATCTGGGCGTGTACTATTGTTTC CAGGGCTCCCACGTGCCACGCACCTTTGGCGGCGGTACC AAGCTGGAGATCAAGACTACGACCCCAGCACCTAGACCT CCCACCCCAGCTCCAACTATAGCTTCCCAGCCATTGTCTC TCCGGCCAGAGGCGTGTCGACCAGCCGCTGGAGGGGCCG TTCATACAAGAGGACTCGATTTCGCTTGCGATATCTACAT ATGGGCCCCTCTTGCCGGGACATGCGGTGTCCTGCTTCTA AGCTTGGTTATTACCCTCTATTGCCATAGGTGGTGCTCAA ACAAAAAGAATGCTGCCGTCATGGACCAGGAGAGCGCG GGCAATCGGACCGCAAACTCAGAGGACTCAGATGAACA AGATCCACAGGAAGTGACCTACACTCAGCTGAACCATTG TGTGTTTACACAGCGCAAGATTACTCGTCCAAGCCAGCG TCCTAAGACCCCCCCGACCGATATCATTGTGTATACCGAG CTTCCTAATGCCGAATCCCGCAGCAAGGTGGTCTCCTGCC CGCGGAGAAAGCGTGGATCCGGGGAAGGCCGAGGCTCC CTTCTAACATGTGGAGATGTCGAGGAAAACCCTGGCCCT ATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCC TGCTTCTCCATGCGGCGCGCCCAGAAGTGCAGCTGGTCG AGAGCGGAGGCGGACTGGTTCAACCCGGAGGCAGCTTGA GACTGTCCTGCGCGGCCAGCGGCTTCAACATCAAGGATA CCTATATCCACTGGGTGAGGCAGGCTCCAGGAAAGGGCC TGGAGTGGGTGGCAAGGATTTACCCTACTAATGGATATA CACGCTACGCTGATTCCGTGAAGGGACGCTTTACAATCTC AGCAGATACATCCAAAAACACGGCCTATTTACAGATGAA TAGTTTGCGGGCCGAAGACACGGCTGTATACTATTGTTCT CGGTGGGGGGGCGATGGATTTTATGCGATGGATTACTGG GGCCAGGGCACCCTGGTAACCGTGTCAAGCGGCTCAACA TCCGGGTCCGGTAAGCCGGGCTCCGGCGAGGGGTCTACA AAGGGAGATATACAGATGACACAGTCCCCCAGTTCCCTG TCCGCCTCAGTGGGAGACCGAGTGACGATTACCTGTCGT GCCAGCCAGGACGTCAATACCGCCGTCGCTTGGTATCAG CAAAAACCAGGCAAGGCCCCGAAACTATTGATCTACAGT

		GCCTCTTTTCTGTACTCCGGGGTGCCGAGCAGATTTAGTG GCTCCAGGAGCGGAACCGATTTCACCCTAACCATTTCCA GTTTGCAGCCAGAGGATTTCGCGACCTATTACTGCCAGC AACACTACACCACACCGCCAACTTTCGGACAAGGAACCA AGGTTGAAATCAAAATTGAAGTTATGTATCCTCCTCCTTA CCTAGACAATGAGAAGAGCAATGGAACCATTATCCATGT GAAAGGGAAACACCTTTGTCCAAGTCCCCTATTTCCCGG GCCTTCGAAGCCCTTTTGGGTGCTGGTGGTGGTTGGTGGA GTCCTGGCTTGCTATAGCTTGCTAGTAACAGTAGCGTTTA TTATTTTCTGGGTGAAACGCGGCCGCAAGAAACTGCTCT ACATCTTTAAACAGCCGTTCATGAGGCCTGTGCAGACAA CGCAGGAAGAGGATGGCTGTAGTTGTCGGTTTCCGGAAG AGGAAGAGGGGGGCTGCGAGTTGCGTGTCAAATTTTCTC GGTCTGCCGACGCCCCCGCGTACCAGCAAGGGCAGAACC AGCTTTATAATGAGCTGAATCTTGGACGACGGGAGGAAT ATGACGTGCTTGACAAGAGGCGAGGTAGGGACCCTGAGA TGGGGGGAAAACCTCGGAGGAAAAACCCACAGGAAGGC CTGTATAACGAACTGCAGAAGGACAAGATGGCTGAAGCC TACTCTGAGATTGGAATGAAAGGGGAACGCAGACGCGGC AAGGGCCATGATGGCCTCTACCAAGGTCTAAGCACTGCC ACCAAGGACACCTATGACGCACTCCACATGCAAGCTCTA CCTCCCCGTTGATAA
MC00297: BB7.2_CD8 _KIR2DL1_ HER2 protein Sequence (VR297)	SEQ ID NO:36	MALPVTALLLPLALLLHAARPQVQLQQSGPELVKPGASVK MSCKASGYTFTSYHIQWVKQRPGQGLEWIGWIYPGDGSTQ YNEKFKGKTTLTADKSSSTAYMLLSSLTSEDSAIYFCAREGT YYAMDYWGQGTSVTVSSGGGGSGGGGSGGGGSDVLMTQ TPLSLPVSLGDQVSISCRSSQSIVHSNGNTYLEWYLQKPGQS PKLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGV YYCFQGSHVPRTFGGGTKLEIKTTTPAPRPPTPAPTIASQPLS LRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLS LVITLYCHRWCSNKKNAAVMDQESAGNRTANSEDSDEQDP QEVTYTQLNHCVFTQRKITRPSQRPKTPPTDIIVYTELPNAES RSKVVSCPRRKRGSGEGRGSLLTCGDVEENPGPMALPVTAL LLPLALLLHAARPEVQLVESGGGLLVQPGGSLRLSCAASGF NIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKGR FTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAM DYWGQGTLVTVSSGSTSGSGKPGSGEGSTKGDIQMTQSPSS LSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYS ASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHY TTPPTFGQGTKVEIKIEVMYPPPYLDNEKSNGTIIHVKGKHL CPSPLFPGPSKPFWVLVVVGGVLACYSLLVTVAFIIFWVKR GRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELR VKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGR DPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGER RRGKGHDGLYQGLSTATKDTYDALHMQALPPR
MC0421 HzBB7.2.2_ LIR1(52)_2 A_HER2	SEQ ID NO: 275	ATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCC TGCTTCTCCATGCGGCAAGGCCACAGGTGCAACTGGTTC AATCTGGTGCTGAGGTGAAAAAGCCCGGCGCATCCGTGA AAGTGAGCTGTAAGGCATCAGGGTACACCTTCACCAGCT ATCACATACAATGGGTCCGCCAGGCCCCCGGACAGAGGT

nucleotide sequence (VR421)		TGGAATGGATTGGGTGGATTTACCCGGGTGACGGCTCAA CCCAGTACAATGAGAAGTTCAAGGGCAGGGTGACTATCA CACGCGATACCTCCGCGAGCACAGCTTACATGGAGTTAT CTAGCCTGAGATCCGAAGATACGGCGGTGTATTACTGCG CGCGGGAAGGGACCTACTATGCCATGGACTATTGGGGAC AAGGGACCCTGGTTACCGTGAGTTCTGGGGGCGGGGGTT CCGGGGGAGGGGGATCTGGGGGTGGAGGGAGCGATGTG GTAATGACCCAGACACCTTTGTCTTTGAGTGTCACCCCCG GACAGCCGGCAAGTATATCCTGTAGATCATCCCAATCAA TCGTGCACTCCAACGGAAACACATACTTGGAATGGTATC TCCAGAAACCTGGACAGTCCCCACAGTTGCTCATCTACA AAGTGTCAAATCGCTTTTCAGGCGTGCCCGATCGTTTCAG CGGCTCAGGCTCCGGGACAGACTTTACATTGAAGATTAG CCGCGTAGAGGCAGAGGATGTGGGCGTTTACTATTGTTTT CAAGGGTCACACGTGCCACGCACATTCGGCGGCGGTACC AAGGTGGAAATTAAGCACCCCAGCGACCCGCTGGAGCTC GTTGTGTCCGGACCATCAGGGGGCCCGAGTAGCCCTACA ACCGGCCCCACTTCTACCAGTGGACCGGAAGATCAACCA CTTACACCAACGGGCAGCGACCCCCAGTCAGGCCTAGGG CGCCACCTGGGTGTGGTCATCGGGATACTGGTCGCTGTC ATCCTGCTTCTGCTCCTTCTCTTGCTCCTATTCCTAATCCT GCGCCACAGGAGACAGGGCAAGCACTGGACCAGCACCC AGCGGAAGGCCGACTTTCAGCACCCTGCCGGCGCCGTGG GCCCTGAGCCTACCGACAGGGGCCTGCAGTGGAGGAGCT CCCCAGCCGCCGATGCCCAGGAGGAGAATCTGTACGCCG CCGTGAAGCACACCCAGCCAGAGGACGGCGTGGAGATG GACACCCGCTCCCCACACGACGAGGACCCACAGGCCGTG ACCTACGCCGAGGTGAAGCACAGCCGCCCCAGACGCGAG ATGGCCAGCCCACCCAGCCCCCTGTCCGGCGAGTTCCTG GACACCAAGGACAGGCAGGCCGAGGAGGACCGGCAGAT GGACACCGAGGCCGCCGCCTCCGAGGCCCCCCAGGACGT GACCTACGCCCAGCTGCACTCCCTGACCCTGCGGAGAGA GGCCACCGAGCCCCCACCCAGCCAGGAGGGCCCCTCCCC CGCCGTGCCTAGCATCTACGCCACCCTGGCCATCCACCG GAGAAAGCGTGGATCCGGGGAAGGCCGAGGCTCCCTTCT AACATGTGGAGATGTCGAGGAAAACCCTGGCCCTATGGC GCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCCTGCTT CTCCATGCGGCGCGCCCAGACATCCAGATGACCCAATCC CCAAGCAGTCTCTCAGCCAGCGTGGGAGACAGGGTTACA ATCACGTGCCGCGCCAGCCAGGACGTCAACACCGCTGTG GCTTGGTATCAGCAAAAGCCCGGGAAGGCACCAAAGCTG CTTATTTATAGCGCCTCCTTCTTGTATTCTGGAGTGCCATC CAGGTTTTCCGGGTCACGTAGCGGGACTGACTTTACCCTC ACCATATCCAGCCTCCAGCCCGAGGATTTCGCCACCTATT ACTGTCAGCAACACTACACGACTCCACCGACTTTTGGAC AGGGCACTAAAGTGGAGATTAAGGGCAGCACGAGTGGG AGTGGAAAGCCCGGCAGCGGGGAGGGGTCTACCAAGGG AGAGGTCCAGCTGGTTGAATCCGGAGGCGGGCTTGTGCA ACCTGGAGGCTCCCTGAGGCTTAGTTGTGCCGCGTCAGG ATTCAACATTAAGGATACCTATATTCATTGGGTCCGACAA

		GCCCCGGGCAAGGGCTTGGAGTGGGTGGCCAGAATCTAT CCGACCAACGGATATACAAGGTACGCCGATTCTGTGAAA GGACGCTTCACCATCAGCGCGGACACATCCAAAAACACA GCCTATCTGCAGATGAACTCCCTTCGCGCCGAGGATACA GCCGTGTACTATTGTAGTCGGTGGGGAGGCGACGGCTTC TACGCGATGGACTATTGGGGACAAGGAACACTGGTGACT GTCAGTAGCACTACGACCCCAGCACCTAGACCTCCCACC CCAGCTCCAACTATAGCTTCCCAGCCATTGTCTCTCCGGC CAGAGGCGTGTCGACCAGCCGCTGGAGGGGCCGTTCATA CAAGAGGACTCGATTTCGCTTGCGATATCTACATATGGG CCCCTCTTGCCGGGACATGCGGTGTCCTGCTTCTAAGCTT GGTTATTACCCTCTATTGCAAAAGAGGACGAAAGAAACT GCTTTATATATTCAAGCAACCTTTCATGCGCCCCGTACAG ACCACGCAGGAGGAAGATGGGTGTAGCTGTCGCTTCCCT GAGGAAGAGGAAGGTGGATGCGAGTTGCGGGTGAAGTT CAGTCGATCCGCCGATGCGCCTGCCTATCAGCAAGGGCA GAACCAGCTTTATAACGAGTTAAACCTTGGCCGCCGGGA AGAGTATGACGTGTTGGACAAGCGTCGCGGGAGAGACCC TGAGATGGGCGGAAAACCAAGGAGAAAAAATCCACAGG AAGGCTTATATAACGAGTTGCAGAAAGACAAGATGGCCG AGGCATACTCCGAAATCGGAATGAAGGGCGAGCGACGG CGCGGCAAAGGCCACGATGGACTCTATCAGGGCTTAAGC ACCGCCACCAAAGACACCTACGATGCACTTCATATGCAG GCACTCCCACCTAGATGATAA
MC0421 HzBB7.2.2_ LIR1(52)_2 A_HER2 Protein Sequence (VR421)	SEQ ID NO: 276	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVK VSCKASGYTFTSYHIQWVRQAPGQRLEWIGWIYPGDGSTQ YNEKFKGRVTITRDTSASTAYMELSSLRSEDTAVYYCAREG TYYAMDYWGQGTLVTVSSGGGGSGGGGSGGGGSDVVMT QTPLSLSVTPGQPASISCRSSQSIVHSNGNTYLEWYLQKPGQ SPQLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVG VYYCFQGSHVPRTFGGGTKVEIKHPSDPLELVVSGPSGGPSS PTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGVVIGILVAVIL LLLLLLLLFLILRHRRQGKHWTSTQRKADFQHPAGAVGPEP TDRGLQWRSSPAADAQEENLYAAVKHTQPEDGVEMDTRSP HDEDPQAVTYAEVKHSRPRREMASPPSPLSGEFLDTKDRQA EEDRQMDTEAAASEAPQDVTYAQLHSLTLRREATEPPPSQE GPSPAVPSIYATLAIHRRKRGSGEGRGSLLTCGDVEENPGPM ALPVTALLLPLALLLHAARPDIQMTQSPSSLSASVGDRVTIT CRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVPSRFS GSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKVE IKGSTSGSGKPGSGEGSTKGEVQLVESGGGLVQPGGSLRLS CAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYA DSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGG DGFYAMDYWGQGTLVTVSSTTTPAPRPPTPAPTIASQPLSLR PEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLV ITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEE GGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVL DKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIG MKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR

MC00428 HzBB7.2.1_ LIR1(52)_ (IRESL)_H ER2 nucleotide sequence (VR428)	SEQ ID NO: 277	ATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCC TGCTTCTCCATGCGGCAAGGCCACAGGTGCAACTGGTTC AATCTGGTGCTGAGGTGAAAAAGCCCGGCAGCTCTGTGA AAGTGAGCTGTAAGGCATCAGGGTATACCTTCACCAGCT ATCACATACAATGGGTCCGCCAGGCCCCCGGACAGGGAT TGGAATGGATGGGGTGGATTTACCCGGGTGACGGCTCAA CCCAGTACAATGAGAAGTTCAAGGGCAGGACAACTATCA CAGCCGATAAGTCCACGAGCACAGCTTACATGGAGTTAT CTAGCCTGAGATCCGAAGATACGGCGGTGTATTACTGCG CGCGGGAAGGGACCTACTATGCCATGGACTATTGGGGAC AAGGGACCCTGGTTACCGTGAGTTCTGGGGGCGGGGGTT CCGGGGGAGGGGGATCTGGGGGTGGAGGGAGCGATGTG GTAATGACCCAGACACCTTTGTCTTTGAGTGTCACCCCCG GACAGCCGGCAAGTATATCCTGTAGATCATCCCAATCAA TCGTGCACTCCAACGGAAACACATACTTGGAATGGTATC TCCAGAAACCTGGACAGTCCCCACAGTTGCTCATCTACA AAGTGTCAAATCGCTTTTCAGGCGTGCCCGATCGTTTCAG CGGCTCAGGCTCCGGGACAGACTTTACATTGAAGATTAG CCGCGTAGAGGCAGAGGATGTGGGCGTTTACTATTGTTTT CAAGGGTCACACGTGCCACGCACATTCGGCGGCGGTACC AAGGTGGAAATTAAGCACCCCAGCGACCCGCTGGAGCTC GTTGTGTCCGGACCATCAGGGGGCCCGAGTAGCCCTACA ACCGGCCCCACTTCTACCAGTGGACCGGAAGATCAACCA CTTACACCAACGGGCAGCGACCCCCAGTCAGGCCTAGGG CGCCACCTGGGTGTGGTCATCGGGATACTGGTCGCTGTC ATCCTGCTTCTGCTCCTTCTCTTGCTCCTATTCCTAATCCT GCGCCACAGGAGACAGGGCAAGCACTGGACCAGCACCC AGCGGAAGGCCGACTTTCAGCACCCTGCCGGCGCCGTGG GCCCTGAGCCTACCGACAGGGGCCTGCAGTGGAGGAGCT CCCCAGCCGCCGATGCCCAGGAGGAGAATCTGTACGCCG CCGTGAAGCACACCCAGCCAGAGGACGGCGTGGAGATG GACACCCGCTCCCCACACGACGAGGACCCACAGGCCGTG ACCTACGCCGAGGTGAAGCACAGCCGCCCCAGACGCGAG ATGGCCAGCCCACCCAGCCCCCTGTCCGGCGAGTTCCTG GACACCAAGGACAGGCAGGCCGAGGAGGACCGGCAGAT GGACACCGAGGCCGCCGCCTCCGAGGCCCCCCAGGACGT GACCTACGCCCAGCTGCACTCCCTGACCCTGCGGAGAGA GGCCACCGAGCCCCCACCCAGCCAGGAGGGCCCCTCCCC CGCCGTGCCTAGCATCTACGCCACCCTGGCCATCCACTGA TAACCCCCCCCCCTAACGTTACTGGCCGAAGCCGCTTGG AATAAGGCCGGTGTGCGTTTGTCTATATGTTATTTTCCAC CATATTGCCGTCTTTTGGCAATGTGAGGGCCCGGAAACCT GGCCCTGTCTTCTTGACGAGCATTCCTAGGGGTCTTTCCC CTCTCGCCAAAGGAATGCAAGGTCTGTTGAATGTCGTGA AGGAAGCAGTTCCTCTGGAAGCTTCTTGAAGACAAACAA CGTCTGTAGCGACCCTTTGCAGGCAGCGGAACCCCCCAC CTGGCGACAGGTGCCTCTGCGGCCAAAAGCCACGTGTAT AAGATACACCTGCAAAGGCGGCACAACCCCAGTGCCACG TTGTGAGTTGGATAGTTGTGGAAAGAGTCAAATGGCTCT CCTCAAGCGTATTCAACAAGGGGCTGAAGGATGCCCAGA

		AGGTACCCCATTGTATGGGATCTGATCTGGGGCCTCGGT GCACATGCTTTACATGTGTTTAGTCGAGGTTAAAAAAAC GTCTAGGCCCCCCGAACCACGGGGACGTGGTTTTCCTTTG AAAAACACGATGATAATATGATGGCGCTGCCAGTCACTG CATTGTTATTGCCTCTGGCCCTGCTTCTCCATGCGGCGCG CCCAGACATCCAGATGACCCAATCCCCAAGCAGTCTCTC AGCCAGCGTGGGAGACAGGGTTACAATCACGTGCCGCGC CAGCCAGGACGTCAACACCGCTGTGGCTTGGTATCAGCA AAAGCCCGGGAAGGCACCAAAGCTGCTTATTTATAGCGC CTCCTTCTTGTATTCTGGAGTGCCATCCAGGTTTTCCGGG TCACGTAGCGGGACTGACTTTACCCTCACCATATCCAGCC TCCAGCCCGAGGATTTCGCCACCTATTACTGTCAGCAACA CTACACGACTCCACCGACTTTTGGACAGGGCACTAAAGT GGAGATTAAGGGCAGCACGAGTGGGAGTGGAAAGCCCG GCAGCGGGGAGGGGTCTACCAAGGGAGAGGTCCAGCTG GTTGAATCCGGAGGCGGGCTTGTGCAACCTGGAGGCTCC CTGAGGCTTAGTTGTGCCGCGTCAGGATTCAACATTAAG GATACCTATATTCATTGGGTCCGACAAGCCCCGGGCAAG GGCTTGGAGTGGGTGGCCAGAATCTATCCGACCAACGGA TATACAAGGTACGCCGATTCTGTGAAAGGACGCTTCACC ATCAGCGCGGACACATCCAAAAACACAGCCTATCTGCAG ATGAACTCCCTTCGCGCCGAGGATACAGCCGTGTACTATT GTAGTCGGTGGGGAGGCGACGGCTTCTACGCGATGGACT ATTGGGGACAAGGAACACTGGTGACTGTCAGTAGCACTA CGACCCCAGCACCTAGACCTCCCACCCCAGCTCCAACTA TAGCTTCCCAGCCATTGTCTCTCCGGCCAGAGGCGTGTCG ACCAGCCGCTGGAGGGGCCGTTCATACAAGAGGACTCGA TTTCGCTTGCGATATCTACATATGGGCCCCTCTTGCCGGG ACATGCGGTGTCCTGCTTCTAAGCTTGGTTATTACCCTCT ATTGCAAAAGAGGACGAAAGAAACTGCTTTATATATTCA AGCAACCTTTCATGCGCCCCGTACAGACCACGCAGGAGG AAGATGGGTGTAGCTGTCGCTTCCCTGAGGAAGAGGAAG GTGGATGCGAGTTGCGGGTGAAGTTCAGTCGATCCGCCG ATGCGCCTGCCTATCAGCAAGGGCAGAACCAGCTTTATA ACGAGTTAAACCTTGGCCGCCGGGAAGAGTATGACGTGT TGGACAAGCGTCGCGGGAGAGACCCTGAGATGGGCGGA AAACCAAGGAGAAAAAATCCACAGGAAGGCTTATATAA CGAGTTGCAGAAAGACAAGATGGCCGAGGCATACTCCGA AATCGGAATGAAGGGCGAGCGACGGCGCGGCAAAGGCC ACGATGGACTCTATCAGGGCTTAAGCACCGCCACCAAAG ACACCTACGATGCACTTCATATGCAGGCACTCCCACCTA GATGATAA
MC0428 HzBB7.2.1_ LIR1(52)_ (IRESL)_H ER2 Protein sequence (VR428)	SEQ ID NO: 278	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGSSVK VSCKASGYTFTSYHIQWVRQAPGQGLEWMGWIYPGDGSTQ YNEKFKGRTTITADKSTSTAYMELSSLRSEDTAVYYCAREG TYYAMDYWGQGTLVTVSSGGGGSGGGGSGGGGSDVVMT QTPLSLSVTPGQPASISCRSSQSIVHSNGNTYLEWYLQKPGQ SPQLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVG VYYCFQGSHVPRTFGGGTKVEIKHPSDPLELVVSGPSGGPSS

		PTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGVVIGILVAVIL LLLLLLLLFLILRHRRQGKHWTSTQRKADFQHPAGAVGPEP TDRGLQWRSSPAADAQEENLYAAVKHTQPEDGVEMDTRSP HDEDPQAVTYAEVKHSRPRREMASPPSPLSGEFLDTKDRQA EEDRQMDTEAAASEAPQDVTYAQLHSLTLRREATEPPPSQE GPSPAVPSIYATLAIH* MALPVTALLLPLALLLHAARPDIQMTQSPSSLSASVGDRVTI TCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVPSRF SGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKV EIKGSTSGSGKPGSGEGSTKGEVQLVESGGGLVQPGGSLRLS CAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYA DSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGG DGFYAMDYWGQGTLVTVSSTTTPAPRPPTPAPTIASQPLSLR PEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLV ITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEE GGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVL DKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIG MKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR*
MC0447 SN66E3.2(LH)_LIR1(30)_(IRESL)_HER2 nucleotide Sequence (VR447)	SEQ ID NO:279	ATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCC TGCTTCTCCATGCGGCAAGGCCAGATATAGTGATGACAC AGTCCCCCGACTCCCTGGCTGTCTCACTGGGAGAACGAG CGACGATTAGTTGTAAGTCTAGCCAGAGCGTCCTGTATTC AAGCAATAACAAGAATTACCTCGCCTGGTATCAGCAAAA GCCGGGACAGCCACCCAAACTGTTGATTTACTGGGCCAG CACGAGAGAGAGCGGAGTGCCCGACCGCTTCAGCGGATC CGGGTCAGGCACAGATTTTACCCTGACTATTAGCTCCCTT CAAGCGGAAGATGTCGCCGTCTACTATTGCCAGCAATAT TACGGAACTCCATTCACATTCGGCGGTGGGACCAAAGTA GAGATAAAGGGTGGCGGGGGATCCGGCGGTGGCGGTAG CGGGGGAGGCGGGTCCCAAGTGCAACTAGTCCAATCAGG TGCCGAAGTCAAGAAACCAGGTGCATCCGTGAAAGTGTC TTGCAAAGCCAGTGGCTACACTTTTACTGACTACTATCTG CACTGGGTGCGTCAAGCACCCGGCCAGGGGCTTGAATGG ATGGGCTGGATTAACCCTTATACTGGAGGGACAAATTAC GCTCAGAAGTTCCAGGGACGCGTTACAATGACCCGAGAC ACCAGCATCAGCACAGCGTACATGGAGTTAAGTGGGCTG ACTTCCGACGATACCGCCGTGTATTACTGCGCTCGGGCA GGGGCCTCTTACTATGATTTTTGGTCCGGTTGGGTCTTCG ATTACTGGGGGCAGGGAACCCTGGTGACAGTGTCCTCAG GCCCCACTTCTACCAGTGGACCGGAAGATCAACCACTTA CACCAACGGGCAGCGACCCCCAGTCAGGCCTAGGGCGCC ACCTGGGTGTGGTCATCGGGATACTGGTCGCTGTCATCCT GCTTCTGCTCCTTCTCTTGCTCCTATTCCTAATCCTGCGCC ACAGGAGACAGGGCAAGCACTGGACCAGCACCCAGCGG AAGGCCGACTTTCAGCACCCTGCCGGCGCCGTGGGCCCT GAGCCTACCGACAGGGGCCTGCAGTGGAGGAGCTCCCCA GCCGCCGATGCCCAGGAGGAGAATCTGTACGCCGCCGTG

		AAGCACACCCAGCCAGAGGACGGCGTGGAGATGGACAC CCGCTCCCCACACGACGAGGACCCACAGGCCGTGACCTA CGCCGAGGTGAAGCACAGCCGCCCCAGACGCGAGATGG CCAGCCCACCCAGCCCCCTGTCCGGCGAGTTCCTGGACA CCAAGGACAGGCAGGCCGAGGAGGACCGGCAGATGGAC ACCGAGGCCGCCGCCTCCGAGGCCCCCCAGGACGTGACC TACGCCCAGCTGCACTCCCTGACCCTGCGGAGAGAGGCC ACCGAGCCCCCACCCAGCCAGGAGGGCCCCTCCCCCGCC GTGCCTAGCATCTACGCCACCCTGGCCATCCACTGATAAC CCCCCCCCCTAACGTTACTGGCCGAAGCCGCTTGGAATA AGGCCGGTGTGCGTTTGTCTATATGTTATTTTCCACCATA TTGCCGTCTTTTGGCAATGTGAGGGCCCGGAAACCTGGC CCTGTCTTCTTGACGAGCATTCCTAGGGGTCTTTCCCCTC TCGCCAAAGGAATGCAAGGTCTGTTGAATGTCGTGAAGG AAGCAGTTCCTCTGGAAGCTTCTTGAAGACAAACAACGT CTGTAGCGACCCTTTGCAGGCAGCGGAACCCCCCACCTG GCGACAGGTGCCTCTGCGGCCAAAAGCCACGTGTATAAG ATACACCTGCAAAGGCGGCACAACCCCAGTGCCACGTTG TGAGTTGGATAGTTGTGGAAAGAGTCAAATGGCTCTCCT CAAGCGTATTCAACAAGGGGCTGAAGGATGCCCAGAAG GTACCCCATTGTATGGGATCTGATCTGGGGCCTCGGTGCA CATGCTTTACATGTGTTTAGTCGAGGTTAAAAAAACGTCT AGGCCCCCCGAACCACGGGGACGTGGTTTTCCTTTGAAA AACACGATGATAATATGATGGCGCTGCCAGTCACTGCAT TGTTATTGCCTCTGGCCCTGCTTCTCCATGCGGCGCGCCC AGACATCCAGATGACCCAATCCCCAAGCAGTCTCTCAGC CAGCGTGGGAGACAGGGTTACAATCACGTGCCGCGCCAG CCAGGACGTCAACACCGCTGTGGCTTGGTATCAGCAAAA GCCCGGGAAGGCACCAAAGCTGCTTATTTATAGCGCCTC CTTCTTGTATTCTGGAGTGCCATCCAGGTTTTCCGGGTCA CGTAGCGGGACTGACTTTACCCTCACCATATCCAGCCTCC AGCCCGAGGATTTCGCCACCTATTACTGTCAGCAACACT ACACGACTCCACCGACTTTTGGACAGGGCACTAAAGTGG AGATTAAGGGCAGCACGAGTGGGAGTGGAAAGCCCGGC AGCGGGGAGGGGTCTACCAAGGGAGAGGTCCAGCTGGTT GAATCCGGAGGCGGGCTTGTGCAACCTGGAGGCTCCCTG AGGCTTAGTTGTGCCGCGTCAGGATTCAACATTAAGGAT ACCTATATTCATTGGGTCCGACAAGCCCCGGGCAAGGGC TTGGAGTGGGTGGCCAGAATCTATCCGACCAACGGATAT ACAAGGTACGCCGATTCTGTGAAAGGACGCTTCACCATC AGCGCGGACACATCCAAAAACACAGCCTATCTGCAGATG AACTCCCTTCGCGCCGAGGATACAGCCGTGTACTATTGTA GTCGGTGGGGAGGCGACGGCTTCTACGCGATGGACTATT GGGGACAAGGAACACTGGTGACTGTCAGTAGCACTACGA CCCCAGCACCTAGACCTCCCACCCCAGCTCCAACTATAG CTTCCCAGCCATTGTCTCTCCGGCCAGAGGCGTGTCGACC AGCCGCTGGAGGGGCCGTTCATACAAGAGGACTCGATTT

		CGCTTGCGATATCTACATATGGGCCCCTCTTGCCGGGACA TGCGGTGTCCTGCTTCTAAGCTTGGTTATTACCCTCTATT GCAAAAGAGGACGAAAGAAACTGCTTTATATATTCAAGC AACCTTTCATGCGCCCCGTACAGACCACGCAGGAGGAAG ATGGGTGTAGCTGTCGCTTCCCTGAGGAAGAGGAAGGTG GATGCGAGTTGCGGGTGAAGTTCAGTCGATCCGCCGATG CGCCTGCCTATCAGCAAGGGCAGAACCAGCTTTATAACG AGTTAAACCTTGGCCGCCGGGAAGAGTATGACGTGTTGG ACAAGCGTCGCGGGAGAGACCCTGAGATGGGCGGAAAA CCAAGGAGAAAAAATCCACAGGAAGGCTTATATAACGA GTTGCAGAAAGACAAGATGGCCGAGGCATACTCCGAAAT CGGAATGAAGGGCGAGCGACGGCGCGGCAAAGGCCACG ATGGACTCTATCAGGGCTTAAGCACCGCCACCAAAGACA CCTACGATGCACTTCATATGCAGGCACTCCCACCTAGATG ATAA
MC0447 SN66E3.2(LH)_LIR1(30)_(IRESL)_HER2 Protein Sequence (VR447)	SEQ ID NO: 280	MALPVTALLLPLALLLHAARPDIVMTQSPDSLAVSLGERATI SCKSSQSVLYSSNNKNYLAWYQQKPGQPPKLLIYWASTRES GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYGTPFTF GGGTKVEIKGGGGSGGGGSGGGGSQVQLVQSGAEVKKPG ASVKVSCKASGYTFTDYYLHWVRQAPGQGLEWMGWINPY TGGTNYAQKFQGRVTMTRDTSISTAYMELSGLTSDDTAVY YCARAGASYYDFWSGWVFDYWGQGTLVTVSSGPTSTSGPE DQPLTPTGSDPQSGLGRHLGVVIGILVAVILLLLLLLLLFLIL RHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSP AADAQEENLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTY AEVKHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTEA AASEAPQDVTYAQLHSLTLRREATEPPPSQEGPSPAVPSIYA TLAIH* MALPVTALLLPLALLLHAARPDIQMTQSPSSLSASVGDRVTI TCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVPSRF SGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKV EIKGSTSGSGKPGSGEGSTKGEVQLVESGGGLVQPGGSLRLS CAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYA DSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGG DGFYAMDYWGQGTLVTVSSTTTPAPRPPTPAPTIASQPLSLR PEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLV ITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEE GGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVL DKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIG MKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR*
MC0449 SN66E3.3(LH)_LIR1(26)_(IRESL)_HER2	SEQ ID NO: 281	ATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCC TGCTTCTCCATGCGGCAAGGCCAGATATAGTGATGACAC AGTCCCCCGACTCCCTGGCTGTCTCACTGGGAGAACGAG CGACGATTAGTTGTAAGTCTAGCCAGAGCGTCCTGTATTC AAGCAATAACAAGAATTACCTCGCCTGGTATCAGCAAAA GCCGGGACAGCCACCCAAACTGTTGATTTACTGGGCCAG CACGAGAGAGAGCGGAGTGCCCGACCGCTTCAGCGGATC

Nucleotide Sequence (VR449)		CGGGTCAGGCACAGATTTTACCCTGACTATTAGCTCCCTT CAAGCGGAAGATGTCGCCGTCTACTATTGCCAGCAATAT TACGGAACTCCATTCACATTCGGCGGTGGGACCAAAGTA GAGATAAAGGGTGGCGGGGGATCCGGCGGTGGCGGTAG CGGGGGAGGCGGGTCCCAAGTGCAACTAGTCCAATCAGG TGCCGAAGTCAAGAAACCAGGTGCATCCGTGAAAGTGTC TTGCAAAGCCAGTGGCTACACTTTTACTGACTACTATCTG CACTGGGTGCGTCAAGCACCCGGCCAGGGGCTTGAATGG ATGGGCTGGATTAACCCTTATACTGGAGGGACAAATTAC GCTCAGAAGTTCCAGGGACGCGTTACAATGACCCGAGAC ACCAGCATCAGCACAGCGTACATGGAGTTAAGTAGGCTG AGGTCCGAAGATACCGCCGTGTATTACTGCGCTCGGGCA GGGGCCTCTTACTATGATTTTTGGTCCGGTTGGGTCTTCG ATTACTGGGGGCAGGGAACCCTGGTGACAGTGTCCTCAA CCAGTGGACCGGAAGATCAACCACTTACACCAACGGGCA GCGACCCCCAGTCAGGCCTAGGGCGCCACCTGGGTGTGG TCATCGGGATACTGGTCGCTGTCATCCTGCTTCTGCTCCT TCTCTTGCTCCTATTCCTAATCCTGCGCCACAGGAGACAG GGCAAGCACTGGACCAGCACCCAGCGGAAGGCCGACTTT CAGCACCCTGCCGGCGCCGTGGGCCCTGAGCCTACCGAC AGGGGCCTGCAGTGGAGGAGCTCCCCAGCCGCCGATGCC CAGGAGGAGAATCTGTACGCCGCCGTGAAGCACACCCAG CCAGAGGACGGCGTGGAGATGGACACCCGCTCCCCACAC GACGAGGACCCACAGGCCGTGACCTACGCCGAGGTGAA GCACAGCCGCCCCAGACGCGAGATGGCCAGCCCACCCAG CCCCCTGTCCGGCGAGTTCCTGGACACCAAGGACAGGCA GGCCGAGGAGGACCGGCAGATGGACACCGAGGCCGCCG CCTCCGAGGCCCCCCAGGACGTGACCTACGCCCAGCTGC ACTCCCTGACCCTGCGGAGAGAGGCCACCGAGCCCCCAC CCAGCCAGGAGGGCCCCTCCCCCGCCGTGCCTAGCATCT ACGCCACCCTGGCCATCCACTGATAACCCCCCCCCCTAAC GTTACTGGCCGAAGCCGCTTGGAATAAGGCCGGTGTGCG TTTGTCTATATGTTATTTTCCACCATATTGCCGTCTTTTGG CAATGTGAGGGCCCGGAAACCTGGCCCTGTCTTCTTGAC GAGCATTCCTAGGGGTCTTTCCCCTCTCGCCAAAGGAATG CAAGGTCTGTTGAATGTCGTGAAGGAAGCAGTTCCTCTG GAAGCTTCTTGAAGACAAACAACGTCTGTAGCGACCCTT TGCAGGCAGCGGAACCCCCCACCTGGCGACAGGTGCCTC TGCGGCCAAAAGCCACGTGTATAAGATACACCTGCAAAG GCGGCACAACCCCAGTGCCACGTTGTGAGTTGGATAGTT GTGGAAAGAGTCAAATGGCTCTCCTCAAGCGTATTCAAC AAGGGGCTGAAGGATGCCCAGAAGGTACCCCATTGTATG GGATCTGATCTGGGGCCTCGGTGCACATGCTTTACATGTG TTTAGTCGAGGTTAAAAAAACGTCTAGGCCCCCCGAACC ACGGGGACGTGGTTTTCCTTTGAAAAACACGATGATAAT ATGATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGG CCCTGCTTCTCCATGCGGCGCGCCCAGACATCCAGATGA

		CCCAATCCCCAAGCAGTCTCTCAGCCAGCGTGGGAGACA GGGTTACAATCACGTGCCGCGCCAGCCAGGACGTCAACA CCGCTGTGGCTTGGTATCAGCAAAAGCCCGGGAAGGCAC CAAAGCTGCTTATTTATAGCGCCTCCTTCTTGTATTCTGG AGTGCCATCCAGGTTTTCCGGGTCACGTAGCGGGACTGA CTTTACCCTCACCATATCCAGCCTCCAGCCCGAGGATTTC GCCACCTATTACTGTCAGCAACACTACACGACTCCACCG ACTTTTGGACAGGGCACTAAAGTGGAGATTAAGGGCAGC ACGAGTGGGAGTGGAAAGCCCGGCAGCGGGGAGGGGTC TACCAAGGGAGAGGTCCAGCTGGTTGAATCCGGAGGCGG GCTTGTGCAACCTGGAGGCTCCCTGAGGCTTAGTTGTGCC GCGTCAGGATTCAACATTAAGGATACCTATATTCATTGG GTCCGACAAGCCCCGGGCAAGGGCTTGGAGTGGGTGGCC AGAATCTATCCGACCAACGGATATACAAGGTACGCCGAT TCTGTGAAAGGACGCTTCACCATCAGCGCGGACACATCC AAAAACACAGCCTATCTGCAGATGAACTCCCTTCGCGCC GAGGATACAGCCGTGTACTATTGTAGTCGGTGGGGAGGC GACGGCTTCTACGCGATGGACTATTGGGGACAAGGAACA CTGGTGACTGTCAGTAGCACTACGACCCCAGCACCTAGA CCTCCCACCCCAGCTCCAACTATAGCTTCCCAGCCATTGT CTCTCCGGCCAGAGGCGTGTCGACCAGCCGCTGGAGGGG CCGTTCATACAAGAGGACTCGATTTCGCTTGCGATATCTA CATATGGGCCCCTCTTGCCGGGACATGCGGTGTCCTGCTT CTAAGCTTGGTTATTACCCTCTATTGCAAAAGAGGACGA AAGAAACTGCTTTATATATTCAAGCAACCTTTCATGCGCC CCGTACAGACCACGCAGGAGGAAGATGGGTGTAGCTGTC GCTTCCCTGAGGAAGAGGAAGGTGGATGCGAGTTGCGGG TGAAGTTCAGTCGATCCGCCGATGCGCCTGCCTATCAGC AAGGGCAGAACCAGCTTTATAACGAGTTAAACCTTGGCC GCCGGGAAGAGTATGACGTGTTGGACAAGCGTCGCGGGA GAGACCCTGAGATGGGCGGAAAACCAAGGAGAAAAAAT CCACAGGAAGGCTTATATAACGAGTTGCAGAAAGACAAG ATGGCCGAGGCATACTCCGAAATCGGAATGAAGGGCGA GCGACGGCGCGGCAAAGGCCACGATGGACTCTATCAGGG CTTAAGCACCGCCACCAAAGACACCTACGATGCACTTCA TATGCAGGCACTCCCACCTAGATGATAA
MC0449 SN66E3.3(LH)_LIR1(26)_(IRESL)_HER2 Protein Sequence (VR449)	SEQ ID NO: 282	MALPVTALLLPLALLLHAARPDIVMTQSPDSLAVSLGERATI SCKSSQSVLYSSNNKNYLAWYQQKPGQPPKLLIYWASTRES GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYGTPFTF GGGTKVEIKGGGGSGGGGSGGGGSQVQLVQSGAEVKKPG ASVKVSCKASGYTFTDYYLHWVRQAPGQGLEWMGWINPY TGGTNYAQKFQGRVTMTRDTSISTAYMELSRLRSEDTAVY YCARAGASYYDFWSGWVFDYWGQGTLVTVSSTSGPEDQP LTPTGSDPQSGLGRHLGVVIGILVAVILLLLLLLLLFLILRHR RQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAA DAQEENLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAE VKHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTEAA

		ASEAPQDVTYAQLHSLTLRREATEPPPSQEGPSPAVPSIYAT LAIH* MALPVTALLLPLALLLHAARPDIQMTQSPSSLSASVGDRVTI TCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVPSRF SGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKV EIKGSTSGSGKPGSGEGSTKGEVQLVESGGGLVQPGGSLRLS CAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYA DSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGG DGFYAMDYWGQGTLVTVSSTTTPAPRPPTPAPTIASQPLSLR PEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLV ITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEE GGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVL DKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIG MKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR*
MC0515-HzBB7.2(2)_LIR1(30)_2A_HER2 Nucleotide Sequence (VR515)	SEQ ID NO:321	ATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCC TGCTTCTCCATGCGGCAAGGCCACAGGTGCAACTGGTTC AATCTGGTGCTGAGGTGAAAAAGCCCGGCGCATCCGTGA AAGTGAGCTGTAAGGCATCAGGGTACACCTTCACCAGCT ATCACATACAATGGGTCCGCCAGGCCCCCGGACAGAGGT TGGAATGGATTGGGTGGATTTACCCGGGTGACGGCTCAA CCCAGTACAATGAGAAGTTCAAGGGCAGGGTGACTATCA CACGCGATACCTCCGCGAGCACAGCTTACATGGAGTTAT CTAGCCTGAGATCCGAAGATACGGCGGTGTATTACTGCG CGCGGGAAGGGACCTACTATGCCATGGACTATTGGGGAC AAGGGACCCTGGTTACCGTGAGTTCTGGGGGCGGGGGTT CCGGGGGAGGGGGATCTGGGGGTGGAGGGAGCGATGTG GTAATGACCCAGACACCTTTGTCTTTGAGTGTCACCCCCG GACAGCCGGCAAGTATATCCTGTAGATCATCCCAATCAA TCGTGCACTCCAACGGAAACACATACTTGGAATGGTATC TCCAGAAACCTGGACAGTCCCCACAGTTGCTCATCTACA AAGTGTCAAATCGCTTTTCAGGCGTGCCCGATCGTTTCAG CGGCTCAGGCTCCGGGACAGACTTTACATTGAAGATTAG CCGCGTAGAGGCAGAGGATGTGGGCGTTTACTATTGTTTT CAAGGGTCACACGTGCCACGCACATTCGGCGGCGGTACC AAGGTGGAAATTAAGGGCCCCACTTCTACCAGTGGACCG GAAGATCAACCACTTACACCAACGGGCAGCGACCCCCAG TCAGGCCTAGGGCGCCACCTGGGTGTGGTCATCGGGATA CTGGTCGCTGTCATCCTGCTTCTGCTCCTTCTCTTGCTCCT ATTCCTAATCCTGCGCCACAGGAGACAGGGCAAGCACTG GACCAGCACCCAGCGGAAGGCCGACTTTCAGCACCCTGC CGGCGCCGTGGGCCCTGAGCCTACCGACAGGGGCCTGCA GTGGAGGAGCTCCCCAGCCGCCGATGCCCAGGAGGAGA ATCTGTACGCCGCCGTGAAGCACACCCAGCCAGAGGACG GCGTGGAGATGGACACCCGCTCCCCACACGACGAGGACC CACAGGCCGTGACCTACGCCGAGGTGAAGCACAGCCGCC CCAGACGCGAGATGGCCAGCCCACCCAGCCCCCTGTCCG GCGAGTTCCTGGACACCAAGGACAGGCAGGCCGAGGAG

		GACCGGCAGATGGACACCGAGGCCGCCGCCTCCGAGGCC CCCCAGGACGTGACCTACGCCCAGCTGCACTCCCTGACC CTGCGGAGAGAGGCCACCGAGCCCCCACCCAGCCAGGA GGGCCCCTCCCCCGCCGTGCCTAGCATCTACGCCACCCTG GCCATCCACGGATCCGGGGAAGGCCGAGGCTCCCTTCTA ACATGTGGAGATGTCGAGGAAAACCCTGGCCCTATGGCG CTGCCAGTCACTGCATTGTTATTGCCTCTGGCCCTGCTTC TCCATGCGGCGCGCCCAGACATCCAGATGACCCAATCCC CAAGCAGTCTCTCAGCCAGCGTGGGAGACAGGGTTACAA TCACGTGCCGCGCCAGCCAGGACGTCAACACCGCTGTGG CTTGGTATCAGCAAAAGCCCGGGAAGGCACCAAAGCTGC TTATTTATAGCGCCTCCTTCTTGTATTCTGGAGTGCCATCC AGGTTTTCCGGGTCACGTAGCGGGACTGACTTTACCCTCA CCATATCCAGCCTCCAGCCCGAGGATTTCGCCACCTATTA CTGTCAGCAACACTACACGACTCCACCGACTTTTGGACA GGGCACTAAAGTGGAGATTAAGGGCAGCACGAGTGGGA GTGGAAAGCCCGGCAGCGGGGAGGGGTCTACCAAGGGA GAGGTCCAGCTGGTTGAATCCGGAGGCGGGCTTGTGCAA CCTGGAGGCTCCCTGAGGCTTAGTTGTGCCGCGTCAGGA TTCAACATTAAGGATACCTATATTCATTGGGTCCGACAAG CCCCGGGCAAGGGCTTGGAGTGGGTGGCCAGAATCTATC CGACCAACGGATATACAAGGTACGCCGATTCTGTGAAAG GACGCTTCACCATCAGCGCGGACACATCCAAAAACACAG CCTATCTGCAGATGAACTCCCTTCGCGCCGAGGATACAG CCGTGTACTATTGTAGTCGGTGGGGAGGCGACGGCTTCT ACGCGATGGACTATTGGGGACAAGGAACACTGGTGACTG TCAGTAGCACTACGACCCCAGCACCTAGACCTCCCACCC CAGCTCCAACTATAGCTTCCCAGCCATTGTCTCTCCGGCC AGAGGCGTGTCGACCAGCCGCTGGAGGGGCCGTTCATAC AAGAGGACTCGATTTCGCTTGCGATATCTACATATGGGC CCCTCTTGCCGGGACATGCGGTGTCCTGCTTCTAAGCTTG GTTATTACCCTCTATTGCAAAAGAGGACGAAAGAAACTG CTTTATATATTCAAGCAACCTTTCATGCGCCCCGTACAGA CCACGCAGGAGGAAGATGGGTGTAGCTGTCGCTTCCCTG AGGAAGAGGAAGGTGGATGCGAGTTGCGGGTGAAGTTC AGTCGATCCGCCGATGCGCCTGCCTATCAGCAAGGGCAG AACCAGCTTTATAACGAGTTAAACCTTGGCCGCCGGGAA GAGTATGACGTGTTGGACAAGCGTCGCGGGAGAGACCCT GAGATGGGCGGAAAACCAAGGAGAAAAAATCCACAGGA AGGCTTATATAACGAGTTGCAGAAAGACAAGATGGCCGA GGCATACTCCGAAATCGGAATGAAGGGCGAGCGACGGC GCGGCAAAGGCCACGATGGACTCTATCAGGGCTTAAGCA CCGCCACCAAAGACACCTACGATGCACTTCATATGCAGG CACTCCCACCTAGATGATAA
MC0515 HzBB7.2(2) _LIR1(30)_	SEQ ID NO:322	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVK VSCKASGYTFTSYHIQWVRQAPGQRLEWIGWIYPGDGSTQ YNEKFKGRVTITRDTSASTAYMELSSLRSEDTAVYYCAREG

2A_HER2 Protein Sequence (VR515)		TYYAMDYWGQGTLVTVSSGGGGSGGGGSGGGGSDVVMT QTPLSLSVTPGQPASISCRSSQSIVHSNGNTYLEWYLQKPGQ SPQLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVG VYYCFQGSHVPRTFGGGTKVEIKGPTSTSGPEDQPLTPTGSD PQSGLGRHLGVVIGILVAVILLLLLLLLLFLILRHRRQGKHW TSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEENL YAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPRR EMASPPSPLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDVT YAQLHSLTLRREATEPPPSQEGPSPAVPSIYATLAIHGSGEGR GSLLTCGDVEENPGPMALPVTALLLPLALLLHAARPDIQMT QSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPK LLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYC QQHYTTPPTFGQGTKVEIKGSTSGSGKPGSGEGSTKGEVQL VESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGL EWVARIYPTNGYTRYADSVKGRFTISADTSKNTAYLQMNS LRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSSTTTP APRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDI YIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRP VQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYQQGQ NQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQE GLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLST ATKDTYDALHMQALPPR
MC0516-SN66E3.2(LH)_LIR1(30)_2A_HER2 Nucleotide Sequence (VR516)	SEQ ID NO:323	ATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCC TGCTTCTCCATGCGGCAAGGCCAGATATAGTGATGACAC AGTCCCCCGACTCCCTGGCTGTCTCACTGGGAGAACGAG CGACGATTAGTTGTAAGTCTAGCCAGAGCGTCCTGTATTC AAGCAATAACAAGAATTACCTCGCCTGGTATCAGCAAAA GCCGGGACAGCCACCCAAACTGTTGATTTACTGGGCCAG CACGAGAGAGAGCGGAGTGCCCGACCGCTTCAGCGGATC CGGGTCAGGCACAGATTTTACCCTGACTATTAGCTCCCTT CAAGCGGAAGATGTCGCCGTCTACTATTGCCAGCAATAT TACGGAACTCCATTCACATTCGGCGGTGGGACCAAAGTA GAGATAAAGGGTGGCGGGGGATCCGGCGGTGGCGGTAG CGGGGGAGGCGGGTCCCAAGTGCAACTAGTCCAATCAGG TGCCGAAGTCAAGAAACCAGGTGCATCCGTGAAAGTGTC TTGCAAAGCCAGTGGCTACACTTTTACTGACTACTATCTG CACTGGGTGCGTCAAGCACCCGGCCAGGGGCTTGAATGG ATGGGCTGGATTAACCCTTATACTGGAGGGACAAATTAC GCTCAGAAGTTCCAGGGACGCGTTACAATGACCCGAGAC ACCAGCATCAGCACAGCGTACATGGAGTTAAGTGGGCTG ACTTCCGACGATACCGCCGTGTATTACTGCGCTCGGGCA GGGGCCTCTTACTATGATTTTTGGTCCGGTTGGGTCTTCG ATTACTGGGGGCAGGGAACCCTGGTGACAGTGTCCTCAG GCCCCACTTCTACCAGTGGACCGGAAGATCAACCACTTA CACCAACGGGCAGCGACCCCCAGTCAGGCCTAGGGCGCC ACCTGGGTGTGGTCATCGGGATACTGGTCGCTGTCATCCT GCTTCTGCTCCTTCTCTTGCTCCTATTCCTAATCCTGCGCC

		ACAGGAGACAGGGCAAGCACTGGACCAGCACCCAGCGG AAGGCCGACTTTCAGCACCCTGCCGGCGCCGTGGGCCCT GAGCCTACCGACAGGGGCCTGCAGTGGAGGAGCTCCCCA GCCGCCGATGCCCAGGAGGAGAATCTGTACGCCGCCGTG AAGCACACCCAGCCAGAGGACGGCGTGGAGATGGACAC CCGCTCCCCACACGACGAGGACCCACAGGCCGTGACCTA CGCCGAGGTGAAGCACAGCCGCCCCAGACGCGAGATGG CCAGCCCACCCAGCCCCCTGTCCGGCGAGTTCCTGGACA CCAAGGACAGGCAGGCCGAGGAGGACCGGCAGATGGAC ACCGAGGCCGCCGCCTCCGAGGCCCCCCAGGACGTGACC TACGCCCAGCTGCACTCCCTGACCCTGCGGAGAGAGGCC ACCGAGCCCCCACCCAGCCAGGAGGGCCCCTCCCCCGCC GTGCCTAGCATCTACGCCACCCTGGCCATCCACGGATCC GGGGAAGGCCGAGGCTCCCTTCTAACATGTGGAGATGTC GAGGAAAACCCTGGCCCTATGGCGCTGCCAGTCACTGCA TTGTTATTGCCTCTGGCCCTGCTTCTCCATGCGGCGCGCC CAGACATCCAGATGACCCAATCCCCAAGCAGTCTCTCAG CCAGCGTGGGAGACAGGGTTACAATCACGTGCCGCGCCA GCCAGGACGTCAACACCGCTGTGGCTTGGTATCAGCAAA AGCCCGGGAAGGCACCAAAGCTGCTTATTTATAGCGCCT CCTTCTTGTATTCTGGAGTGCCATCCAGGTTTTCCGGGTC ACGTAGCGGGACTGACTTTACCCTCACCATATCCAGCCTC CAGCCCGAGGATTTCGCCACCTATTACTGTCAGCAACACT ACACGACTCCACCGACTTTTGGACAGGGCACTAAAGTGG AGATTAAGGGCAGCACGAGTGGGAGTGGAAAGCCCGGC AGCGGGGAGGGGTCTACCAAGGGAGAGGTCCAGCTGGTT GAATCCGGAGGCGGGCTTGTGCAACCTGGAGGCTCCCTG AGGCTTAGTTGTGCCGCGTCAGGATTCAACATTAAGGAT ACCTATATTCATTGGGTCCGACAAGCCCCGGGCAAGGGC TTGGAGTGGGTGGCCAGAATCTATCCGACCAACGGATAT ACAAGGTACGCCGATTCTGTGAAAGGACGCTTCACCATC AGCGCGGACACATCCAAAAACACAGCCTATCTGCAGATG AACTCCCTTCGCGCCGAGGATACAGCCGTGTACTATTGTA GTCGGTGGGGAGGCGACGGCTTCTACGCGATGGACTATT GGGGACAAGGAACACTGGTGACTGTCAGTAGCACTACGA CCCCAGCACCTAGACCTCCCACCCCAGCTCCAACTATAG CTTCCCAGCCATTGTCTCTCCGGCCAGAGGCGTGTCGACC AGCCGCTGGAGGGGCCGTTCATACAAGAGGACTCGATTT CGCTTGCGATATCTACATATGGGCCCCTCTTGCCGGGACA TGCGGTGTCCTGCTTCTAAGCTTGGTTATTACCCTCTATT GCAAAAGAGGACGAAAGAAACTGCTTTATATATTCAAGC AACCTTTCATGCGCCCCGTACAGACCACGCAGGAGGAAG ATGGGTGTAGCTGTCGCTTCCCTGAGGAAGAGGAAGGTG GATGCGAGTTGCGGGTGAAGTTCAGTCGATCCGCCGATG CGCCTGCCTATCAGCAAGGGCAGAACCAGCTTTATAACG AGTTAAACCTTGGCCGCCGGGAAGAGTATGACGTGTTGG ACAAGCGTCGCGGGAGAGACCCTGAGATGGGCGGAAAA

		CCAAGGAGAAAAAATCCACAGGAAGGCTTATATAACGA GTTGCAGAAAGACAAGATGGCCGAGGCATACTCCGAAAT CGGAATGAAGGGCGAGCGACGGCGCGGCAAAGGCCACG ATGGACTCTATCAGGGCTTAAGCACCGCCACCAAAGACA CCTACGATGCACTTCATATGCAGGCACTCCCACCTAGATG ATAA
MC0516-SN66E3.2(LH)_LIR1(30)_2A_HER2 Protein Sequence (VR516)	SEQ ID NO:324	MALPVTALLLPLALLLHAARPDIVMTQSPDSLAVSLGERATI SCKSSQSVLYSSNNKNYLAWYQQKPGQPPKLLIYWASTRES GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYGTPFTF GGGTKVEIKGGGGSGGGGSGGGGSQVQLVQSGAEVKKPG ASVKVSCKASGYTFTDYYLHWVRQAPGQGLEWMGWINPY TGGTNYAQKFQGRVTMTRDTSISTAYMELSGLTSDDTAVY YCARAGASYYDFWSGWVFDYWGQGTLVTVSSGPTSTSGPE DQPLTPTGSDPQSGLGRHLGVVIGILVAVILLLLLLLLLFLIL RHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSP AADAQEENLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTY AEVKHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTEA AASEAPQDVTYAQLHSLTLRREATEPPPSQEGPSPAVPSIYA TLAIHGSGEGRGSLLTCGDVEENPGPMALPVTALLLPLALLL HAARPDIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWY QQKPGKAPKLLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQ PEDFATYYCQQHYTTPPTFGQGTKVEIKGSTSGSGKPGSGE GSTKGEVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHW VRQAPGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSK NTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGT LVTVSSTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHT RGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYI FKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSAD APAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGK PRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHD GLYQGLSTATKDTYDALHMQALPPR
MC0517-SN66E3.3(LH)_LIR1(26)_2A_HER2 Nuclotide Sequence (VR517)	SEQ ID NO:325	ATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCC TGCTTCTCCATGCGGCAAGGCCAGATATAGTGATGACAC AGTCCCCCGACTCCCTGGCTGTCTCACTGGGAGAACGAG CGACGATTAGTTGTAAGTCTAGCCAGAGCGTCCTGTATTC AAGCAATAACAAGAATTACCTCGCCTGGTATCAGCAAAA GCCGGGACAGCCACCCAAACTGTTGATTTACTGGGCCAG CACGAGAGAGAGCGGAGTGCCCGACCGCTTCAGCGGATC CGGGTCAGGCACAGATTTTACCCTGACTATTAGCTCCCTT CAAGCGGAAGATGTCGCCGTCTACTATTGCCAGCAATAT TACGGAACTCCATTCACATTCGGCGGTGGGACCAAAGTA GAGATAAAGGGTGGCGGGGGATCCGGCGGTGGCGGTAG CGGGGGAGGCGGGTCCCAAGTGCAACTAGTCCAATCAGG TGCCGAAGTCAAGAAACCAGGTGCATCCGTGAAAGTGTC TTGCAAAGCCAGTGGCTACACTTTTACTGACTACTATCTG CACTGGGTGCGTCAAGCACCCGGCCAGGGGCTTGAATGG ATGGGCTGGATTAACCCTTATACTGGAGGGACAAATTAC

		GCTCAGAAGTTCCAGGGACGCGTTACAATGACCCGAGAC ACCAGCATCAGCACAGCGTACATGGAGTTAAGTAGGCTG AGGTCCGAAGATACCGCCGTGTATTACTGCGCTCGGGCA GGGGCCTCTTACTATGATTTTTGGTCCGGTTGGGTCTTCG ATTACTGGGGGCAGGGAACCCTGGTGACAGTGTCCTCAA CCAGTGGACCGGAAGATCAACCACTTACACCAACGGGCA GCGACCCCCAGTCAGGCCTAGGGCGCCACCTGGGTGTGG TCATCGGGATACTGGTCGCTGTCATCCTGCTTCTGCTCCT TCTCTTGCTCCTATTCCTAATCCTGCGCCACAGGAGACAG GGCAAGCACTGGACCAGCACCCAGCGGAAGGCCGACTTT CAGCACCCTGCCGGCGCCGTGGGCCCTGAGCCTACCGAC AGGGGCCTGCAGTGGAGGAGCTCCCCAGCCGCCGATGCC CAGGAGGAGAATCTGTACGCCGCCGTGAAGCACACCCAG CCAGAGGACGGCGTGGAGATGGACACCCGCTCCCCACAC GACGAGGACCCACAGGCCGTGACCTACGCCGAGGTGAA GCACAGCCGCCCCAGACGCGAGATGGCCAGCCCACCCAG CCCCCTGTCCGGCGAGTTCCTGGACACCAAGGACAGGCA GGCCGAGGAGGACCGGCAGATGGACACCGAGGCCGCCG CCTCCGAGGCCCCCCAGGACGTGACCTACGCCCAGCTGC ACTCCCTGACCCTGCGGAGAGAGGCCACCGAGCCCCCAC CCAGCCAGGAGGGCCCCTCCCCCGCCGTGCCTAGCATCT ACGCCACCCTGGCCATCCACGGATCCGGGGAAGGCCGAG GCTCCCTTCTAACATGTGGAGATGTCGAGGAAAACCCTG GCCCTATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCT GGCCCTGCTTCTCCATGCGGCGCGCCCAGACATCCAGAT GACCCAATCCCCAAGCAGTCTCTCAGCCAGCGTGGGAGA CAGGGTTACAATCACGTGCCGCGCCAGCCAGGACGTCAA CACCGCTGTGGCTTGGTATCAGCAAAAGCCCGGGAAGGC ACCAAAGCTGCTTATTTATAGCGCCTCCTTCTTGTATTCT GGAGTGCCATCCAGGTTTTCCGGGTCACGTAGCGGGACT GACTTTACCCTCACCATATCCAGCCTCCAGCCCGAGGATT TCGCCACCTATTACTGTCAGCAACACTACACGACTCCACC GACTTTTGGACAGGGCACTAAAGTGGAGATTAAGGGCAG CACGAGTGGGAGTGGAAAGCCCGGCAGCGGGGAGGGGT CTACCAAGGGAGAGGTCCAGCTGGTTGAATCCGGAGGCG GGCTTGTGCAACCTGGAGGCTCCCTGAGGCTTAGTTGTGC CGCGTCAGGATTCAACATTAAGGATACCTATATTCATTGG GTCCGACAAGCCCCGGGCAAGGGCTTGGAGTGGGTGGCC AGAATCTATCCGACCAACGGATATACAAGGTACGCCGAT TCTGTGAAAGGACGCTTCACCATCAGCGCGGACACATCC AAAAACACAGCCTATCTGCAGATGAACTCCCTTCGCGCC GAGGATACAGCCGTGTACTATTGTAGTCGGTGGGGAGGC GACGGCTTCTACGCGATGGACTATTGGGGACAAGGAACA CTGGTGACTGTCAGTAGCACTACGACCCCAGCACCTAGA CCTCCCACCCCAGCTCCAACTATAGCTTCCCAGCCATTGT CTCTCCGGCCAGAGGCGTGTCGACCAGCCGCTGGAGGGG CCGTTCATACAAGAGGACTCGATTTCGCTTGCGATATCTA

		CATATGGGCCCCTCTTGCCGGGACATGCGGTGTCCTGCTT CTAAGCTTGGTTATTACCCTCTATTGCAAAAGAGGACGA AAGAAACTGCTTTATATATTCAAGCAACCTTTCATGCGCC CCGTACAGACCACGCAGGAGGAAGATGGGTGTAGCTGTC GCTTCCCTGAGGAAGAGGAAGGTGGATGCGAGTTGCGGG TGAAGTTCAGTCGATCCGCCGATGCGCCTGCCTATCAGC AAGGGCAGAACCAGCTTTATAACGAGTTAAACCTTGGCC GCCGGGAAGAGTATGACGTGTTGGACAAGCGTCGCGGGA GAGACCCTGAGATGGGCGGAAAACCAAGGAGAAAAAAT CCACAGGAAGGCTTATATAACGAGTTGCAGAAAGACAAG ATGGCCGAGGCATACTCCGAAATCGGAATGAAGGGCGA GCGACGGCGCGGCAAAGGCCACGATGGACTCTATCAGGG CTTAAGCACCGCCACCAAAGACACCTACGATGCACTTCA TATGCAGGCACTCCCACCTAGATGATAA
MC0517-SN66E3.3(LH)_LIR1(26)_2A_HER2 Protein Sequence (VR517)	SEQ ID NO:326	MALPVTALLLPLALLLHAARPDIVMTQSPDSLAVSLGERATI SCKSSQSVLYSSNNKNYLAWYQQKPGQPPKLLIYWASTRES GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYGTPFTF GGGTKVEIKGGGGSGGGGSGGGGSQVQLVQSGAEVKKPG ASVKVSCKASGYTFTDYYLHWVRQAPGQGLEWMGWINPY TGGTNYAQKFQGRVTMTRDTSISTAYMELSRLRSEDTAVY YCARAGASYYDFWSGWVFDYWGQGTLVTVSSTSGPEDQP LTPTGSDPQSGLGRHLGVVIGILVAVILLLLLLLLLFLILRHR RQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAA DAQEENLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAE VKHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTEAA ASEAPQDVTYAQLHSLTLRREATEPPPSQEGPSPAVPSIYAT LAIHGSGEGRGSLLTCGDVEENPGPMALPVTALLLPLALLL HAARPDIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWY QQKPGKAPKLLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQ PEDFATYYCQQHYTTPPTFGQGTKVEIKGSTSGSGKPGSGE GSTKGEVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHW VRQAPGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSK NTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGT LVTVSSTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHT RGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYI FKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSAD APAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGK PRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHD GLYQGLSTATKDTYDALHMQALPPR
VR033 nucleotide sequence	335	ATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCC TGCTTCTCCATGCGGCAAGGCCAGATTATAAAGACGATG ACGATAAGGACATCCAGATGACCCAATCCCCAAGCAGTC TCTCAGCCAGCGTGGGAGACAGGGTTACAATCACGTGCC GCGCCAGCCAGGACGTCAACACCGCTGTGGCTTGGTATC AGCAAAAGCCCGGGAAGGCACCAAAGCTGCTTATTTATA GCGCCTCCTTCTTGTATTCTGGAGTGCCATCCAGGTTTTC CGGGTCACGTAGCGGGACTGACTTTACCCTCACCATATCC

		AGCCTCCAGCCCGAGGATTTCGCCACCTATTACTGTCAGC AACACTACACGACTCCACCGACTTTTGGACAGGGCACTA AAGTGGAGATTAAGGGCAGCACGAGTGGGAGTGGAAAG CCCGGCAGCGGGGAGGGGTCTACCAAGGGAGAGGTCCA GCTGGTTGAATCCGGAGGCGGGCTTGTGCAACCTGGAGG CTCCCTGAGGCTTAGTTGTGCCGCGTCAGGATTCAACATT AAGGATACCTATATTCATTGGGTCCGACAAGCCCCGGGC AAGGGCTTGGAGTGGGTGGCCAGAATCTATCCGACCAAC GGATATACAAGGTACGCCGATTCTGTGAAAGGACGCTTC ACCATCAGCGCGGACACATCCAAAAACACAGCCTATCTG CAGATGAACTCCCTTCGCGCCGAGGATACAGCCGTGTAC TATTGTAGTCGGTGGGGAGGCGACGGCTTCTACGCGATG GACTATTGGGGACAAGGAACACTGGTGACTGTCAGTAGC ACTACAACTCCTGCCCCACGGCCACCTACACCTGCGCCTA CAATTGCCAGCCAGCCACTGTCCTTACGACCAGAGGCTT GCCGCCCCGCTGCGGGAGGCGCCGTCCATACCCGGGGCC TTGACTTCGCATGCGATATTTACATTTGGGCACCCTTGGC CGGCACCTGCGGAGTTTTACTTCTGAGCTTGGTGATAACG CTGTACTGTAAAAGAGGACGAAAGAAACTGCTTTATATA TTCAAGCAACCTTTCATGCGCCCCGTACAGACCACGCAG GAGGAAGATGGGTGTAGCTGTCGCTTCCCTGAGGAAGAG GAAGGTGGATGCGAGTTGCGGGTGAAGTTCAGTCGATCC GCCGATGCGCCTGCCTATCAGCAAGGGCAGAACCAGCTT TATAACGAGTTAAACCTTGGCCGCCGGGAAGAGTATGAC GTGTTGGACAAGCGTCGCGGGAGAGACCCTGAGATGGGC GGAAAACCAAGGAGAAAAAATCCACAGGAAGGCTTATA TAACGAGTTGCAGAAAGACAAGATGGCCGAGGCATACTC CGAAATCGGAATGAAGGGCGAGCGACGGCGCGGCAAAG GCCACGATGGACTCTATCAGGGCTTAAGCACCGCCACCA AAGACACCTACGATGCACTTCATATGCAGGCACTCCCAC CTAGATGATAA
VR033 protein sequence	342	MALPVTALLLPLALLLHAARPDYKDDDDKDIQMTQSPSSLS ASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSAS FLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTP PTFGQGTKVEIKGSTSGSGKPGSGEGSTKGEVQLVESGGGL VQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIY PTNGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTA VYYCSRWGGDGFYAMDYWGQGTLVTVSSTTTPAPRPPTPA PTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAG TCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEED GCSCRFPEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELN LGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQK DKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDA LHMQALPPR
VR492 nucleotide sequence	336	ATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCC TGCTTCTCCATGCGGCAAGGCCACAGGTGCAACTGGTTC AATCTGGTGCTGAGGTGAAAAAGCCCGGCGCATCCGTGA AAGTGAGCTGTAAGGCATCAGGGTACACCTTCACCAGCT ATCACATACAATGGGTCCGCCAGGCCCCCGGACAGAGGT

		TGGAATGGATTGGGTGGATTTACCCGGGTGACGGCTCAA CCCAGTACAATGAGAAGTTCAAGGGCAGGGTGACTATCA CACGCGATACCTCCGCGAGCACAGCTTACATGGAGTTAT CTAGCCTGAGATCCGAAGATACGGCGGTGTATTACTGCG CGCGGGAAGGGACCTACTATGCCATGGACTATTGGGGAC AAGGGACCCTGGTTACCGTGAGTTCTGGGGGCGGGGGTT CCGGGGGAGGGGGATCTGGGGGTGGAGGGAGCGATGTG GTAATGACCCAGACACCTTTGTCTTTGAGTGTCACCCCCG GACAGCCGGCAAGTATATCCTGTAGATCATCCCAATCAA TCGTGCACTCCAACGGAAACACATACTTGGAATGGTATC TCCAGAAACCTGGACAGTCCCCACAGTTGCTCATCTACA AAGTGTCAAATCGCTTTTCAGGCGTGCCCGATCGTTTCAG CGGCTCAGGCTCCGGGACAGACTTTACATTGAAGATTAG CCGCGTAGAGGCAGAGGATGTGGGCGTTTACTATTGTTTT CAAGGGTCACACGTGCCACGCACATTCGGCGGCGGTACC AAGGTGGAAATTAAGCACCCCAGCGACCCGCTGGAGCTC GTTGTGTCCGGACCATCAGGGGGCCCGAGTAGCCCTACA ACCGGCCCCACTTCTACCAGTGGACCGGAAGATCAACCA CTTACACCAACGGGCAGCGACCCCCAGTCAGGCCTAGGG CGCCACCTGGGTGTGGTCATCGGGATACTGGTCGCTGTC ATCCTGCTTCTGCTCCTTCTCTTGCTCCTATTCCTAATCCT GCGCCACAGGAGACAGGGCAAGCACTGGACCAGCACCC AGCGGAAGGCCGACTTTCAGCACCCTGCCGGCGCCGTGG GCCCTGAGCCTACCGACAGGGGCCTGCAGTGGAGGAGCT CCCCAGCCGCCGATGCCCAGGAGGAGAATCTGTTCGCCG CCGTGAAGCACACCCAGCCAGAGGACGGCGTGGAGATG GACACCCGCTCCCCACACGACGAGGACCCACAGGCCGTG ACCTTCGCCGAGGTGAAGCACAGCCGCCCCAGACGCGAG ATGGCCAGCCCACCCAGCCCCCTGTCCGGCGAGTTCCTG GACACCAAGGACAGGCAGGCCGAGGAGGACCGGCAGAT GGACACCGAGGCCGCCGCCTCCGAGGCCCCCCAGGACGT GACCTTCGCCCAGCTGCACTCCCTGACCCTGCGGAGAGA GGCCACCGAGCCCCCACCCAGCCAGGAGGGCCCCTCCCC CGCCGTGCCTAGCATCTTCGCCACCCTGGCCATCCACCGG AGAAAGCGTGGATCCGGGGAAGGCCGAGGCTCCCTTCTA ACATGTGGAGATGTCGAGGAAAACCCTGGCCCTATGGCG CTGCCAGTCACTGCATTGTTATTGCCTCTGGCCCTGCTTC TCCATGCGGCGCGCCCAGACATCCAGATGACCCAATCCC CAAGCAGTCTCTCAGCCAGCGTGGGAGACAGGGTTACAA TCACGTGCCGCGCCAGCCAGGACGTCAACACCGCTGTGG CTTGGTATCAGCAAAAGCCCGGGAAGGCACCAAAGCTGC TTATTTATAGCGCCTCCTTCTTGTATTCTGGAGTGCCATCC AGGTTTTCCGGGTCACGTAGCGGGACTGACTTTACCCTCA CCATATCCAGCCTCCAGCCCGAGGATTTCGCCACCTATTA CTGTCAGCAACACTACACGACTCCACCGACTTTTGGACA GGGCACTAAAGTGGAGATTAAGGGCAGCACGAGTGGGA GTGGAAAGCCCGGCAGCGGGGAGGGGTCTACCAAGGGA

		GAGGTCCAGCTGGTTGAATCCGGAGGCGGGCTTGTGCAA CCTGGAGGCTCCCTGAGGCTTAGTTGTGCCGCGTCAGGA TTCAACATTAAGGATACCTATATTCATTGGGTCCGACAAG CCCCGGGCAAGGGCTTGGAGTGGGTGGCCAGAATCTATC CGACCAACGGATATACAAGGTACGCCGATTCTGTGAAAG GACGCTTCACCATCAGCGCGGACACATCCAAAAACACAG CCTATCTGCAGATGAACTCCCTTCGCGCCGAGGATACAG CCGTGTACTATTGTAGTCGGTGGGGAGGCGACGGCTTCT ACGCGATGGACTATTGGGGACAAGGAACACTGGTGACTG TCAGTAGCACTACGACCCCAGCACCTAGACCTCCCACCC CAGCTCCAACTATAGCTTCCCAGCCATTGTCTCTCCGGCC AGAGGCGTGTCGACCAGCCGCTGGAGGGGCCGTTCATAC AAGAGGACTCGATTTCGCTTGCGATATCTACATATGGGC CCCTCTTGCCGGGACATGCGGTGTCCTGCTTCTAAGCTTG GTTATTACCCTCTATTGCAAAAGAGGACGAAAGAAACTG CTTTATATATTCAAGCAACCTTTCATGCGCCCCGTACAGA CCACGCAGGAGGAAGATGGGTGTAGCTGTCGCTTCCCTG AGGAAGAGGAAGGTGGATGCGAGTTGCGGGTGAAGTTC AGTCGATCCGCCGATGCGCCTGCCTATCAGCAAGGGCAG AACCAGCTTTATAACGAGTTAAACCTTGGCCGCCGGGAA GAGTATGACGTGTTGGACAAGCGTCGCGGGAGAGACCCT GAGATGGGCGGAAAACCAAGGAGAAAAAATCCACAGGA AGGCTTATATAACGAGTTGCAGAAAGACAAGATGGCCGA GGCATACTCCGAAATCGGAATGAAGGGCGAGCGACGGC GCGGCAAAGGCCACGATGGACTCTATCAGGGCTTAAGCA CCGCCACCAAAGACACCTACGATGCACTTCATATGCAGG CACTCCCACCTAGATGATAA
VR492 protein sequence	343	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVK VSCKASGYTFTSYHIQWVRQAPGQRLEWIGWIYPGDGSTQ YNEKFKGRVTITRDTSASTAYMELSSLRSEDTAVYYCAREG TYYAMDYWGQGTLVTVSSGGGGSGGGGSGGGGSDVVMT QTPLSLSVTPGQPASISCRSSQSIVHSNGNTYLEWYLQKPGQ SPQLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVG VYYCFQGSHVPRTFGGGTKVEIKHPSDPLELVVSGPSGGPSS PTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGVVIGILVAVIL LLLLLLLLFLILRHRRQGKHWTSTQRKADFQHPAGAVGPEP TDRGLQWRSSPAADAQEENLFAAVKHTQPEDGVEMDTRSP HDEDPQAVTFAEVKHSRPRREMASPPSPLSGEFLDTKDRQA EEDRQMDTEAAASEAPQDVTFAQLHSLTLRREATEPPPSQE GPSPAVPSIFATLAIHRRKRGSGEGRGSLLTCGDVEENPGPM ALPVTALLLPLALLLHAARPDIQMTQSPSSLSASVGDRVTIT CRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVPSRFS GSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKVE IKGSTSGSGKPGSGEGSTKGEVQLVESGGGLVQPGGSLRLS CAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYA DSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGG DGFYAMDYWGQGTLVTVSSTTTPAPRPPTPAPTIASQPLSLR

		PEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLV ITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEE GGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVL DKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIG MKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
VR442 nucleotide sequence	337	ATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCC TGCTTCTCCATGCGGCAAGGCCACAGGTGCAACTGGTTC AATCTGGTGCTGAGGTGAAAAAGCCCGGCGCATCCGTGA AAGTGAGCTGTAAGGCATCAGGGTACACCTTCACCAGCT ATCACATACAATGGGTCCGCCAGGCCCCCGGACAGAGGT TGGAATGGATTGGGTGGATTTACCCGGGTGACGGCTCAA CCCAGTACAATGAGAAGTTCAAGGGCAGGGTGACTATCA CACGCGATACCTCCGCGAGCACAGCTTACATGGAGTTAT CTAGCCTGAGATCCGAAGATACGGCGGTGTATTACTGCG CGCGGGAAGGGACCTACTATGCCATGGACTATTGGGGAC AAGGGACCCTGGTTACCGTGAGTTCTGGGGGCGGGGGTT CCGGGGGAGGGGGATCTGGGGGTGGAGGGAGCGATGTG GTAATGACCCAGACACCTTTGTCTTTGAGTGTCACCCCCG GACAGCCGGCAAGTATATCCTGTAGATCATCCCAATCAA TCGTGCACTCCAACGGAAACACATACTTGGAATGGTATC TCCAGAAACCTGGACAGTCCCCACAGTTGCTCATCTACA AAGTGTCAAATCGCTTTTCAGGCGTGCCCGATCGTTTCAG CGGCTCAGGCTCCGGGACAGACTTTACATTGAAGATTAG CCGCGTAGAGGCAGAGGATGTGGGCGTTTACTATTGTTTT CAAGGGTCACACGTGCCACGCACATTCGGCGGCGGTACC AAGGTGGAAATTAAGCCGAGTAGCCCTACAACCGGCCCC ACTTCTACCAGTGGACCGGAAGATCAACCACTTACACCA ACGGGCAGCGACCCCCAGTCAGGCCTAGGGCGCCACCTG GGTGTGGTCATCGGGATACTGGTCGCTGTCATCCTGCTTC TGCTCCTTCTCTTGCTCCTATTCCTAATCCTGCGCCACAG GAGACAGGGCAAGCACTGGACCAGCACCCAGCGGAAGG CCGACTTTCAGCACCCTGCCGGCGCCGTGGGCCCTGAGC CTACCGACAGGGGCCTGCAGTGGAGGAGCTCCCCAGCCG CCGATGCCCAGGAGGAGAATCTGTACGCCGCCGTGAAGC ACACCCAGCCAGAGGACGGCGTGGAGATGGACACCCGCT CCCCACACGACGAGGACCCACAGGCCGTGACCTACGCCG AGGTGAAGCACAGCCGCCCCAGACGCGAGATGGCCAGC CCACCCAGCCCCCTGTCCGGCGAGTTCCTGGACACCAAG GACAGGCAGGCCGAGGAGGACCGGCAGATGGACACCGA GGCCGCCGCCTCCGAGGCCCCCCAGGACGTGACCTACGC CCAGCTGCACTCCCTGACCCTGCGGAGAGAGGCCACCGA GCCCCCACCCAGCCAGGAGGGCCCCTCCCCCGCCGTGCC TAGCATCTACGCCACCCTGGCCATCCACTGATAACCCCCC CCCCTAACGTTACTGGCCGAAGCCGCTTGGAATAAGGCC GGTGTGCGTTTGTCTATATGTTATTTTCCACCATATTGCC GTCTTTTGGCAATGTGAGGGCCCGGAAACCTGGCCCTGT CTTCTTGACGAGCATTCCTAGGGGTCTTTCCCCTCTCGCC

		AAAGGAATGCAAGGTCTGTTGAATGTCGTGAAGGAAGCA GTTCCTCTGGAAGCTTCTTGAAGACAAACAACGTCTGTA GCGACCCTTTGCAGGCAGCGGAACCCCCCACCTGGCGAC AGGTGCCTCTGCGGCCAAAAGCCACGTGTATAAGATACA CCTGCAAAGGCGGCACAACCCCAGTGCCACGTTGTGAGT TGGATAGTTGTGGAAAGAGTCAAATGGCTCTCCTCAAGC GTATTCAACAAGGGGCTGAAGGATGCCCAGAAGGTACCC CATTGTATGGGATCTGATCTGGGGCCTCGGTGCACATGCT TTACATGTGTTTAGTCGAGGTTAAAAAAACGTCTAGGCC CCCCGAACCACGGGGACGTGGTTTTCCTTTGAAAAACAC GATGATAATATGATGGCGCTGCCAGTCACTGCATTGTTAT TGCCTCTGGCCCTGCTTCTCCATGCGGCGCGCCCAGACAT CCAGATGACCCAATCCCCAAGCAGTCTCTCAGCCAGCGT GGGAGACAGGGTTACAATCACGTGCCGCGCCAGCCAGGA CGTCAACACCGCTGTGGCTTGGTATCAGCAAAAGCCCGG GAAGGCACCAAAGCTGCTTATTTATAGCGCCTCCTTCTTG TATTCTGGAGTGCCATCCAGGTTTTCCGGGTCACGTAGCG GGACTGACTTTACCCTCACCATATCCAGCCTCCAGCCCGA GGATTTCGCCACCTATTACTGTCAGCAACACTACACGACT CCACCGACTTTTGGACAGGGCACTAAAGTGGAGATTAAG GGCAGCACGAGTGGGAGTGGAAAGCCCGGCAGCGGGGA GGGGTCTACCAAGGGAGAGGTCCAGCTGGTTGAATCCGG AGGCGGGCTTGTGCAACCTGGAGGCTCCCTGAGGCTTAG TTGTGCCGCGTCAGGATTCAACATTAAGGATACCTATATT CATTGGGTCCGACAAGCCCCGGGCAAGGGCTTGGAGTGG GTGGCCAGAATCTATCCGACCAACGGATATACAAGGTAC GCCGATTCTGTGAAAGGACGCTTCACCATCAGCGCGGAC ACATCCAAAAACACAGCCTATCTGCAGATGAACTCCCTT CGCGCCGAGGATACAGCCGTGTACTATTGTAGTCGGTGG GGAGGCGACGGCTTCTACGCGATGGACTATTGGGGACAA GGAACACTGGTGACTGTCAGTAGCACTACGACCCCAGCA CCTAGACCTCCCACCCCAGCTCCAACTATAGCTTCCCAGC CATTGTCTCTCCGGCCAGAGGCGTGTCGACCAGCCGCTG GAGGGGCCGTTCATACAAGAGGACTCGATTTCGCTTGCG ATATCTACATATGGGCCCCTCTTGCCGGGACATGCGGTGT CCTGCTTCTAAGCTTGGTTATTACCCTCTATTGCAAAAGA GGACGAAAGAAACTGCTTTATATATTCAAGCAACCTTTC ATGCGCCCCGTACAGACCACGCAGGAGGAAGATGGGTGT AGCTGTCGCTTCCCTGAGGAAGAGGAAGGTGGATGCGAG TTGCGGGTGAAGTTCAGTCGATCCGCCGATGCGCCTGCCT ATCAGCAAGGGCAGAACCAGCTTTATAACGAGTTAAACC TTGGCCGCCGGGAAGAGTATGACGTGTTGGACAAGCGTC GCGGGAGAGACCCTGAGATGGGCGGAAAACCAAGGAGA AAAAATCCACAGGAAGGCTTATATAACGAGTTGCAGAAA GACAAGATGGCCGAGGCATACTCCGAAATCGGAATGAA GGGCGAGCGACGGCGCGGCAAAGGCCACGATGGACTCT

		ATCAGGGCTTAAGCACCGCCACCAAAGACACCTACGATG CACTTCATATGCAGGCACTCCCACCTAGATGATAA
VR442 protein sequence	344	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVK VSCKASGYTFTSYHIQWVRQAPGQRLEWIGWIYPGDGSTQ YNEKFKGRVTITRDTSASTAYMELSSLRSEDTAVYYCAREG TYYAMDYWGQGTLVTVSSGGGGSGGGGSGGGGSDVVMT QTPLSLSVTPGQPASISCRSSQSIVHSNGNTYLEWYLQKPGQ SPQLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVG VYYCFQGSHVPRTFGGGTKVEIKPSSPTTGPTSTSGPEDQPL TPTGSDPQSGLGRHLGVVIGILVAVILLLLLLLLLFLILRHRR QGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAAD AQEENLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEV KHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTEAAAS EAPQDVTYAQLHSLTLRREATEPPPSQEGPSPAVPSIYATLAI H* MALPVTALLLPLALLLHAARPDIQMTQSPSSLSASVGDRVTI TCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVPSRF SGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKV EIKGSTSGSGKPGSGEGSTKGEVQLVESGGGLVQPGGSLRLS CAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYA DSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGG DGFYAMDYWGQGTLVTVSSTTTPAPRPPTPAPTIASQPLSLR PEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLV ITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEE GGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVL DKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIG MKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR*
VR443 nucleotide sequence	338	ATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCC TGCTTCTCCATGCGGCAAGGCCACAGGTGCAACTGGTTC AATCTGGTGCTGAGGTGAAAAAGCCCGGCGCATCCGTGA AAGTGAGCTGTAAGGCATCAGGGTACACCTTCACCAGCT ATCACATACAATGGGTCCGCCAGGCCCCCGGACAGAGGT TGGAATGGATTGGGTGGATTTACCCGGGTGACGGCTCAA CCCAGTACAATGAGAAGTTCAAGGGCAGGGTGACTATCA CACGCGATACCTCCGCGAGCACAGCTTACATGGAGTTAT CTAGCCTGAGATCCGAAGATACGGCGGTGTATTACTGCG CGCGGGAAGGGACCTACTATGCCATGGACTATTGGGGAC AAGGGACCCTGGTTACCGTGAGTTCTGGGGGCGGGGGTT CCGGGGGAGGGGGATCTGGGGGTGGAGGGAGCGATGTG GTAATGACCCAGACACCTTTGTCTTTGAGTGTCACCCCCG GACAGCCGGCAAGTATATCCTGTAGATCATCCCAATCAA TCGTGCACTCCAACGGAAACACATACTTGGAATGGTATC TCCAGAAACCTGGACAGTCCCCACAGTTGCTCATCTACA AAGTGTCAAATCGCTTTTCAGGCGTGCCCGATCGTTTCAG CGGCTCAGGCTCCGGGACAGACTTTACATTGAAGATTAG CCGCGTAGAGGCAGAGGATGTGGGCGTTTACTATTGTTTT CAAGGGTCACACGTGCCACGCACATTCGGCGGCGGTACC

		AAGGTGGAAATTAAGGGCCCCACTTCTACCAGTGGACCG GAAGATCAACCACTTACACCAACGGGCAGCGACCCCCAG TCAGGCCTAGGGCGCCACCTGGGTGTGGTCATCGGGATA CTGGTCGCTGTCATCCTGCTTCTGCTCCTTCTCTTGCTCCT ATTCCTAATCCTGCGCCACAGGAGACAGGGCAAGCACTG GACCAGCACCCAGCGGAAGGCCGACTTTCAGCACCCTGC CGGCGCCGTGGGCCCTGAGCCTACCGACAGGGGCCTGCA GTGGAGGAGCTCCCCAGCCGCCGATGCCCAGGAGGAGA ATCTGTACGCCGCCGTGAAGCACACCCAGCCAGAGGACG GCGTGGAGATGGACACCCGCTCCCCACACGACGAGGACC CACAGGCCGTGACCTACGCCGAGGTGAAGCACAGCCGCC CCAGACGCGAGATGGCCAGCCCACCCAGCCCCCTGTCCG GCGAGTTCCTGGACACCAAGGACAGGCAGGCCGAGGAG GACCGGCAGATGGACACCGAGGCCGCCGCCTCCGAGGCC CCCCAGGACGTGACCTACGCCCAGCTGCACTCCCTGACC CTGCGGAGAGAGGCCACCGAGCCCCCACCCAGCCAGGA GGGCCCCTCCCCCGCCGTGCCTAGCATCTACGCCACCCTG GCCATCCACTGATAACCCCCCCCCCTAACGTTACTGGCCG AAGCCGCTTGGAATAAGGCCGGTGTGCGTTTGTCTATAT GTTATTTTCCACCATATTGCCGTCTTTTGGCAATGTGAGG GCCCGGAAACCTGGCCCTGTCTTCTTGACGAGCATTCCTA GGGGTCTTTCCCCTCTCGCCAAAGGAATGCAAGGTCTGTT GAATGTCGTGAAGGAAGCAGTTCCTCTGGAAGCTTCTTG AAGACAAACAACGTCTGTAGCGACCCTTTGCAGGCAGCG GAACCCCCCACCTGGCGACAGGTGCCTCTGCGGCCAAAA GCCACGTGTATAAGATACACCTGCAAAGGCGGCACAACC CCAGTGCCACGTTGTGAGTTGGATAGTTGTGGAAAGAGT CAAATGGCTCTCCTCAAGCGTATTCAACAAGGGGCTGAA GGATGCCCAGAAGGTACCCCATTGTATGGGATCTGATCT GGGGCCTCGGTGCACATGCTTTACATGTGTTTAGTCGAGG TTAAAAAAACGTCTAGGCCCCCCGAACCACGGGGACGTG GTTTTCCTTTGAAAAACACGATGATAATATGATGGCGCTG CCAGTCACTGCATTGTTATTGCCTCTGGCCCTGCTTCTCC ATGCGGCGCGCCCAGACATCCAGATGACCCAATCCCCAA GCAGTCTCTCAGCCAGCGTGGGAGACAGGGTTACAATCA CGTGCCGCGCCAGCCAGGACGTCAACACCGCTGTGGCTT GGTATCAGCAAAAGCCCGGGAAGGCACCAAAGCTGCTTA TTTATAGCGCCTCCTTCTTGTATTCTGGAGTGCCATCCAG GTTTTCCGGGTCACGTAGCGGGACTGACTTTACCCTCACC ATATCCAGCCTCCAGCCCGAGGATTTCGCCACCTATTACT GTCAGCAACACTACACGACTCCACCGACTTTTGGACAGG GCACTAAAGTGGAGATTAAGGGCAGCACGAGTGGGAGT GGAAAGCCCGGCAGCGGGGAGGGGTCTACCAAGGGAGA GGTCCAGCTGGTTGAATCCGGAGGCGGGCTTGTGCAACC TGGAGGCTCCCTGAGGCTTAGTTGTGCCGCGTCAGGATTC AACATTAAGGATACCTATATTCATTGGGTCCGACAAGCC CCGGGCAAGGGCTTGGAGTGGGTGGCCAGAATCTATCCG

		ACCAACGGATATACAAGGTACGCCGATTCTGTGAAAGGA CGCTTCACCATCAGCGCGGACACATCCAAAAACACAGCC TATCTGCAGATGAACTCCCTTCGCGCCGAGGATACAGCC GTGTACTATTGTAGTCGGTGGGGAGGCGACGGCTTCTAC GCGATGGACTATTGGGGACAAGGAACACTGGTGACTGTC AGTAGCACTACGACCCCAGCACCTAGACCTCCCACCCCA GCTCCAACTATAGCTTCCCAGCCATTGTCTCTCCGGCCAG AGGCGTGTCGACCAGCCGCTGGAGGGGCCGTTCATACAA GAGGACTCGATTTCGCTTGCGATATCTACATATGGGCCCC TCTTGCCGGGACATGCGGTGTCCTGCTTCTAAGCTTGGTT ATTACCCTCTATTGCAAAAGAGGACGAAAGAAACTGCTT TATATATTCAAGCAACCTTTCATGCGCCCCGTACAGACCA CGCAGGAGGAAGATGGGTGTAGCTGTCGCTTCCCTGAGG AAGAGGAAGGTGGATGCGAGTTGCGGGTGAAGTTCAGTC GATCCGCCGATGCGCCTGCCTATCAGCAAGGGCAGAACC AGCTTTATAACGAGTTAAACCTTGGCCGCCGGGAAGAGT ATGACGTGTTGGACAAGCGTCGCGGGAGAGACCCTGAGA TGGGCGGAAAACCAAGGAGAAAAAATCCACAGGAAGGC TTATATAACGAGTTGCAGAAAGACAAGATGGCCGAGGCA TACTCCGAAATCGGAATGAAGGGCGAGCGACGGCGCGG CAAAGGCCACGATGGACTCTATCAGGGCTTAAGCACCGC CACCAAAGACACCTACGATGCACTTCATATGCAGGCACT CCCACCTAGATGATAA
VR443 protein sequence	345	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVK VSCKASGYTFTSYHIQWVRQAPGQRLEWIGWIYPGDGSTQ YNEKFKGRVTITRDTSASTAYMELSSLRSEDTAVYYCAREG TYYAMDYWGQGTLVTVSSGGGGSGGGGSGGGGSDVVMT QTPLSLSVTPGQPASISCRSSQSIVHSNGNTYLEWYLQKPGQ SPQLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVG VYYCFQGSHVPRTFGGGTKVEIKGPTSTSGPEDQPLTPTGSD PQSGLGRHLGVVIGILVAVILLLLLLLLLFLILRHRRQGKHW TSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEENL YAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPRR EMASPPSPLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDVT YAQLHSLTLRREATEPPPSQEGPSPAVPSIYATLAIH* MALPVTALLLPLALLLHAARPDIQMTQSPSSLSASVGDRVTI TCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVPSRF SGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKV EIKGSTSGSGKPGSGEGSTKGEVQLVESGGGLVQPGGSLRLS CAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYA DSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGG DGFYAMDYWGQGTLVTVSSTTTPAPRPPTPAPTIASQPLSLR PEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLV ITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEE GGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVL DKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIG MKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR*

VR506 nucleotide sequence	339	ATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCC TGCTTCTCCATGCGGCAAGGCCACAGGTGCAACTGGTTC AATCTGGTGCTGAGGTGAAAAAGCCCGGCGCATCCGTGA AAGTGAGCTGTAAGGCATCAGGGTACACCTTCACCAGCT ATCACATACAATGGGTCCGCCAGGCCCCCGGACAGAGGT TGGAATGGATTGGGTGGATTTACCCGGGTGACGGCTCAA CCCAGTACAATGAGAAGTTCAAGGGCAGGGTGACTATCA CACGCGATACCTCCGCGAGCACAGCTTACATGGAGTTAT CTAGCCTGAGATCCGAAGATACGGCGGTGTATTACTGCG CGCGGGAAGGGACCTACTATGCCATGGACTATTGGGGAC AAGGGACCCTGGTTACCGTGAGTTCTGGGGGCGGGGGTT CCGGGGGAGGGGGATCTGGGGGTGGAGGGAGCGATGTG GTAATGACCCAGACACCTTTGTCTTTGAGTGTCACCCCCG GACAGCCGGCAAGTATATCCTGTAGATCATCCCAATCAA TCGTGCACTCCAACGGAAACACATACTTGGAATGGTATC TCCAGAAACCTGGACAGTCCCCACAGTTGCTCATCTACA AAGTGTCAAATCGCTTTTCAGGCGTGCCCGATCGTTTCAG CGGCTCAGGCTCCGGGACAGACTTTACATTGAAGATTAG CCGCGTAGAGGCAGAGGATGTGGGCGTTTACTATTGTTTT CAAGGGTCACACGTGCCACGCACATTCGGCGGCGGTACC AAGGTGGAAATTAAGGAATCTAAGTACGGACCGCCCTGC CCCCCTTGCCCTGGCCCCACTTCTACCAGTGGACCGGAAG ATCAACCACTTACACCAACGGGCAGCGACCCCCAGTCAG GCCTAGGGCGCCACCTGGGTGTGGTCATCGGGATACTGG TCGCTGTCATCCTGCTTCTGCTCCTTCTCTTGCTCCTATTC CTAATCCTGCGCCACAGGAGACAGGGCAAGCACTGGACC AGCACCCAGCGGAAGGCCGACTTTCAGCACCCTGCCGGC GCCGTGGGCCCTGAGCCTACCGACAGGGGCCTGCAGTGG AGGAGCTCCCCAGCCGCCGATGCCCAGGAGGAGAATCTG TACGCCGCCGTGAAGCACACCCAGCCAGAGGACGGCGTG GAGATGGACACCCGCTCCCCACACGACGAGGACCCACAG GCCGTGACCTACGCCGAGGTGAAGCACAGCCGCCCCAGA CGCGAGATGGCCAGCCCACCCAGCCCCCTGTCCGGCGAG TTCCTGGACACCAAGGACAGGCAGGCCGAGGAGGACCG GCAGATGGACACCGAGGCCGCCGCCTCCGAGGCCCCCCA GGACGTGACCTACGCCCAGCTGCACTCCCTGACCCTGCG GAGAGAGGCCACCGAGCCCCCACCCAGCCAGGAGGGCC CCTCCCCCCGCCGTGCCTAGCATCTACGCCACCCTGGCCAT CCACCGGAGAAAGCGTGGATCCGGGGAAGGCCGAGGCT CCCTTCTAACATGTGGAGATGTCGAGGAAAACCCTGGCC CTATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGC CCTGCTTCTCCATGCGGCGCGCCCAGACATCCAGATGAC CCAATCCCCAAGCAGTCTCTCAGCCAGCGTGGGAGACAG GGTTACAATCACGTGCCGCGCCAGCCAGGACGTCAACAC CGCTGTGGCTTGGTATCAGCAAAAGCCCGGGAAGGCACC AAAGCTGCTTATTTATAGCGCCTCCTTCTTGTATTCTGGA GTGCCATCCAGGTTTTCCGGGTCACGTAGCGGGACTGAC

		TTTACCCTCACCATATCCAGCCTCCAGCCCGAGGATTTCG CCACCTATTACTGTCAGCAACACTACACGACTCCACCGA CTTTTGGACAGGGCACTAAAGTGGAGATTAAGGGCAGCA CGAGTGGGAGTGGAAAGCCCGGCAGCGGGGAGGGGTCT ACCAAGGGAGAGGTCCAGCTGGTTGAATCCGGAGGCGG GCTTGTGCAACCTGGAGGCTCCCTGAGGCTTAGTTGTGCC GCGTCAGGATTCAACATTAAGGATACCTATATTCATTGG GTCCGACAAGCCCCGGGCAAGGGCTTGGAGTGGGTGGCC AGAATCTATCCGACCAACGGATATACAAGGTACGCCGAT TCTGTGAAAGGACGCTTCACCATCAGCGCGGACACATCC AAAAACACAGCCTATCTGCAGATGAACTCCCTTCGCGCC GAGGATACAGCCGTGTACTATTGTAGTCGGTGGGGAGGC GACGGCTTCTACGCGATGGACTATTGGGGACAAGGAACA CTGGTGACTGTCAGTAGCACTACGACCCCAGCACCTAGA CCTCCCACCCCAGCTCCAACTATAGCTTCCCAGCCATTGT CTCTCCGGCCAGAGGCGTGTCGACCAGCCGCTGGAGGGG CCGTTCATACAAGAGGACTCGATTTCGCTTGCGATATCTA CATATGGGCCCCTCTTGCCGGGACATGCGGTGTCCTGCTT CTAAGCTTGGTTATTACCCTCTATTGCAAAAGAGGACGA AAGAAACTGCTTTATATATTCAAGCAACCTTTCATGCGCC CCGTACAGACCACGCAGGAGGAAGATGGGTGTAGCTGTC GCTTCCCTGAGGAAGAGGAAGGTGGATGCGAGTTGCGGG TGAAGTTCAGTCGATCCGCCGATGCGCCTGCCTATCAGC AAGGGCAGAACCAGCTTTATAACGAGTTAAACCTTGGCC GCCGGGAAGAGTATGACGTGTTGGACAAGCGTCGCGGGA GAGACCCTGAGATGGGCGGAAAACCAAGGAGAAAAAAT CCACAGGAAGGCTTATATAACGAGTTGCAGAAAGACAAG ATGGCCGAGGCATACTCCGAAATCGGAATGAAGGGCGA GCGACGGCGCGGCAAAGGCCACGATGGACTCTATCAGGG CTTAAGCACCGCCACCAAAGACACCTACGATGCACTTCA TATGCAGGCACTCCCACCTAGATGATAA
VR506 protein sequence	346	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVK VSCKASGYTFTSYHIQWVRQAPGQRLEWIGWIYPGDGSTQ YNEKFKGRVTITRDTSASTAYMELSSLRSEDTAVYYCAREG TYYAMDYWGQGTLVTVSSGGGGSGGGGSGGGGSDVVMT QTPLSLSVTPGQPASISCRSSQSIVHSNGNTYLEWYLQKPGQ SPQLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVG VYYCFQGSHVPRTFGGGTKVEIKESKYGPPCPPCPGPTSTSG PEDQPLTPTGSDPQSGLGRHLGVVIGILVAVILLLLLLLLLFLI LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRS SPAADAQEENLYAAVKHTQPEDGVEMDTRSPHDEDPQAVT YAEVKHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTE AAASEAPQDVTYAQLHSLTLRREATEPPPSQEGPSPAVPSIY ATLAIHRRKRGSGEGRGSLLTCGDVEENPGPMALPVTALLL PLALLLHAARPDIQMTQSPSSLSASVGDRVTITCRASQDVNT AVAWYQQKPGKAPKLLIYSASFLYSGVPSRFSGSRSGTDFT LTISSLQPEDFATYYCQQHYTTPPTFGQGTKVEIKGSTSGSG

		KPGSGEGSTKGEVQLVESGGGLVQPGGSLRLSCAASGFNIK DTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKGRFTI SADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDY WGQGTLVTVSSTTTPAPRPPTPAPTIASQPLSLRPEACRPAA GGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRG RKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRV KFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRD PEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERR RGKGHDGLYQGLSTATKDTYDALHMQALPPR
VR507 nucleotide sequence	340	ATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCC TGCTTCTCCATGCGGCAAGGCCACAGGTGCAACTGGTTC AATCTGGTGCTGAGGTGAAAAAGCCCGGCGCATCCGTGA AAGTGAGCTGTAAGGCATCAGGGTACACCTTCACCAGCT ATCACATACAATGGGTCCGCCAGGCCCCCGGACAGAGGT TGGAATGGATTGGGTGGATTTACCCGGGTGACGGCTCAA CCCAGTACAATGAGAAGTTCAAGGGCAGGGTGACTATCA CACGCGATACCTCCGCGAGCACAGCTTACATGGAGTTAT CTAGCCTGAGATCCGAAGATACGGCGGTGTATTACTGCG CGCGGGAAGGGACCTACTATGCCATGGACTATTGGGGAC AAGGGACCCTGGTTACCGTGAGTTCTGGGGGCGGGGGTT CCGGGGGAGGGGGATCTGGGGGTGGAGGGAGCGATGTG GTAATGACCCAGACACCTTTGTCTTTGAGTGTCACCCCCG GACAGCCGGCAAGTATATCCTGTAGATCATCCCAATCAA TCGTGCACTCCAACGGAAACACATACTTGGAATGGTATC TCCAGAAACCTGGACAGTCCCCACAGTTGCTCATCTACA AAGTGTCAAATCGCTTTTCAGGCGTGCCCGATCGTTTCAG CGGCTCAGGCTCCGGGACAGACTTTACATTGAAGATTAG CCGCGTAGAGGCAGAGGATGTGGGCGTTTACTATTGTTTT CAAGGGTCACACGTGCCACGCACATTCGGCGGCGGTACC AAGGTGGAAATTAAGGAATCTAAGTACGGACCGCCCTGC CCCCCTTGCCCTGAAGATCAACCACTTACACCAACGGGC AGCGACCCCCAGTCAGGCCTAGGGCGCCACCTGGGTGTG GTCATCGGGATACTGGTCGCTGTCATCCTGCTTCTGCTCC TTCTCTTGCTCCTATTCCTAATCCTGCGCCACAGGAGACA GGGCAAGCACTGGACCAGCACCCAGCGGAAGGCCGACTT TCAGCACCCTGCCGGCGCCGTGGGCCCTGAGCCTACCGA CAGGGGCCTGCAGTGGAGGAGCTCCCCAGCCGCCGATGC CCAGGAGGAGAATCTGTACGCCGCCGTGAAGCACACCCA GCCAGAGGACGGCGTGGAGATGGACACCCGCTCCCCACA CGACGAGGACCCACAGGCCGTGACCTACGCCGAGGTGAA GCACAGCCGCCCCAGACGCGAGATGGCCAGCCCACCCAG CCCCCTGTCCGGCGAGTTCCTGGACACCAAGGACAGGCA GGCCGAGGAGGACCGGCAGATGGACACCGAGGCCGCCG CCTCCGAGGCCCCCCAGGACGTGACCTACGCCCAGCTGC ACTCCCTGACCCTGCGGAGAGAGGCCACCGAGCCCCCAC CCAGCCAGGAGGGCCCCTCCCCCGCCGTGCCTAGCATCT ACGCCACCCTGGCCATCCACCGGAGAAAGCGTGGATCCG

		GGGAAGGCCGAGGCTCCCTTCTAACATGTGGAGATGTCG AGGAAAACCCTGGCCCTATGGCGCTGCCAGTCACTGCAT TGTTATTGCCTCTGGCCCTGCTTCTCCATGCGGCGCGCCC AGACATCCAGATGACCCAATCCCCAAGCAGTCTCTCAGC CAGCGTGGGAGACAGGGTTACAATCACGTGCCGCGCCAG CCAGGACGTCAACACCGCTGTGGCTTGGTATCAGCAAAA GCCCGGGAAGGCACCAAAGCTGCTTATTTATAGCGCCTC CTTCTTGTATTCTGGAGTGCCATCCAGGTTTTCCGGGTCA CGTAGCGGGACTGACTTTACCCTCACCATATCCAGCCTCC AGCCCGAGGATTTCGCCACCTATTACTGTCAGCAACACT ACACGACTCCACCGACTTTTGGACAGGGCACTAAAGTGG AGATTAAGGGCAGCACGAGTGGGAGTGGAAAGCCCGGC AGCGGGGAGGGGTCTACCAAGGGAGAGGTCCAGCTGGTT GAATCCGGAGGCGGGCTTGTGCAACCTGGAGGCTCCCTG AGGCTTAGTTGTGCCGCGTCAGGATTCAACATTAAGGAT ACCTATATTCATTGGGTCCGACAAGCCCCGGGCAAGGGC TTGGAGTGGGTGGCCAGAATCTATCCGACCAACGGATAT ACAAGGTACGCCGATTCTGTGAAAGGACGCTTCACCATC AGCGCGGACACATCCAAAAACACAGCCTATCTGCAGATG AACTCCCTTCGCGCCGAGGATACAGCCGTGTACTATTGTA GTCGGTGGGGAGGCGACGGCTTCTACGCGATGGACTATT GGGGACAAGGAACACTGGTGACTGTCAGTAGCACTACGA CCCCAGCACCTAGACCTCCCACCCCAGCTCCAACTATAG CTTCCCAGCCATTGTCTCTCCGGCCAGAGGCGTGTCGACC AGCCGCTGGAGGGGCCGTTCATACAAGAGGACTCGATTT CGCTTGCGATATCTACATATGGGCCCCTCTTGCCGGGACA TGCGGTGTCCTGCTTCTAAGCTTGGTTATTACCCTCTATT GCAAAAGAGGACGAAAGAAACTGCTTTATATATTCAAGC AACCTTTCATGCGCCCCGTACAGACCACGCAGGAGGAAG ATGGGTGTAGCTGTCGCTTCCCTGAGGAAGAGGAAGGTG GATGCGAGTTGCGGGTGAAGTTCAGTCGATCCGCCGATG CGCCTGCCTATCAGCAAGGGCAGAACCAGCTTTATAACG AGTTAAACCTTGGCCGCCGGGAAGAGTATGACGTGTTGG ACAAGCGTCGCGGGAGAGACCCTGAGATGGGCGGAAAA CCAAGGAGAAAAAATCCACAGGAAGGCTTATATAACGA GTTGCAGAAAGACAAGATGGCCGAGGCATACTCCGAAAT CGGAATGAAGGGCGAGCGACGGCGCGGCAAAGGCCACG ATGGACTCTATCAGGGCTTAAGCACCGCCACCAAAGACA CCTACGATGCACTTCATATGCAGGCACTCCCACCTAGATG ATAA
VR507 protein sequence	347	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVK VSCKASGYTFTSYHIQWVRQAPGQRLEWIGWIYPGDGSTQ YNEKFKGRVTITRDTSASTAYMELSSLRSEDTAVYYCAREG TYYAMDYWGQGTLVTVSSGGGGSGGGGSGGGGSDVVMT QTPLSLSVTPGQPASISCRSSQSIVHSNGNTYLEWYLQKPGQ SPQLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVG VYYCFQGSHVPRTFGGGTKVEIKESKYGPPCPPCPEDQPLTP

		TGSDPQSGLGRHLGVVIGILVAVILLLLLLLLLFLILRHRRQG KHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQ EENLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVKHS RPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTEAAASEAP QDVTYAQLHSLTLRREATEPPPSQEGPSPAVPSIYATLAIHR RKRGSGEGRGSLLTCGDVEENPGPMALPVTALLLPLALLLH AARPDIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQ QKPGKAPKLLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQP EDFATYYCQQHYTTPPTFGQGTKVEIKGSTSGSGKPGSGEG STKGEVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWV RQAPGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKNT AYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLV TVSSTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRG LDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFK QPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAP AYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPR RKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGL YQGLSTATKDTYDALHMQALPPR
VR508 nucleotide sequence	341	ATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCTGGCCC TGCTTCTCCATGCGGCAAGGCCACAGGTGCAACTGGTTC AATCTGGTGCTGAGGTGAAAAAGCCCGGCGCATCCGTGA AAGTGAGCTGTAAGGCATCAGGGTACACCTTCACCAGCT ATCACATACAATGGGTCCGCCAGGCCCCCGGACAGAGGT TGGAATGGATTGGGTGGATTTACCCGGGTGACGGCTCAA CCCAGTACAATGAGAAGTTCAAGGGCAGGGTGACTATCA CACGCGATACCTCCGCGAGCACAGCTTACATGGAGTTAT CTAGCCTGAGATCCGAAGATACGGCGGTGTATTACTGCG CGCGGGAAGGGACCTACTATGCCATGGACTATTGGGGAC AAGGGACCCTGGTTACCGTGAGTTCTGGGGGCGGGGGTT CCGGGGGAGGGGGATCTGGGGGTGGAGGGAGCGATGTG GTAATGACCCAGACACCTTTGTCTTTGAGTGTCACCCCCG GACAGCCGGCAAGTATATCCTGTAGATCATCCCAATCAA TCGTGCACTCCAACGGAAACACATACTTGGAATGGTATC TCCAGAAACCTGGACAGTCCCCACAGTTGCTCATCTACA AAGTGTCAAATCGCTTTTCAGGCGTGCCCGATCGTTTCAG CGGCTCAGGCTCCGGGACAGACTTTACATTGAAGATTAG CCGCGTAGAGGCAGAGGATGTGGGCGTTTACTATTGTTTT CAAGGGTCACACGTGCCACGCACATTCGGCGGCGGTACC AAGGTGGAAATTAAGGAATCTAAGTACGGACCGCCCTGC CCCCCTTGCCCTCTTACACCAACGGGCAGCGACCCCCAGT CAGGCCTAGGGCGCCACCTGGGTGTGGTCATCGGGATAC TGGTCGCTGTCATCCTGCTTCTGCTCCTTCTCTTGCTCCTA TTCCTAATCCTGCGCCACAGGAGACAGGGCAAGCACTGG ACCAGCACCCAGCGGAAGGCCGACTTTCAGCACCCTGCC GGCGCCGTGGGCCCTGAGCCTACCGACAGGGGCCTGCAG TGGAGGAGCTCCCCAGCCGCCGATGCCCAGGAGGAGAAT CTGTACGCCGCCGTGAAGCACACCCAGCCAGAGGACGGC

		GTGGAGATGGACACCCGCTCCCCACACGACGAGGACCCA CAGGCCGTGACCTACGCCGAGGTGAAGCACAGCCGCCCC AGACGCGAGATGGCCAGCCCACCCAGCCCCCTGTCCGGC GAGTTCCTGGACACCAAGGACAGGCAGGCCGAGGAGGA CCGGCAGATGGACACCGAGGCCGCCGCCTCCGAGGCCCC CCAGGACGTGACCTACGCCCAGCTGCACTCCCTGACCCT GCGGAGAGAGGCCACCGAGCCCCCACCCAGCCAGGAGG GCCCCTCCCCCGCCGTGCCTAGCATCTACGCCACCCTGGC CATCCACCGGAGAAAGCGTGGATCCGGGGAAGGCCGAG GCTCCCTTCTAACATGTGGAGATGTCGAGGAAAACCCTG GCCCTATGGCGCTGCCAGTCACTGCATTGTTATTGCCTCT GGCCCTGCTTCTCCATGCGGCGCGCCCAGACATCCAGAT GACCCAATCCCCAAGCAGTCTCTCAGCCAGCGTGGGAGA CAGGGTTACAATCACGTGCCGCGCCAGCCAGGACGTCAA CACCGCTGTGGCTTGGTATCAGCAAAAGCCCGGGAAGGC ACCAAAGCTGCTTATTTATAGCGCCTCCTTCTTGTATTCT GGAGTGCCATCCAGGTTTTCCGGGTCACGTAGCGGGACT GACTTTACCCTCACCATATCCAGCCTCCAGCCCGAGGATT TCGCCACCTATTACTGTCAGCAACACTACACGACTCCACC GACTTTTGGACAGGGCACTAAAGTGGAGATTAAGGGCAG CACGAGTGGGAGTGGAAAGCCCGGCAGCGGGGAGGGGT CTACCAAGGGAGAGGTCCAGCTGGTTGAATCCGGAGGCG GGCTTGTGCAACCTGGAGGCTCCCTGAGGCTTAGTTGTGC CGCGTCAGGATTCAACATTAAGGATACCTATATTCATTGG GTCCGACAAGCCCCGGGCAAGGGCTTGGAGTGGGTGGCC AGAATCTATCCGACCAACGGATATACAAGGTACGCCGAT TCTGTGAAAGGACGCTTCACCATCAGCGCGGACACATCC AAAAACACAGCCTATCTGCAGATGAACTCCCTTCGCGCC GAGGATACAGCCGTGTACTATTGTAGTCGGTGGGGAGGC GACGGCTTCTACGCGATGGACTATTGGGGACAAGGAACA CTGGTGACTGTCAGTAGCACTACGACCCCAGCACCTAGA CCTCCCACCCCAGCTCCAACTATAGCTTCCCAGCCATTGT CTCTCCGGCCAGAGGCGTGTCGACCAGCCGCTGGAGGGG CCGTTCATACAAGAGGACTCGATTTCGCTTGCGATATCTA CATATGGGCCCCTCTTGCCGGGACATGCGGTGTCCTGCTT CTAAGCTTGGTTATTACCCTCTATTGCAAAAGAGGACGA AAGAAACTGCTTTATATATTCAAGCAACCTTTCATGCGCC CCGTACAGACCACGCAGGAGGAAGATGGGTGTAGCTGTC GCTTCCCTGAGGAAGAGGAAGGTGGATGCGAGTTGCGGG TGAAGTTCAGTCGATCCGCCGATGCGCCTGCCTATCAGC AAGGGCAGAACCAGCTTTATAACGAGTTAAACCTTGGCC GCCGGGAAGAGTATGACGTGTTGGACAAGCGTCGCGGGA GAGACCCTGAGATGGGCGGAAAACCAAGGAGAAAAAAT CCACAGGAAGGCTTATATAACGAGTTGCAGAAAGACAAG ATGGCCGAGGCATACTCCGAAATCGGAATGAAGGGCGA GCGACGGCGCGGCAAAGGCCACGATGGACTCTATCAGGG

		CTTAAGCACCGCCACCAAAGACACCTACGATGCACTTCA TATGCAGGCACTCCCACCTAGATGATAA
VR508 protein sequence	348	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVK VSCKASGYTFTSYHIQWVRQAPGQRLEWIGWIYPGDGSTQ YNEKFKGRVTITRDTSASTAYMELSSLRSEDTAVYYCAREG TYYAMDYWGQGTLVTVSSGGGGSGGGGSGGGGSDVVMT QTPLSLSVTPGQPASISCRSSQSIVHSNGNTYLEWYLQKPGQ SPQLLIYKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVG VYYCFQGSHVPRTFGGGTKVEIKESKYGPPCPPCPLTPTGSD PQSGLGRHLGVVIGILVAVILLLLLLLLFLILRHRRQGKHW TSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEENL YAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPRR EMASPPSPLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDVT YAQLHSLTLRREATEPPPSQEGPSPAVPSIYATLAIHRRKRGS GEGRGSLLTCGDVEENPGPMALPVTALLLPLALLLHAARPD IQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPG KAPKLLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFAT YYCQQHYTTPPTFGQGTKVEIKGSTSGSGKPGSGEGSTKGE VQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPG KGLEWVARIYPTNGYTRYADSVKGRFTISADTSKNTAYLQ MNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSS TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDF ACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPF MRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYQ QGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKN PQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQG LSTATKDTYDALHMQALPPR

ii. BICISTRONIC iCAR PORTION

[0400] In some embodiments, the bicistronic iCAR portions described below can be included as part of monocistronic iCAR constructs for use in co-transduction methods along with a described monocistronic aCAR construct.

1. iCAR portion: scFv Component

[0401] In some embodiments, the bicistronic construct comprises an iCAR portion comprising a single chain variable fragment (scFv) component. In some embodiments, the iCAR portion comprises a single chain variable fragment (scFv) component. In some embodiments, the scFv targets an HLA antigen. In some embodiments, the HLA antigen is selected from the group consisting of HLA-A2, HLA-A3, HLA-A, HLA-B, HLA-C, HLA-G, HLA-E, HLA-F, HLA-DPA1, HLA-DQA1, HLA-DQB1, HLA-DQB2, HLA-DRB1, and HLA-DRB5. In some embodiments, the iCAR comprises an scFv. In some embodiments, the scFv is selected from the group consisting of BB7.2, 3PF12, 3PF12/C4, 3PF12/F12, 3PF12/B11, W6/32, BBM.1,

SN66E3.1, SN66E3.2, SN66E.3, Ha5C2.A2, MWB1, MWB1-mod, Hz.BB7.2VH1-69 _A18VK, Hz.BB7.2VH1-69 (27,30)_A18, HzBB7.2VH1-69 (27,30,48) A18, Hz.BB7.2 VH1-69 (27,30,67)_A18, Hz.BB7.2 VH1-69 (27,30,69) _A18, Hz.BB7.2 VH1-69 (27,30,67,69)_A18, Hz.BB7.2 VH1-3_A18, Hz.BB7.2 VH1-3(48)_ A18, Hz.BB7.2 VH1-3(67)_A18, Hz.BB7.2 VH1-3(69)_A18, Hz.BB7.2 VH1-3(71)_A18, Hz.BB7.2 VH1-3(73)_A18, and MWB1.2, . In some embodiments, the scFv has the VL and VH sequences of BB7.2 (SEQ ID NOs: 37 and 38). In some embodiments, the scFv has the VL and VH sequences of 3PF12/C4 (SEQ ID NOs: 39 and 40). In some embodiments, the scFv has the VL and VH sequences of 3PF12/F12 (SEQ ID NOs: 41 and 42). In some embodiments, the scFv has the VL and VH sequences of 3PF12/B11 (SEQ ID NOs: 43 and 44). In some embodiments, the scFv has the VL and VH sequences of W6/32 (SEQ ID NOs: 45 and 46). In some embodiments, the scFv has the VL and VH sequences of BBM.1 (SEQ ID NOs: 47 and 48). In some embodiments, the scFv has the VL and VH sequences of SN66E3.1 (SEQ ID NOs: 49 and 50). In some embodiments, the scFv has the VL and VH sequences of Ha5C2.A2 (SEQ ID NOs: 51 and 52). In some embodiments, the scFv has the VL and VH sequences of MWB1 (SEQ ID NOs: 53 and 54). In some embodiments, the scFv has the VL and VH sequences of MWB1.1 (SEQ ID NOs: 55 and 56). In some embodiments, the scFv has the VL and VH sequences of Hz.BB7.2 VH1-69 _A18VK (SEQ ID NOs: 57 and 58). In some embodiments, the scFv has the VL and VH sequences of Hz.BB7.2 VH1-69 (27,30)_A18 (SEQ ID NOs: 59 and 60). In some embodiments, the scFv has the VL and VH sequences of Hz.BB7.2 VH1-69 (27,30,48) _ A18 (SEQ ID NOs: 61 and 62). In some embodiments, the scFv has the VL and VH sequences of Hz.BB7.2 VH1-69 (27,30,67)_A18 (SEQ ID NOs: 63 and 64). In some embodiments, the scFv has the VL and VH sequences of Hz.BB7.2 VH1-69 (27,30,69) _A18 (SEQ ID NOs: 65 and 66). In some embodiments, the scFv has the VL and VH sequences of Hz.BB7.2 VH1-69 (27,30,67,69)_A18 (SEQ ID NOs: 67 and 68). In some embodiments, the scFv has the VL and VH sequences of Hz.BB7.2 VH1-3_A18 (SEQ ID NOs: 69 and 70). In some embodiments, the scFv has the VL and VH sequences of Hz.BB7.2 VH1-3(48)_ A18 (SEQ ID NOs: 71 and 72). In some embodiments, the scFv has the VL and VH sequences of Hz.BB7.2 VH1-3(67)_A18 (SEQ ID NOs: 73 and 74). In some embodiments, the scFv has the VL and VH sequences of Hz.BB7.2 VH1-3(69)_A18 (SEQ ID NOs: 75 and 76). In some embodiments, the scFv has the VL and VH sequences of Hz.BB7.2 VH1-3(71)_A18 (SEQ ID NOs: 77 and 78). In some embodiments, the scFv has the VL and VH sequences of Hz.BB7.2 VH1-3(73)_A18 (SEQ ID NOs: 79 and 80). In some embodiments, the scFv has the VL and VH sequences of MWB1.2 (SEQ ID NOs: 163 and 164). In some embodiments, the scFv has

the VL and VH sequences of SN66E3.2 (SEQ ID NOs: 165 and 166). In some embodiments, the scFv has the VL and VH sequences of SN66E3.3 (SEQ ID NOs: 283 and 284) In some embodiments, the scFv is BB7.2 (SEQ ID NO:167). In some embodiments, the scFv is 3PF12 (SEQ ID NO:168). In some embodiments, the scFv is SN66E3.1 (SEQ ID NO:169). In some embodiments, the scFv is SN66E3.2 (SEQ ID NO:285). In some embodiments, the scFv is SN66E3.3 (SEQ ID NO:286). In some embodiments, the scFv is Hz BB7.2.1 (SEQ ID NO:287). In some embodiments, the scFv is HzBB7.2.2 (SEQ ID NO:288). In some embodiments, the scFv is MWB1.1 (SEQ ID NO:273). In some embodiments, the scFv is MWB1.2 (SEQ ID NO:274). In some embodiments, the scFv is 3PF12/C4. In some embodiments, the scFv is 3PF12/F12. In some embodiments, the scFv is 3PF12/B11. In some embodiments, the scFv is W6/32. In some embodiments, the scFv is BBM.1. In some embodiments, the scFv is Ha5C2.A2. In some embodiments, the scFv is MWB1. In some embodiments, the scFv is MWB1-mod. In some embodiments, the scFv is BB7.2. In some embodiments, the scFv is 3PF12. In some embodiments, the scFv is SN66E3.1. In some embodiments, the scFv is SN66E3.2. In some embodiments, the scFv is SN66E3.3. In some embodiments, the scFv is Hz BB7.2.1. In some embodiments, the scFv is HzBB7.2.2. In some embodiments, the scFv is MWB1.1. In some embodiments, the scFv is MWB1.2. In some embodiments, the scFv is Hz.BB7.2 VH1-69 _A18VK. In some embodiments, the scFv is Hz.BB7.2 VH1-69 (27,30)_A18. In some embodiments, the scFv is Hz.BB7.2 VH1-69 (27,30,48) _ A18. In some embodiments, the scFv is Hz.BB7.2 VH1-69 (27, 30, 67)_A18. In some embodiments, the scFv is Hz.BB7.2 VH1-69 (27, 30, 69) _A18. In some embodiments, the scFv is Hz.BB7.2 VH1-69 (27, 30, 67, 69)_A18. In some embodiments, the scFv is Hz.BB7.2VH1-3_A18. In some embodiments, the scFv is Hz.BB7.2 VH1-3(48)_ A18. In some embodiments, the scFv is Hz.BB7.2 -3(67)_A18. In some embodiments, the scFv is Hz.BB7.2 VH1-3(69)_A18. In some embodiments, the scFv is Hz.BB7.2 VH1-3(71)_A18. In some embodiments, the scFv is Hz.BB7.2 VH1-3(73)_A18. In some embodiments, the scFv is MWB1.2. In some embodiments, the scFv is SN66E3.2. In some embodiments, the scFv is MWB1.1. In some embodiments, the scFv is MWB1.2. In some embodiments, the scFv comprises Hz.BB7.2 heavy chain Hz.BB7.2VH1-69. In some embodiments, the scFv comprises Hz.BB7.2 Heavy chain Hz.BB7.2VH1-69(H27Y, H30S. In some embodiments, the scFv comprises Hz.BB7.2 heavy chain HZ.BB7.2VH1-69(H27Y, H30S, H48I). In some embodiments, the scFv comprises Hz.BB7.2 Heavy chain Hz.BB7.2VH1-69(H27Y, H30S, H67T). In some embodiments, the scFv comprises Hz. BB7.2 Heavy chain Hz.BB7.2VH1-69 (H27Y, H30S, H69L). In some embodiments, the scFv comprises Hz.BB7.2 Heavy Chain

HZ.BB7.2VH1-69 (H27Y, H30S, VH67T, H69L). In some embodiments, the scFv comprises Hz.BB7.2 Heavy Chain Hz.BB7.2 VH1-3. In some embodiments, the scFv comprises Hz.BB7.2 Heavy Chain Hz.BB7.2 VH1-3 (H48I). In some embodiments, the scFv comprises Hz.BB7.2 Heavy Chain VH1-3 (H67T). In some embodiments, the scFv comprises Hz.BB7.2 Heavy Chain Hz.BB7.2 VH1-3 (H69L). In some embodiments, the scFv comprises Hz.BB7.2 Heavy Chain Hz.BB7.2 VH1-3 (H71A). In some embodiments, the scFv comprises Hz.BB7.2 Heavy Chain Hz.BB7.2 VH1-3 (H73A). In some embodiments, the scFv comprises Hz.BB7.2 Light chain VKA18. The 6 CDR sequences for the variable heavy and variable light chains are shown in bold and underline in Table 2 for each sequence, also referred to as vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3. In some embodiments, the iCAR comprises the 6 CDR sequences for the variable heavy and variable light chains as show in bold and underline in Table 2 for each sequence, also referred to as vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3. In some embodiments, the iCAR comprises the 6 CDR sequences for the variable heavy and variable light chains as show in bold and underline in Table 2 for each sequence, also referred to as vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3, wherein each CDR individually optionally comprises one more substitutions. In some embodiments, the iCAR comprises the 6 CDR sequences for the variable heavy and variable light chains as show in bold and underline in Table 2 for each sequence, also referred to as vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3, wherein each CDR individually optionally comprises 1, 2, and/or 3 substitutions. In some embodiments, the iCAR comprises the 6 CDR sequences for the variable heavy and variable light chains as show in bold and underline in Table 2 for each sequence, also referred to as vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3, wherein each CDR individually comprises one more substitutions. In some embodiments, the iCAR comprises the 6 CDR sequences for the variable heavy and variable light chains as show in bold and underline in Table 2 for each sequence, also referred to as vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2, and vlCDR3, wherein each CDR individually comprises 1, 2, and/or 3 substitutions.

Table 2: iCAR vh, vl, and scFv sequences

Sequence Information	**SEQ ID NO**	**Amino acid sequence**
BB7.2 variable light chain	37	DVLMTQTPLSLPVSLGDQVSISC**RSSQSIVHSNGNTYLE** WYLQKPGQSPKLLIY**KVSNRFS**GVPDRFSGSGSGTDFTL KISRVEAEDLGVYYC**FQGSHVPRT**FGGGTKLEIK

BB7.2 variable heavy chain	38	QVQLQQSGPELVKPGASVKMSCKASGYTFT**SYHIQ**WV KQRPGQGLEWIG**WIYPGDGSTQYNEKFKG**KTTLTADK SSSTAYMLLSSLTSEDSAIYFCAR**EGTYYAMDY**WGQGT SVTVSS
3PF12/C4 variable light chain	39	DIVMTQSPSFLSASVGDRVTITC**RASHGINNYLA**WYQQ KPGKAPKLLIY**AASTLQS**GVPSRFSGSGSGTEFTLTISSL QPEDFATYYC**QQYDSYPPT**FGRGTKVEIK
3PF12/C4 variable heavy chain	40	QVQLVQSGGGVVQPGGSLRVSCAASGVTLS**DYGMH**W VRQAPGKGLEWMA**FIRNDGSDKYYADSVKG**RFTISRD NSKKTVSLQMSSLRAEDTAVYYCAK**NGESGPLDYWYF DL**WGRGTLVTVSS
3PF12/F12 variable light chain	41	DVVMTQSPSSLSASVGDRVTITC**QASQDISNYLN**WYQQ KPGKAPKLLIY**DASNLET**GVPSRFSGSGSGTDFTFTISSL QPEDFATYYC**QQYSSFPLT**FGGGTKVDIK
3PF12/F12 variable heavy chain	42	QVQLVQSGGGVVQPGGSLRVSCAASGVTLS**DYGMH**W VRQAPGKGLEWMA**FIRNDGSDKYYADSVKG**RFTISRD NSKKTVSLQMSSLRAEDTAVYYCAK**NGESGPLDYWYF DL**WGRGTLVTVSS
3PF12/B11 variable light chain	43	DVVMTQSPSSLSASVGDRVTITC**QASQDISNYLN**WYQQ KPGKAPKLLIY**DASNLET**GVPSRFSGSGSGTDFTFTISSL QPEDIATYYC**QQYDNLPPT**FGGGTKLEIV
3PF12/B11 variable heavy chain	44	QVQLVQSGGGVVQPGGSLRVSCAASGVTLS**DYGMH**W VRQAPGKGLEWMA**FIRNDGSDKYYADSVKG**RFTISRD NSKKTVSLQMSSLRAEDTAVYYCAK**NGESGPLDYWYF DL**WGRGTLVTVSS
W6/32 variable light chain	45	SIVMTQTPKFLLVSAGDRVTITC**KASQSVSNDVA**WYQQ KPGQSPKLLIY**YASNRYT**GVPDRFTGSGYGTDFTFTISTV QAEDLAVYFC**QQDYSSPPWT**FGGGTKLEIR
W6/32 variable heavy chain	46	QVQLKQSGPGLVQPSQSLSLTCTVSGFSLT**SYGVH**WVR QPPGKGLEWLG**VIWSGGSTDYNAAFIS**RLSIRKDNSKS QVFFKMNSLQADDTAIYYCAR**TFTTSTSAWFAY**WGQG TLVTVSA
BBM.1 variable light chain	47	DIQMTQSPASQSASLGESVTITC**LASQTIGTWLA**WYQQ KPGKSPQLLIY**AATSLAD**GVPSRFSGSGSGTKFSLKIRTL QAEDFVSYYC**QQLYSKPYT**FGGGTKLEIK
BBM.1 variable heavy chain	48	EVQLQQSGAELVKPGASVKLSCTPSGFNVK**DTYIH**WVK QRPKQGLEWIG**RIDPSDGDIKYDPKFQG**KATITADTSSN TVSLQLSSLTSEDTAVYYCAR**WFGDYGAMNY**WGQGTS VTVSS
SN66E3.1 variable light chain	49	DIVMTQSPDSLAVSLGERATISC**KSSQSVLYSSNNKNYL A**WYQQKLGQPPKLLIY**WASTRES**GVPDRFSGSGSGTNF TLTISSLQAENVAVYYC**QQYYGTPFT**FGGGTKVEIK

SN66E3.1 variable heavy chain	50	QVQLVQSGAEVKKPGASVKVSCKASGYTFT**DYYLH**WV RQAPGQGLEWMG**WINPYTGGTNYAQKFQG**RVTMTR DASISTVYMELSGLTSDDTAVHFCAR**AGASYYDFWSG WVFDY**WGQGTLVTVSS
Ha5C2.A2 variable light chain	51	DIQMTQSPSSLSASVGDRVTITCR**ASQSISTYLN**WYQQK PGKAPKLLIY**AASSLQS**GVPSRFSGSGSGTDFTLTISSLQP EDFATYQC**QQSYSTPFTF**GGGTKVEIK
Ha5C2.A2 variable heavy chain	52	QVQLQESGPGLVKPSETLSLTCTVSGGSIS**SYYWS**WIRQ PAGKGLEWIG**RIYISGGTNYNPSLKS**RVTMSVDTSKNQ VSLKLSSVTAADTAVYYCAR**DILGGVSGWSHYGMDV** WGQGTTVTVSS
MWB1 variable light chain	53	QSALTQPPSASGSPGQSVTISC**TGTSSDVGGYKYVS**WY QHHPDKAPKLMIY**EVNKRPS**GVPDRFSGSKSDNTASLT VSGLQAEDEADYYC**SSYAGSNNWV**FGGGTKLTVL
MWB1 variable heavy chain	54	QVQLVESGGGVVQPGGSLRLSCAASGFTFS**TYGMH**WV RQAPGKGLEWAA**SVSYDGSNKYYADSGQG**RFTISRDTS MNSLYLQVNSLRDETAVYYCAI**GIYGAYSFDY**WGQGT LVTVSS
MWB1.1 (MWB1.1) variable light chain	55	QSALTQPPSASGSPGQSVTISC**TGTSSDVGGYKYVS**WY QHHPDKAPKLMIY**EVNKR**PSGVPDRFSGSKSDNTASLT VSGLQAEDEADYYC**SSYAGSNNWV**FGGGTKLTVL
MWB1.1(MWB1 .1) variable heavy chain	56	QVQLVESGGGVVQPGGSLRLSCAASGFTFS**TYGMH**WV RQAPGKGLEWVA**SISYDGSNKYYADSGQG**RFTISRDTS KNSLYLQMNSLRAEDTAVYYCAI**GIYGAYSFDY**WGQG TLVTVSS
Hz.BB7.2 _A18VK variable light chain	57	DVVMTQTPLSLSVTPGQPASISC**RSSQSIVHSNGNTYLE** WYLQKPGQSPQLLIY**KVSNRFS**GVPDRFSGSGSGTDFTL KISRVEAEDVGVYYC**FQGSHVPRT**FGGGTKVEIK
Hz. BB7.2 VH1-69 variable heavy chain	58	QVQLVQSGAEVKKPGSSVKVSCKASGGTFS**SYHIQ**WVR QAPGQGLEWMG**WIYPGDGSTQYNEKFKG**RVTITADK STSTAYMELSSLRSEDTAVYYCAR**EGTYYAMDY**WGQG TLVTVSS
Hz.BB7.2 VH1-69 (27,30) variable light chain	59	DVVMTQTPLSLSVTPGQPASISC**RSSQSIVHSNGNTYLE** WYLQKPGQSPQLLIY**KVSNRFS**GVPDRFSGSGSGTDFTL KISRVEAEDVGVYYC**FQGSHVPRT**FGGGTKVEIK
Hz.BB7.2 Heavy chain VH1-69(H27Y, H30S)	60	QVQLVQSGAEVKKPGSSVKVSCKASGYTFT**SYHIQ**WVR QAPGQGLEWMG**WIYPGDGSTQYNEKFKG**RVTITADK STSTAYMELSSLRSEDTAVYYCAR**EGTYYAMDY**WGQG TLVTVSS
HZ.BB7.2VH1-69 (27,30,48) _	61	DVVMTQTPLSLSVTPGQPASISC**RSSQSIVHSNGNTYLE** WYLQKPGQSPQLLIY**KVSNRFS**GVPDRFSGSGSGTDFTL KISRVEAEDVGVYYC**FQGSHVPRT**FGGGTKVEIK

A18 variable light chain		
Hz.BB7.2 heavy chain VH1-69(H27Y,H30S, H48I))	62	QVQLVQSGAEVKKPGSSVKVSCKASGYTFT**SYHIQ**WVR QAPGQGLEWIG**WIYPGDGSTQYNEKFKG**RVTITADKS TSTAYMELSSLRSEDTAVYYCAR**EGTYYAMDY**WGQGT LVTVSS
Hz.BB7.2 VH1-69 (27,30,67)_A18 variable light chain	63	DVVMTQTPLSLSVTPGQPASISC**RSSQSIVHSNGNTYLE** WYLQKPGQSPQLLIY**KVSNRFS**GVPDRFSGSGSGTDFTL KISRVEAEDVGVYYC**FQGSHVPRT**FGGGTKVEIK
Hz.BB7.2 Heavy chain VH1-69(H27Y,H30S, H67T))	64	QVQLVQSGAEVKKPGSSVKVSCKASGYTFT**SYHIQ**WVR QAPGQGLEWMG**WIYPGDGSTQYNEKFKG**RTTITADKS TSTAYMELSSLRSEDTAVYYCAR**EGTYYAMDY**WGQGT LVTVSS
HZ.BB7.2VH1-69 (27,30,69) _A18 variable light chain	65	DVVMTQTPLSLSVTPGQPASISC**RSSQSIVHSNGNTYLE** WYLQKPGQSPQLLIY**KVSNRFS**GVPDRFSGSGSGTDFTL KISRVEAEDVGVYYC**FQGSHVPRT**FGGGTKVEIK
Hz. BB7.2 Heavy chain VH1-69 (H27Y,H30S,H69L))	66	QVQLVQSGAEVKKPGSSVKVSCKASGYTFT**SYHIQ**WVR QAPGQGLEWMG**WIYPGDGSTQYNEKFKG**RVTLTADK STSTAYMELSSLRSEDTAVYYCAR**EGTYYAMDY**WGQG TLVTVSS
Hz.BB7.2 VH1-69 (27,30,67,69)_A18 variable light chain	67	DVVMTQTPLSLSVTPGQPASISC**RSSQSIVHSNGNTYLE** WYLQKPGQSPQLLIY**KVSNRFS**GVPDRFSGSGSGTDFTL KISRVEAEDVGVYYC**FQGSHVPRT**FGGGTKVEIK
Hz.BB7.2 Heavy Chain VH1-69 (H27Y, H30S, VH67T,H69L))	68	QVQLVQSGAEVKKPGSSVKVSCKASGYTFT**SYHIQ**WVR QAPGQGLEWMG**WIYPGDGSTQYNEKFKG**RTTLTADK STSTAYMELSSLRSEDTAVYYCAR**EGTYYAMDY**WGQG TLVTVSS
Hz.BB7.2VH1-3_A18 variable light chain	69	DVVMTQTPLSLSVTPGQPASISC**RSSQSIVHSNGNTYLE** WYLQKPGQSPQLLIY**KVSNRFS**GVPDRFSGSGSGTDFTL KISRVEAEDVGVYYC**FQGSHVPRT**FGGGTKVEIK
Hz.BB7.2 Heavy Chain VH1-3)	70	QVQLVQSGAEVKKPGASVKVSCKASGYTFT**SYHIQ**WV RQAPGQRLEWMG**WIYPGDGSTQYNEKFK**GRVTITRDT SASTAYMELSSLRSEDTAVYYCAR**EGTYYAMDY**WGQG TLVTVSS
Hz.BB7.2VH1-3(48)_ A18 variable light chain	71	DVVMTQTPLSLSVTPGQPASISC**RSSQSIVHSNGNTYLE** WYLQKPGQSPQLLIY**KVSNRFS**GVPDRFSGSGSGTDFTL KISRVEAEDVGVYYC**FQGSHVPRT**FGGGTKVEIK

Hz.BB7.2 Heavy Chain VH1-3 (H48I))	72	QVQLVQSGAEVKKPGASVKVSCKASGYTFT**SYHIQ**WV RQAPGQRLEWIG**WIYPGDGSTQYNEKFK**GRVTITRDTS ASTAYMELSSLRSEDTAVYYCAR**EGTYYAMDY**WGQG TLVTVSS
Hz.BB7.2VH1-3(67)_A18 variable light chain (Hz.BB7.2 Light chain VKA18)	73	DVVMTQTPLSLSVTPGQPASISC**RSSQSIVHSNGNTYLE** WYLQKPGQSPQLLIY**KVSNRFS**GVPDRFSGSGSGTDFTL KISRVEAEDVGVYYC**FQGSHVPRT**FGGGTKVEIK
Hz.BB7.2 Heavy Chain VH1-3 (H67T))	74	QVQLVQSGAEVKKPGASVKVSCKASGYTFT**SYHIQ**WV RQAPGQRLEWMG**WIYPGDGSTQYNEKFK**GRTTITRDT SASTAYMELSSLRSEDTAVYYCAR**EGTYYAMDY**WGQG TLVTVSS
Hz.BB.2VH1-3(69)_A18 variable light chain	75	DVVMTQTPLSLSVTPGQPASISC**RSSQSIVHSNGNTYLE** WYLQKPGQSPQLLIY**KVSNRFS**GVPDRFSGSGSGTDFTL KISRVEAEDVGVYYC**FQGSHVPRT**FGGGTKVEIK
Hz.BB7.2 Heavy Chain VH1-3 (H69L))	76	QVQLVQSGAEVKKPGASVKVSCKASGYTFT**SYHIQ**WV RQAPGQRLEWMG**WIYPGDGSTQYNEKFK**GRVTLTRD TSASTAYMELSSLRSEDTAVYYCAR**EGTYYAMDY**WGQ GTLVTVSS
Hz.BB7.2VH1-3(71)_A18 variable light chain	77	DVVMTQTPLSLSVTPGQPASISC**RSSQSIVHSNGNTYLE** WYLQKPGQSPQLLIY**KVSNRFS**GVPDRFSGSGSGTDFTL KISRVEAEDVGVYYC**FQGSHVPRT**FGGGTKVEIK
Hz. BB7.2 VH1-3(71)_ variable heavy chain	78	QVQLVQSGAEVKKPGASVKVSCKASGYTFT**SYHIQ**WV RQAPGQRLEWMG**WIYPGDGSTQYNEKFK**GRVTITADT SASTAYMELSSLRSEDTAVYYCAR**EGTYYAMDY**WGQG TLVTVSS
Hz.BB7.2VH1-3(73)_A18 variable light chain	79	DVVMTQTPLSLSVTPGQPASISC**RSSQSIVHSNGNTYLE** WYLQKPGQSPQLLIY**KVSNRFS**GVPDRFSGSGSGTDFTL KISRVEAEDVGVYYC**FQGSHVPRT**FGGGTKVEIK
Hz.BB7.2VH1-3(73)_A18 variable heavy chain	80	QVQLVQSGAEVKKPGASVKVSCKASGYTFT**SYHIQ**WV RQAPGQRLEWMG**WIYPGDGSTQYNEKFKG**RVTITRD KSASTAYMELSSLRSEDTAVYYCAR**EGTYYAMDY**WGQ GTLVTVSS
MWB1.2 variable light chain	163	QSALTQPPSASGSPGQSVTISC**TGTSSDVGGYKYVS**WY QQHPGKAPKLMIY**EVNKRPS**GVPDRFSGSKSGNTASLT VSGLQAEDEADYYC**SSYAGSNNWV**FGGGTKLTVL
MWB1.2 variable heavy chain	164	QVQLVESGGGVVQPGGSLRLSCAASGFTFS**TYGMH**WV RQAPGKGLEWVA**SISYDGSNKYYADSGQG**RFTISRDTS

		KNSLYLQMNSLRAEDTAVYYCAI**GIYGAYSFDY**WGQG TLVTVSS
SN66E3.2 variable light chain	165	DIVMTQSPDSLAVSLGERATISC**KSSQSVLYSSNNKNYL AW**YQQKPGQPPKLLIY**WASTRES**GVPDRFSGSGSGTDF TLTISSLQAEDVAVYYC**QQYYGTPFTF**GGGTKVEIK
SN66E3.2 variable heavy chain	166	QVQLVQSGAEVKKPGASVKVSCKASGYTFT**DYYLH**WV RQAPGQGLEWMG**WINPYTGGTNYAQKFQGR**VTMTR DTSISTAYMELSGLTSDDTAVYYC**ARAGASYYDFWSG WVFDY**WGQGTLVTVSS
MWB1.1 scFvVH_VL	273	QVQLVESGGGVVQPGGSLRLSCAASGFTFS**TYGMH**WV RQAPGKGLEWVA**SISYDGSNKYYADSGQG**RFTISRDTS KNSLYLQMNSLRAEDTAVYYCAI**GIYGAYSFDY**WGQG TLVTVSSGGGGSGGGGSGGGGSQSALTQPPSASGSPGQS VTISC**TGTSSDVGGYKYVS**WYQHHPDKAPKLMIY**EVN KRPS**GVPDRFSGSKSDNTASLTVSGLQAEDEADYYC**SSY AGSNNWV**FGGGTKLTVL
MWB1.2scFvVH_VL	274	QVQLVESGGGVVQPGGSLRLSCAASGFTFS**TYGMH**WV RQAPGKGLEWVA**SISYDGSNKYYADSGQG**RFTISRDTS KNSLYLQMNSLRAEDTAVYYCAI**GIYGAYSFDY**WGQG TLVTVSSGGGGSGGGGSGGGGSQSALTQPPSASGSPGQS VTISC**TGTSSDVGGYKYVS**WYQQHPGKAPKLMIY**EVN KRPS**GVPDRFSGSKSGNTASLTVSGLQAEDEADYYC**SSY AGSNNWV**FGGGTKLTVL
SN66E3.3 Variable Light chain	283	DIVMTQSPDSLAVSLGERATISC**KSSQSVLYSSNNKNYL A**WYQQKPGQPPKLLIY**WASTRES**GVPDRFSGSGSGTDF TLTISSLQAEDVAVYYC**QQYYGTPFT**FGGGTKVEIK
SN66E3.3 variable Heavy chain	284	QVQLVQSGAEVKKPGASVKVSCKASGYTFT**DYYLH**WV RQAPGQGLEWMG**WINPYTGGTNYAQKFQG**RVTMTRD TSISTAYMELSRLRSEDTAVYYCAR**AGASYYDFWSGW VFDY**WGQGTLVTVSS

[0402] In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH.

[0403] In some embodiments, the iCAR scFv comprises a linker that covalently connects the VH and the VL to form the iCAR scFv.

[0404] In some embodiments, the heavy and light chains of the scFv are covalently connected via a linker. In some embodiments, the linker is a gly-ser polypeptide linker, *i.e.*, a peptide that consists of glycine and serine residues. Exemplary gly-ser polypeptide linkers comprise the amino acid sequence $Ser(Gly_4Ser)_n$, as well as $(Gly_4Ser)_n$ and/or $(Gly_4Ser_3)_n$. In some embodiments, n=l. In some embodiments, n=2. In some embodiments, n=3, *i.e.*, $Ser(Gly_4Ser)_3$. In some embodiments, n=4, *i.e.*, $Ser(Gly_4Ser)_4$. In some embodiments, n=5. In some

embodiments, n=6. In some embodiments, n=7. In some embodiments, n=8. In some embodiments, n=9. In some embodiments, n=10. Another exemplary gly-ser polypeptide linker comprises the amino acid sequence $Ser(Gly_4Ser)_n$. In some embodiments, n=l. In some embodiments, n=2. In some embodiments, n=3. In another embodiment, n=4. In some embodiments, n=5. In some embodiments, n=6. Another exemplary gly-ser polypeptide linker comprises $(Gly_4Ser)_n$. In some embodiments, n=l. In some embodiments, n=2. In some embodiments, n=3. In some embodiments, n=4. In some embodiments, n=5. In some embodiments, n=6. Another exemplary gly-ser polypeptide linker comprises $(Gly_3Ser)_n$. In some embodiments, n=l. In some embodiments, n=2. In some embodiments, n=3. In some embodiments, n=4. In another embodiment, n=5. In yet another embodiment, n=6. Another exemplary gly-ser polypeptide linker comprises $(Gly_4Ser_3)_n$. In some embodiments, n=l. In some embodiments, n=2. In some embodiments, n=3. In some embodiments, n=4. In some embodiments, n=5. In some embodiments, n=6. Another exemplary gly-ser polypeptide linker comprises $(Gly_3Ser)_n$. In some embodiments, n=l. In some embodiments, n=2. In some embodiments, n=3. In some embodiments, n=4. In another embodiment, n=5. In yet another embodiment, n=6.

[0405] In some embodiments, the iCAR comprises a GS based linker sequence, connecting the VH and VL or the VL and VH to form the scFv. In some embodiments, the GS linker comprises GGGGS (SEQ ID NO:153). In some embodiments, the iCAR comprises a Whitlow linker sequence, e.g., GSTSGSGKPGSGEGSTKG (SEQ ID NO:82). In some embodiments, the iCAR comprises the Vh and Vl sequences in the Vh-Vl orientation. In some embodiments, the iCAR comprises the Vh and Vl sequences in the Vl-Vh orientation. In some embodiments, the iCAR comprises a linker between the Vh and Vl sequences. In some embodiments, the iCAR does not comprise a linker between the Vh and Vl sequences.

Table 3: iCAR linkers

Sequence Information	SEQ ID NO	Amino acid sequence
(G4S)X3 linker	81	GGGGSGGGGSGGGGS
Whitlow linker	82	GSTSGSGKPGSGEGSTKG
PD1 linker	83	DFQWREKTPEPPVPCVPEQ
G4S	153	GGGGS

[0406] In some embodiments, the iCAR scFv comprises a linker. In some embodiments, the iCAR scFv is selected from the group consisting of BB7.2 scFv (SEQ ID NO: 167), 3PF12 scFv (SEQ ID NO: 168), SN66E3.1 scFv (SEQ ID NO: 169), SN66E3.2 scFv (SEQ ID NO:

285), SN66E3.3 scFv (SEQ ID NO: 286), Hz BB7.2.1 scFv (SEQ ID NO: 287), and Hz BB7.2.2 scFv (SEQ ID NO: 288). In some embodiments, the iCAR scFv is BB7.2 scFv (SEQ ID NO: 167). In some embodiments, the iCAR scFv is 3PF12 scFv (SEQ ID NO: 168). In some embodiments, the iCAR scFv is SN66E3.1 scFv (SEQ ID NO: 169). In some embodiments, the iCAR scFv is SN66E3.2 scFv (SEQ ID NO: 285). In some embodiments, the iCAR scFv is SN66E3.3 scFv (SEQ ID NO: 286). In some embodiments, the iCAR scFv is Hz BB7.2.1 scFv (SEQ ID NO: 287). In some embodiments, the iCAR scFv is Hz BB7.2.2 scFv (SEQ ID NO: 288).

Table 4: iCAR scFv sequences with linkers

Sequence Information	**SEQ ID NO**	**Amino acid sequence**
BB7.2 scFv	167	QVQLQQSGPELVKPGASVKMSCKASGYTFTSYHIQWVKQR PGQGLEWIGWIYPGDGSTQYNEKFKGKTTLTADKSSSTAY MLLSSLTSEDSAIYFCAREGTYYAMDYWGQGTSVTVSSGG GGSGGGGSGGGGSDVLMTQTPLSLPVSLGDQVSISCRSSQSI VHSNGNTYLEWYLQKPGQSPKLLIYKVSNRFSGVPDRFSGS GSGTDFTLKISRVEAEDLGVYYCFQGSHVPRTFGGGTKLEIK
3PF12 scFv	168	QVQLVQSGGGVVQPGGSLRVSCAASGVTLSDYGMHWVRQ APGKGLEWMAFIRNDGSDKYYADSVKGRFTISRDNSKKTV SLQMSSLRAEDTAVYYCAKNGESGPLDYWYFDLWGRGTL VTVSSGGGGSGGGGSGGGGSDIVMTQSPSFLSASVGDRVTI TCRASHGINNYLAWYQQKPGKAPKLLIYAASTLQSGVPSRF SGSGSGTEFTLTISSLQPEDFATYYCQQYDSYPPTFGRGTKV EIK
SN66E3.1 scFv	169	QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYYLHWVRQ APGQGLEWMGWINPYTGGTNYAQKFQGRVTMTRDASISTV YMELSGLTSDDTAVHFCARAGASYYDFWSGWVFDYWGQG TLVTVSSGGGGSGGGGSGGGGSDIVMTQSPDSLAVSLGERA TISCKSSQSVLYSSNNKNYLAWYQQKLGQPPKLLIYWASTR ESGVPDRFSGSGSGTNFTLTISSLQAENVAVYYCQQYYGTPF TFGGGTKVEIK
SN66E3.2 scFv	285	DIVMTQSPDSLAVSLGERATISCKSSQSVLYSSNNKNYLAW YQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISS LQAEDVAVYYCQQYYGTPFTFGGGTKVEIKGGGGSGGGGS GGGGSQVQLVQSGAEVKKPGASVKVSCKASGYTFTDYYLH WVRQAPGQGLEWMGWINPYTGGTNYAQKFQGRVTMTRD TSISTAYMELSGLTSDDTAVYYCARAGASYYDFWSGWVFD YWGQGTLVTVSS
SN66E3.3 scFv	286	DIVMTQSPDSLAVSLGERATISCKSSQSVLYSSNNKNYLAW YQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISS LQAEDVAVYYCQQYYGTPFTFGGGTKVEIKGGGGSGGGGS GGGGSQVQLVQSGAEVKKPGASVKVSCKASGYTFTDYYLH WVRQAPGQGLEWMGWINPYTGGTNYAQKFQGRVTMTRD

		TSISTAYMELSRLRSEDTAVYYCARAGASYYDFWSGWVFD YWGQGTLVTVSS
Hz BB7.2.1 scFv	287	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYHIQWVRQA PGQGLEWMGWIYPGDGSTQYNEKFKGRTTITADKSTSTAY MELSSLRSEDTAVYYCAREGTYYAMDYWGQGTLVTVSSG GGGSGGGGSGGGGSDVVMTQTPLSLSVTPGQPASISCRSSQ SIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGVPDRFSG SGSGTDFTLKISRVEAEDVGVYYCFQGSHVPRTFGGGTKVEI K
HzBB7.2.2 scFV	288	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYHIQWVRQA PGQRLEWIGWIYPGDGSTQYNEKFKGRVTITRDTSASTAYM ELSSLRSEDTAVYYCAREGTYYAMDYWGQGTLVTVSSGGG GSGGGGSGGGGSDVVMTQTPLSLSVTPGQPASISCRSSQSIV HSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGVPDRFSGSG SGTDFTLKISRVEAEDVGVYYCFQGSHVPRTFGGGTKVEIK

[0407] In some embodiments, the iCAR scFv linker is a gly-ser polypeptide linker, *i.e.*, a peptide that consists of glycine and serine residues. Exemplary gly-ser polypeptide linkers comprise the amino acid sequence $Ser(Gly_4Ser)_n$, as well as $(Gly_4Ser)_n$ and/or $(Gly_4Ser_3)_n$. In some embodiments, n=l. In some embodiments, n=2. In some embodiments, n=3, *i.e.*, $Ser(Gly_4Ser)_3$. In some embodiments, n=4, *i.e.*, $Ser(Gly_4Ser)_4$. In some embodiments, n=5. In some embodiments, n=6. In some embodiments, n=7. In some embodiments, n=8. In some embodiments, n=9. In some embodiments, n=10. Another exemplary gly-ser polypeptide linker comprises the amino acid sequence $Ser(Gly_4Ser)_n$. In some embodiments, n=l. In some embodiments, n=2. In some embodiments, n=3. In another embodiment, n=4. In some embodiments, n=5. In some embodiments, n=6. Another exemplary gly-ser polypeptide linker comprises $(Gly_4Ser)_n$. In some embodiments, n=l. In some embodiments, n=2. In some embodiments, n=3. In some embodiments, n=4. In some embodiments, n=5. In some embodiments, n=6. Another exemplary gly-ser polypeptide linker comprises $(Gly_3Ser)_n$. In some embodiments, n=l. In some embodiments, n=2. In some embodiments, n=3. In some embodiments, n=4. In another embodiment, n=5. In yet another embodiment, n=6. Another exemplary gly-ser polypeptide linker comprises $(Gly_4Ser_3)_n$. In some embodiments, n=l. In some embodiments, n=2. In some embodiments, n=3. In some embodiments, n=4. In some embodiments, n=5. In some embodiments, n=6. Another exemplary gly-ser polypeptide linker comprises $(Gly_3Ser)_n$. In some embodiments, n=l. In some embodiments, n=2. In some embodiments, n=3. In some embodiments, n=4. In another embodiment, n=5. In yet another embodiment, n=6.

2. iCAR portion: Hinge domain

[0408] In some embodiments, the bicistronic construct comprises an iCAR portion comprising a hinge domain component. In some embodiments, the hinge domain comprises a hinge selected from the group consisting of a PD-1 hinge domain, a CD28 hinge domain, and a CD8 hinge domain (including a CD8a hinge domain) a LIR1 Ig3-4 hinge domain, a LIR1 Ig-4 hinge domain, a LIR1 52 aa hinge domain, a LIR1 36 aa hinge domain, a LIR1 30 aa hinge domain, a LIR1 8 aa hinge domain, a CD33 hinge domain, and a KIR2DL1 hinge domain. In some embodiments, the hinge domain is a PD-1 hinge (SEQ ID NO: 86). In some embodiments, the hinge domain is a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the vector comprises a CD8 hinge domain. In some embodiments, the vector comprises a CD8a hinge domain (SEQ ID NO:84). In some embodiments, the vector comprises aLIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the vector comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the vector comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the vector comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the vector comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the vector comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the vector comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the vector comprises aKIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) (SEQ ID NO: 295).

Table 5: iCAR hinge sequences

Sequence Information	**SEQ ID NO**	**Amino acid sequence**
CD8 alpha	84	TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTR GLDFACD
IgG4	449	ESKYGPPCPPCP
CD28	85	IEVMYPPPYLDNEKSNGTIIHVKGKHLCPSPLFPGPSKP
PD-1	86	TERRAEVPTAHPSPSPRPAGQFQTLV
LIR1 Ig3-4	87	VSKKPSLSVQPGPIVAPEETLTLQCGSDAGYNRFVLYK DGERDFLQLAGAQPQAGLSQANFTLGPVSRSYGGQY RCYGAHNLSSEWSAPSDPLDILIAGQFYDRVSLSVQPG PTVASGENVTLLCQSQGWMQTFLLTKEGAADDPWRL

		RSTYQSQKYQAEFPMGPVTSAHAGTYRCYGSQSSKP YLLTHPSDPLELVVSGPSGGPSSPTTGPTSTSGPEDQPL TPTGSDPQSGLGRHLGV
LIR1 Ig-4	88	PLDILIAGQFYDRVSLSVQPGPTVASGENVTLLCQSQG WMQTFLLTKEGAADDPWRLRSTYQSQKYQAEFPMG PVTSAHAGTYRCYGSQSSKPYLLTHPSDPLELVVSGPS GGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGV
LIR1 52 aa	89	HPSDPLELVVSGPSGGPSSPTTGPTSTSGPEDQPLTPTG SDPQSGLGRHLGV
LIR1 36 aa	90	PSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGV
LIR1 30 aa	91	GPTSTSGPEDQPLTPTGSDPQSGLGRHLGV
LIR1 8 aa	92	GLGRHLGV
CD33	93	LNVTYVPQNPTTGIFPGDGSGKQETRAGVVH
KIR2DL1	94	PYEWSKSSDPLLVSVTGNPSNSWPSPTEPSSKTGNPRH LH
LIR1 26 aa	289	TSGPEDQPLTPTGSDPQSGLGRHLGV
PD-1 (47)	290	GAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRP AGQFQTLV
PD-1 (42)	291	APKAQIKESLRAELRVTERRAEVPTAHPSPSPRPAGQF QTLV
PD-1 (36)	292	KESLRAELRVTERRAEVPTAHPSPSPRPAGQFQTLV
PD-1 (30)	293	ELRVTERRAEVPTAHPSPSPRPAGQFQTLV
PD-1 (26)	294	TERRAEVPTAHPSPSPRPAGQFQTLV
PD-1 (20)	295	VPTAHPSPSPRPAGQFQTLV

3. iCAR portion: transmembrane domain

[0409] In some embodiments, the bicistronic construct comprises an iCAR portion comprising a transmembrane (TM) domain component. In some embodiments, the TM domain comprises a TM domain selected from the group consisting of a PD-1 TM domain, a CD28 TM domain, a CD8 TM domain (including a CD8a TM domain), a LIR1 TM domain, a CD33 TM domain, and a KIR2DL1 TM domain. In some embodiments, the TM domain is a PD-1 TM domain (SEQ ID NO:97). In some embodiments, the TM domain is a CD28 TM domain (SEQ ID NO:96). In some embodiments, the vector comprises a CD8 TM domain. In some embodiments, the vector comprises a CD8a TM domain (SEQ ID NO:95). In some embodiments, the vector comprises a LIR1 TM domain (SEQ ID NO:98). In some embodiments, the vector comprises a CD33 TM domain (SEQ ID NO:99). In some embodiments, the vector comprises a KIR2DL1 TM domain (SEQ ID NO:100).

Table 6: iCAR transmembrane sequences

Sequence Information	**SEQ ID NO**	**Amino acid sequence**
CD8 alpha	95	IYIWAPLAGTCGVLLLSLVITLYC

CD28	96	FWVLVVVGGVLACYSLLVTVAFIIFWV
PD-1	97	VGVVGGLLGSLVLLVWVLAVI
LIR1	98	VIGILVAVILLLLLLLLLFLI
CD33	99	GAIGGAGVTALLALCLCLIFFIV
KIR2DL1	100	ILIGTSVVIILFILLFFLL

4. iCAR portion: Inhibitory domain

[0410] In some embodiments, the bicistronic construct comprises an iCAR portion comprising an inhibitory domain component. In some embodiments, the iCAR portion comprises an inhibitory domain. In some embodiments, the inhibitory domain is selected from the group consisting of PD-1, KIR2DL1, KIR2DL2, KIR2DL3, KIR2DL4, KIR2DL5A, KIR3DL1, KIR3DL2, KIR3DL3, LAIR1, CD22, CD33, SIGLEC5, SIGLEC6, SIGLEC7, SIGLEC8, SIGLEC9, SIGLEC10, SIGLEC11, SIGLEC12, PECAM1/CD31, CD200R1, FCRL1, FCRL2, FCRL3, FCRL4, FCRL5, SLAMF1, SLAMF5, BTLA, LAG3, 2B4, CD160, CEACAM1, TIM3, VISTA, TIGIT, SIRPalpha, FcγRIIB, CD5, CD300a, CD300f, LIR1, LIR2, LIR3, LIR5, LIR8, Ly9, 2xPD1(G4S), 2xPD1(PD1), PVRIg, and AA2ARKIR2DL1, LIR1, and PD-1. In some embodiments, the inhibitory domain is KIR2DL1 (SEQ ID NO:102). In some embodiments, the inhibitory domain is LIR1 (SEQ ID NO:143). In some embodiments, the inhibitory domain is PD-1 (SEQ ID NO:101). In some embodiments, the inhibitory domain is KIR2DL2 (SEQ ID NO:103). In some embodiments, the inhibitory domain is KIR2DL3 (SEQ ID NO:104). In some embodiments, the inhibitory domain is KIR2DL4 (SEQ ID NO:105). In some embodiments, the inhibitory domain is KIR2DL5A (SEQ ID NO:106). In some embodiments, the inhibitory domain is KIR3DL1 (SEQ ID NO:107). In some embodiments, the inhibitory domain is KIR3DL2 (SEQ ID NO:108). In some embodiments, the inhibitory domain is KIR3DL3 (SEQ ID NO:109). In some embodiments, the inhibitory domain is LAIR1 (SEQ ID NO:110). In some embodiments, the inhibitory domain is CD22 (SEQ ID NO:111). In some embodiments, the inhibitory domain is CD33 (SEQ ID NO:112). In some embodiments, the inhibitory domain is SIGLEC5 (SEQ ID NO:113). In some embodiments, the inhibitory domain is SIGLEC6 (SEQ ID NO:114). In some embodiments, the inhibitory domain is SIGLEC7 (SEQ ID NO:115). In some embodiments, the inhibitory domain is SIGLEC8 (SEQ ID NO:116). In some embodiments, the inhibitory domain is SIGLEC9 (SEQ ID NO:117). In some embodiments, the inhibitory domain is SIGLEC10 (SEQ ID NO:118). In some embodiments, the inhibitory domain is SIGLEC11 (SEQ ID NO:119). In some embodiments, the inhibitory domain is SIGLEC12 (SEQ ID NO:120). In some embodiments, the inhibitory domain is PECAM1/CD31 (SEQ ID NO:121). In some embodiments, the

inhibitory domain is CD200R1 (SEQ ID NO:122). In some embodiments, the inhibitory domain is FCRL1 (SEQ ID NO:123). In some embodiments, the inhibitory domain is FCRL2 (SEQ ID NO:124). In some embodiments, the inhibitory domain is FCRL3 (SEQ ID NO:125). In some embodiments, the inhibitory domain is FCRL4 (SEQ ID NO:126). In some embodiments, the inhibitory domain is FCRL5 (SEQ ID NO:127). In some embodiments, the inhibitory domain is SLAMF1 (SEQ ID NO:128). In some embodiments, the inhibitory domain is SLAMF5 (SEQ ID NO:129). In some embodiments, the inhibitory domain is BTLA (SEQ ID NO:130). In some embodiments, the inhibitory domain is LAG3 (SEQ ID NO:131). In some embodiments, the inhibitory domain is 2B4 (SEQ ID NO:132). In some embodiments, the inhibitory domain is CD160 (SEQ ID NO:133). In some embodiments, the inhibitory domain is CEACAM1 (SEQ ID NO:134). In some embodiments, the inhibitory domain is TIM3 (SEQ ID NO:135). In some embodiments, the inhibitory domain is VISTA (SEQ ID NO:136). In some embodiments, the inhibitory domain is TIGIT (SEQ ID NO:137). In some embodiments, the inhibitory domain is SIRPalpha (SEQ ID NO:138). In some embodiments, the inhibitory domain is FcγRIIB (SEQ ID NO:139). In some embodiments, the inhibitory domain is CD5 (SEQ ID NO:140). In some embodiments, the inhibitory domain is CD300a (SEQ ID NO:141). In some embodiments, the inhibitory domain is CD300f (SEQ ID NO:142). In some embodiments, the inhibitory domain is LIR2 (SEQ ID NO:144). In some embodiments, the inhibitory domain is LIR3 (SEQ ID NO:145). In some embodiments, the inhibitory domain is LIR5 (SEQ ID NO:146). In some embodiments, the inhibitory domain is LIR8 (SEQ ID NO:147). In some embodiments, the inhibitory domain is Ly9 (SEQ ID NO:148). In some embodiments, the inhibitory domain is 2xPD1(G4S) (SEQ ID NO:149). In some embodiments, the inhibitory domain is 2xPD1(PD1) (SEQ ID NO:150). In some embodiments, the inhibitory domain is PVRIg (SEQ ID NO:151). In some embodiments, the inhibitory domain is AA2AR (SEQ ID NO:152).

Table 7: iCAR inhibitory domain sequences

Sequence Information	SEQ ID NO	Amino acid sequence
PD-1	101	CSRAARGTIGARRTGQPLKEDPSAVPVFSVDYGELDFQW REKTPEPPVPCVPEQTEYATIVFPSGMGTSSPARRGSADG PRSAQPLRPEDGHCSWPL
KIR2DL1	102	HRWCSNKKNAAVMDQESAGNRTANSEDSDEQDPQEVT YTQLNHCVFTQRKITRPSQRPKTPPTDIIVYTELPNAESRS KVVSCP

KIR2DL2	103	HRWCSNKKNAAVMDQESAGNRTANSEDSDEQDPQEVT YTQLNHCVFTQRKITRPSQRPKTPPTDIIVYAELPNAESRS KVVSCP
KIR2DL3	104	HRWCCNKKNAVVMDQEPAGNRTVNREDSDEQDPQEVT YAQLNHCVFTQRKITRPSQRPKTPPTDIIVYTELPNAEP
KIR2DL4	105	RWCSKKKDAAVMNQEPAGHRTVNREDSDEQDPQEVTY AQLDHCIFTQRKITGPSQRSKRPSTDTSVCIELPNAEPRAL SPAHEHHSQALMGSSRETTALSQTQLASSNVPAAGI
KIR2DL5A	106	LHCCCSNKKNAAVMDQEPAGDRTVNREDSDDQDPQEVT YAQLDHCVFTQTKITSPSQRPKTPPTDTTMYMELPNAKPR SLSPAHKHHSQALRGSSRETTALSQNRVASSHVPAAGI
KIR3DL1	107	HLWCSNKKNAAVMDQEPAGNRTANSEDSDEQDPEEVTY AQLDHCVFTQRKITRPSQRPKTPPTDTILYTELPNAKPRSK VVSCP
KIR3DL2	108	YRWCSNKKNAAVMDQEPAGDRTVNRQDSDEQDPQEVT YAQLDHCVFIQRKISRPSQRPKTPLTDTSVYTELPNAEPRS KVVSCPRAPQSGLEGVF
KIR3DL3	109	HRWCANKKNAVVMDQEPAGNRTVNREDSDEQDPQEVT YAQLNHCVFTQRKITRPSQRPKTPPTDTSV
LAIR1	110	HRQNQIKQGPPRSKDEEQKPQQRPDLAVDVLERTADKAT VNGLPEKDRETDTSALAAGSSQEVTYAQLDHWALTQRT ARAVSPQSTKPMAESITYAAVARH
CD22	111	KLQRRWKRTQSQQGLQENSSGQSFFVRNKKVRRAPLSEG PHSLGCYNPMMEDGISYTTLRFPEMNIPRTGDAESSEMQR PPPDCDDTVTYSALHKRQVGDYENVIPDFPEDEGIHYSEL IQFGVGERPQAQENVDYVILKH
CD33	112	KTHRRKAARTAVGRNDTHPTTGSASPKHQKKSKLHGPTE TSSCSGAAPTVEMDEELHYASLNFHGMNPSKDTSTEYSE VRTQ
SIGLEC5	113	KARRKQAAGRPEKMDDEDPIMGTITSGSRKKPWPDSPGD QASPPGDAPPLEEQKELHYASLSFSEMKSREPKDQEAPST TEYSEIKTSK
SIGLEC6	114	RVKTRRKKAAQPVQNTDDVNPVMVSGSRGHQHQFQTGI VSDHPAEAGPISEDEQELHYAVLHFHKVQPQEPKVTDTE YSEIKIHK
SIGLEC7	115	RSCRKKSARPAADVGDIGMKDANTIRGSASQGNLTESWA DDNPRHHGLAAHSSGEEREIQYAPLSFHKGEPQDLSGQE ATNNEYSEIKIPK
SIGLEC8	116	RSCRKKSARPAAGVGDTGMEDAKAIRGSASQGPLTESW KDGNPLKKPPPAVAPSSGEEGELHYATLSFHKVKPQDPQ GQEATDSEYSEIKIHKRETAETQACLRNHNPSSKEVRG
SIGLEC9	117	VRSCRKKSARPAAGVGDTGIEDANAVRGSASQGPLTEPW AEDSPPDQPPPASARSSVGEGELQYASLSFQMVKPWDSR GQEATDTEYSEIKIHR
SIGLEC10	118	KILPKRRTQTETPRPRFSRHSTILDYINVVPTAGPLAQKRN QKATPNSPRTPLPPGAPSPESKKNQKKQYQLPSFPEPKSST QAPESQESQEELHYATLNFPGVRPRPEARMPKGTQADYA EVKFQ

SIGLEC11	119	KICRKEARKRAAAEQDVPSTLGPISQGHQHECSAGSSQD HPPPGAATYTPGKGEEQELHYASLSFQGLRLWEPADQEA PSTTEYSEIKIHTGQPLRGPGFGLQLEREMSGMVPK
SIGLEC12	120	RSCRKKSARPAVGVGDTGMEDANAVRGSASQGPLIESPA DDSPPHHAPPALATPSPEEGEIQYASLSFHKARPQYPQEQ EAIGYEYSEINIPK
PECAM1/CD31	121	KCYFLRKAKAKQMPVEMSRPAVPLLNSNNEKMSDPNME ANSHYGHNDDVRNHAMKPINDNKEPLNSDVQYTEVQVS SAESHKDLGKKDTETVYSEVRKAVPDAVESRYSRTEGSL DGT
CD200R1	122	KVNGCRKYKLNKTESTPVVEEDEMQPYASYTEKNNPLY DTTNKVKASEALQSEVDTDLHTL
FCRL1	123	GLKRKIGRRSARDPLRSLPSPLPQEFTYLNSPTPGQLQPIY ENVNVVSGDEVYSLAYYNQPEQESVAAETLGTHMEDKV SLDIYSRLRKANITDVDYEDAM
FCRL2	124	HKISGESSATNEPRGASRPNPQEFTYSSPTPDMEELQPVY VNVGSVDVDVVYSQVWSMQQPESSANIRTLLENKDSQVI YSSVKKS
FCRL3	125	HYARARRKPGGLSATGTSSHSPSECQEPSSSRPSRIDPQEP THSKPLAPMELEPMYSNVNPGDSNPIYSQIWSIQHTKENS ANCPMMHQEHEELTVLYSELKKTHPDDSAGEASSRGRA HEEDDEENYENVPRVLLASDH
FCRL4	126	HCWRRRKSGVGFLGDETRLPPAPGPGESSHSICPAQVELQ SLYVDVHPKKGDLVYSEIQTTQLGEEEEANTSRTLLEDK DVSVVYSEVKTQHPDNSAGKISSKDEES
FCRL5	127	LSRKAGRKPASDPARSPSDSDSQEPTYHNVPAWEELQPV YTNANPRGENVVYSEVRIIQEKKKHAVASDPRHLRNKGS PIIYSEVKVASTPVSGSLFLASSAPHR
SLAMF1	128	QLRRRGKTNHYQTTVEKKSLTIYAQVQKPGPLQKKLDSF PAQDPCTTIYVAATEPVPESVQETNSITVYASVTLPES
SLAMF5	129	RLFKRRQGRIFPEGSCLNTFTKNPYAASKKTIYTYIMASR NTQPAESRIYDEILQSKVLPSKEEPVNTVYSEVQFADKMG KASTQDSKPPGTSSYEIVI
BTLA	130	RRHQGKQNELSDTAGREINLVDAHLKSEQTEASTRQNSQ VLLSETGIYDNDPDLCFRMQEGSEVYSNPCLEENKPGIVY ASLNHSVIGPNSRLARNVKEAPTEYASICVRS
LAG3	131	HLWRRQWRPRRFSALEQGIHPPQAQSKIEELEQEPEPEPE PEPEPEPEPEPEQL
2B4	132	WRRKRKEKQSETSPKEFLTIYEDVKDLKTRRNHEQEQTF PGGGSTIYSMIQSQSSAPTSQEPAYTLYSLIQPSRKSGSRK RNHSPSFNSTIYEVIGKSQPKAQNPARLSRKELENFDVYS
CD160	133	GCINITSSASQEGTRLNLICTVWHKKEEAEGFVVFLCKDR SGDCSPETSLKQLRLKRDPGIDGVGEISSQLMFTISQVTPL HSGTYQCCARSQKSGIRLQGHFFSILFTETGNYTVTGLKQ RQHLEFSHNEGTLS
CEACAM1	134	HFGKTGRASDQRDLTEHKPSVSNHTQDHSNDPPNKMNE VTYSTLNFEAQQPTQPTSASPSLTATEIIYSEVKKQ
TIM3	135	FKWYSHSKEKIQNLSLISLANLPPSGLANAVAEGIRSEENI YTIEENVYEVEEPNEYYCYVSSRQQPSQPLGCRFAMP

VISTA	136	YKQRQAASNRRAQELVRMDSNIQGIENPGFEASPPAQGIP EAKVRHPLSYVAQRQPSESGRHLLSEPSTPLSPPGPGDVFF PSLDPVPDSPNFEVI
TIGIT	137	LTRKKKALRIHSVEGDLRRKSAGQEEWSPSAPSPPGSCVQ AEAAPAGLCGEQRGEDCAELHDYFNVLSYRSLGNCSFFT ETG
SIRPalpha	138	RIRQKKAQGSTSSTRLHEPEKNAREITQDTNDITYADLNL PKGKKPAPQAAEPNNHTEYASIQTSPQPASEDTLTYADLD MVHLNRTPKQPAPKPEPSFSEYASVQVPRK
FcγRIIB	139	VVALIYCRKKRISALPGYPECREMGETLPEKPANPTNPDE ADKVGAENTITYSLLMHPDALEEPDDQNRI
CD5	140	KKLVKKFRQKKQRQWIGPTGMNQNMSFHRNHTATVRS HAENPTASHVDNEYSQPPRNSHLSAYPALEGALHRSSMQ PDNSSDSDYDLHGAQRL
CD300a	141	RMFQKWIKAGDHSELSQNPKQAATQSELHYANLELLMW PLQEKPAPPREVEVEYSTVASPREELHYASVVFDSNTNRI AAQRPREEEPDSDYSVIRKT
CD300f	142	WRMMKYQQKAAGMSPEQVLQPLEGDLCYADLTLQLAG TSPQKATTKLSSAQVDQVEVEYVTMASLPKEDISYASLTL GAEDQEPTYCNMGHLSSHLPGRGPEEPTEYSTISRP
LIR1	143	LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWR SSPAADAQEENLYAAVKHTQPEDGVEMDTRSPHDEDPQ AVTYAEVKHSRPRREMASPPSPLSGEFLDTKDRQAEEDR QMDTEAAASEAPQDVTYAQLHSLTLRREATEPPPSQEGP SPAVPSIYATLAIH
LIR2	144	LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWR SSPAADAQEENLYAAVKDTQPEDGVEMDTRAAASEAPQ DVTYAQLHSLTLRRKATEPPPSQEREPPAEPSIYATLAIH
LIR3	145	RRQRHSKHRTSDQRKTDFQRPAGAAETEPKDRGLLRRSS PAADVQEENLYAAVKDTQSEDRVELDSQSPHDEDPQAV TYAPVKHSSPRREMASPPSSLSGEFLDTKDRQVEEDRQM DTEAAASEASQDVTYAQLHSLTLRRKATEPPPSQEGEPPA EPSIYATLAIH
LIR5	146	QHWRQGKHRTLAQRQADFQRPPGAAEPEPKDGGLQRRS SPAADVQGENFCAAVKNTQPEDGVEMDTRQSPHDEDPQ AVTYAKVKHSRPRREMASPPSPLSGEFLDTKDRQAEEDR QMDTEAAASEAPQDVTYAQLHSFTLRQKATEPPPSQEGA SPAEPSVYATLAIH
LIR8	147	RHRHQSKHRTSAHFYRPAGAAGPEPKDQGLQKRASPVA DIQEEILNAAVKDTQPKDGVEMDARAAASEAPQDVTYA QLHSLTLRREATEPPPSQEREPPAEPSIYAPLAIH
Ly9	148	KRKGRCSVPAFCSSQAEAPADTPEPTAGHTLYSVLSQGY EKLDTPLRPARQQPTPTSDSSSDSNLTTEEDEDRPEVHKPI SGRYEVFDQVTQEGAGHDPAPEGQADYDPVTPYVTEVES VVGENTMYAQVFNLQGKTPVSQKEESSATIYCSIRKPQV VPPPQQNDLEIPESPTYENFT
2xPD1(G4S)	149	CSRAARGTIGARRTGQPLKEDPSAVPVFSVDYGELDFQW REKTPEPPVPCVPEQTEYATIVFPSGMGTSSPARRGSADG PRSAQPLRPEDGHCSWPLGGGGSGGGGSCSRAARGTIGA RRTGQPLKEDPSAVPVFSVDYGELDFQWREKTPEPPVPC

		VPEQTEYATIVFPSGMGTSSPARRGSADGPRSAQPLRPED GHCSWPL
2xPD1(PD1)	150	CSRAARGTIGARRTGQPLKEDPSAVPVFSVDYGELDFQW REKTPEPPVPCVPEQTEYATIDFQWREKTPEPPVPCVPEQ VDYGELDFQWREKTPEPPVPCVPEQTEYATIVFPSGMGTS SPARRGSADGPRSAQPLRPEDGHCSWPL
PVRIg	151	LRRHKHRPAPRLQPSRTSPQAPRARAWAPSQASQAALHV PYATINTSCRPATLDTAHPHGGPSWWASLPTHAAHRPQG PAAWASTPIPARGSFVSVENGLYAQAGERPPHTGPGLTLF PDPRGPRAMEGPLGVR
AA2AR	152	RIREFRQTFRKIIRSHVLRQQEPFKAAGTSARVLAAHGSD GEQVSLRLNGHPPGVWANGSAPHPERRPNGYALGLVSG GSAQESQGNTGLPDVELLSHELKGVCPEPPGLDDPLAQD GAGVS
LIR1 mutated (Y to F)	450	LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWR SSPAADAQEENLFAAVKHTQPEDGVEMDTRSPHDEDPQA VTFAEVKHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQ MDTEAAASEAPQDVTFAQLHSLTLRREATEPPPSQEGPSP AVPSIFATLAIH

5. Optional synthetic PD-1

[0411] In some embodiments, the iCAR construct comprises an optional synthetic PD-1 sequence. In some embodiments, the iCAR comprises a synthetic PD-1 sequence shown in Table 8. In some embodiments, the iCAR construct comprises an optional synthetic LIR1 sequence. In some embodiments, the iCAR comprises a synthetic LIR1 sequence shown in Table 8.

Table 8: synthetic PD-1 and LIR1 sequences

SEQ ID NO	Sequence intracellular synPD-1
243	CSRAARGTIGARRTGQPLKEDPSAVPVFSVDYGELVFPSGMGTSSPARR GSADGPRSAQPLRPEDGHCSWPL
244	CSRAARGTIGARRTGQPLKEDPSAVPVFSVDYGELDFQWREKTPEPPVP CVPEQVDYGELVFPSGMGTSSPARRGSADGPRSAQPLRPEDGHCSWPL
245	CSRAARGTIGARRTGQPLKEDPSAVPVFSVDYGELDFQWREKTPEPPVP CVPEQVDYGELDFQWREKTPEPPVPCVPEQVDYGELVFPSGMGTSSPAR RGSADGPRSAQPLRPEDGHCSWPL
246	CSRAARGTIGARRTGQPLKEDPSAVPVFSVDYGELDFQWREKTPEPPVP CVPEQVDYGELDFQWREKTPEPPVPCVPEQVDYGELDFQWREKTPEPP VPCVPEQVDYGELVFPSGMGTSSPARRGSADGPRSAQPLRPEDGHCSWP L
247	CSRAARGTIGARRTGQPLKEDPSAVPVFSVDYGELDFQWREKTPEPPVP CVPEQVDYGELDFQWREKTPEPPVPCVPEQVDYGELDFQWREKTPEPP VPCVPEQVDYGELDFQWREKTPEPPVPCVPEQVDYGELVFPSGMGTSSP ARRGSADGPRSAQPLRPEDGHCSWPL

248	CSRAARGTIGARRTGQPLKEDPSAVPVFSTEYATIVFPSGMGTSSPARRG SADGPRSAQPLRPEDGHCSWPL
249	CSRAARGTIGARRTGQPLKEDPSAVPVFSTEYATIDFQWREKTPEPPVPC VPEQTEYATIVFPSGMGTSSPARRGSADGPRSAQPLRPEDGHCSWPL
250	CSRAARGTIGARRTGQPLKEDPSAVPVFSTEYATIDFQWREKTPEPPVPC VPEQTEYATIDFQWREKTPEPPVPCVPEQTEYATIVFPSGMGTSSPARRG SADGPRSAQPLRPEDGHCSWPL
251	CSRAARGTIGARRTGQPLKEDPSAVPVFSTEYATIDFQWREKTPEPPVPC VPEQTEYATIDFQWREKTPEPPVPCVPEQTEYATIDFQWREKTPEPPVPC VPEQTEYATIVFPSGMGTSSPARRGSADGPRSAQPLRPEDGHCSWPL
252	CSRAARGTIGARRTGQPLKEDPSAVPVFSTEYATIDFQWREKTPEPPVPC VPEQTEYATIDFQWREKTPEPPVPCVPEQTEYATIDFQWREKTPEPPVPC VPEQTEYATIDFQWREKTPEPPVPCVPEQTEYATIVFPSGMGTSSPARRG SADGPRSAQPLRPEDGHCSWPL
253	CSRAARGTIGARRTGQPLKEDPSAVPVFSVDYGELDFQWREKTPEPPVP CVPEQTEYATIVFPSGMGTSSPARRGSADGPRSAQPLRPEDGHCSWPLG GGGSGGGGSCSRAARGTIGARRTGQPLKEDPSAVPVFSVDYGELDFQW REKTPEPPVPCVPEQTEYATIVFPSGMGTSSPARRGSADGPRSAQPLRPE DGHCSWPL
254	CSRAARGTIGARRTGQPLKEDPSAVPVFSVDYGELDFQWREKTPEPPVP CVPEQTEYATIDFQWREKTPEPPVPCVPEQVDYGELDFQWREKTPEPPV PCVPEQTEYATIVFPSGMGTSSPARRGSADGPRSAQPLRPEDGHCSWPL
296	LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQE ENLYAAVKHTQPEDGVEMDTRSPHDEDPQANLYAAVKHSRPRREMAS PPSPLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDNLYAAVHSLTLRRE ATEPPPSQEGPSPAVPNLYAAVAIH
297	LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQE EVTYAEVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPRREMASP PSPLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYAEVHSLTLRREA TEPPPSQEGPSPAVPVTYAEVAIH
298	LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQE EVTYAQLKHTQPEDGVEMDTRSPHDEDPQAVTYAQLKHSRPRREMASP PSPLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYAQLHSLTLRREA TEPPPSQEGPSPAVPVTYAQLAIH
299	LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQE ESIYATLKHTQPEDGVEMDTRSPHDEDPQASIYATLKHSRPRREMASPPS PLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDSIYATLHSLTLRREATE PPPSQEGPSPAVPSIYATLAIH
300	LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQE EVTYAQLKHTQPEDGVEMDTRSPHDEDPQASIYATLKHSRPRREMASPP SPLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYAQLHSLTLRREAT EPPPSQEGPSPAVPSIYATLAIH
301	LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQE ETEYATIKHTQPEDGVEMDTRSPHDEDPQATEYATIKHSRPRREMASPPS PLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYAQLHSLTLRREAT EPPPSQEGPSPAVPSIYATLAIH
302	LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQE EVTYAQLKHTQPEDGVEMDTRSPHDEDPQASIYATLKHSRPRREMASPP SPLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDTEYATIHSLTLRREAT EPPPSQEGPSPAVPTEYATIAIH

304	LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQE EVTYAQLKHTQPEDGVEMDTRSPHDEDPQATEYATIKHSRPRREMASPP SPLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDTEYATIHSLTLRREAT EPPPSQEGPSPAVPSIYATLAIH

6. Exemplary iCARs

[0412] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of BB7.2 (SEQ ID NOs: 37 and 38). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a $(G_4S)X3$ linker (SEQ ID NO:81) linker that covalently connects the VH and the VLto form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR

comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:]122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some

embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of 3PF12/C4 (SEQ ID NOs: 39 and 40). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. . In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa

hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID

NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain

(SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0413] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of 3PF12/F12 (SEQ ID NOs: 41 and 42). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In

some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ

ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0414] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of 3PF12/B11 (SEQ ID NOs: 43 and 44). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. . In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some

embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID

NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID

NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0415] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of W6/32 (SEQ ID NOs: 45 and 46). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In

some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain

(SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0416] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of BBM.1 (SEQ ID NOs: 47 and 48). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some

embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID

NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID

NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0417] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of SN66E3.1 (SEQ ID NOs: 49 and 50). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. . In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some

embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain

(SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0418] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of Ha5C2.A2 (SEQ ID NOs: 51 and 52). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. In some

embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID

NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID

NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0419] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of MWB1 (SEQ ID NOs: 53 and 54). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. . In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some

embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain

(SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0420] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of MWB1-mod (MWB1.1) (SEQ ID NOs: 55 and 56). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the

VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ

ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID

NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0421] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of Hz.BB7.2 VH1-69 _A18VK (SEQ ID NOs: 57 and 58). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291).

In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain

(SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0422] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of Hz.BB7.2 VH1-69 (27,30)_A18 (SEQ ID NOs: 59 and 60). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some

embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. . In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ

ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID

NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0423] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of Hz.BB7.2VH1-69 (27,30,48) _ A18 (SEQ ID NOs: 61 and 62). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID

NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain

(SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0424] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of Hz.BB7.2 VH1-69 (27,30,67)_A18 (SEQ ID NOs: 63 and 64). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv.. In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID

NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID

NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0425] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of Hz.BB7.2 VH1-69 (27,30,69) _A18 (SEQ ID NOs: 65 and 66). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge

domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ

ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of

the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0426] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of Hz.BB7.2 VH1-69 (27,30,67,69)_A18 (SEQ ID NOs: 67 and 68). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID

NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID

NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0427] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of Hz.BB7.2 VH1-3_A18 (SEQ ID NOs: 69 and 70). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some

embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID

NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain

(SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0428] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of Hz.BB7.2 VH1-3(48)_ A18 (SEQ ID NOs: 71 and 72). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. . In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In

some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID

NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0429] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of Hz.BB7.2 VH1-3(67)_A18 (SEQ ID NOs: 73 and 74). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some

embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID

NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ

ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0430] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of Hz.Bb7.2 VH1-3(69)_A18 (SEQ ID NOs: 75 and 76). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In

some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain

(SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0431] In some embodiments, the scFv has the VL and VH sequences of Hz.BB7.2 VH1-3(71)_A18 (SEQ ID NOs: 77 and 78). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. . In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1

Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID

NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID

NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0432] In some embodiments, the iCAR comprises an scFv component comprising the VL and VH sequences of Hz. BB7.2VH1-3(73)_A18 (SEQ ID NOs: 79 and 80). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In

some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain

(SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0433] In some embodiments, the scFv has the VL and VH sequences of MWB1.2 (SEQ ID NOs: 163 and 164). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. . In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge

domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID

NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID

NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0434] In some embodiments, the scFv has the VL and VH sequences of SN66E3.2 (SEQ ID NOs: 165 and 166). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. . In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In

some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain

(SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0435] In some embodiments, the scFv has the VL and VH sequences of MWB1.1 (SEQ ID NOs: 273). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. . In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge

domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID

NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID

NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0436] In some embodiments, the scFv has the VL and VH sequences of MWB1.2 (SEQ ID NOs: 274). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. . In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In

some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain

(SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0437] In some embodiments, the scFv has the VL and VH sequences of SN66E3.3 (SEQ ID NOs: 283 and 284). In some embodiments, the orientation of the iCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the iCAR VH and VL regions is VL-VH. In some embodiments, the iCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the iCAR scFv. In some embodiments, the iCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the iCAR scFv. . In some embodiments, the iCAR comprises a CD8 alpha hinge domain (SEQ ID NO:84). In some embodiments, the iCAR comprises a CD28 hinge domain (SEQ ID NO:85). In some embodiments, the iCAR comprises a PD-1 hinge

domain (SEQ ID NO:86). In some embodiments, the iCAR comprises a LIR1 Ig3-4 hinge domain (SEQ ID NO:87). In some embodiments, the iCAR comprises a LIR1 Ig-4 hinge domain (SEQ ID NO:88). In some embodiments, the iCAR comprises a LIR1 52 aa hinge domain (SEQ ID NO:89). In some embodiments, the iCAR comprises a LIR1 36 aa hinge domain (SEQ ID NO:90). In some embodiments, the iCAR comprises a LIR1 30 aa hinge domain (SEQ ID NO:91). In some embodiments, the iCAR comprises a LIR1 8 aa hinge domain (SEQ ID NO:92). In some embodiments, the iCAR comprises a CD33 hinge domain (SEQ ID NO:93). In some embodiments, the iCAR comprises a KIR2DL1 hinge domain (SEQ ID NO:94). In some embodiments, the iCAR comprises aLIR1 26 aa hinge domain (SEQ ID NO: 289). In some embodiments, the iCAR comprises PD-1 (47) hinge domain (SEQ ID NO: 290). In some embodiments, the iCAR comprises PD-1 (42) hinge domain (SEQ ID NO: 291). In some embodiments, the iCAR comprises PD-1 (36) hinge domain (SEQ ID NO: 292). In some embodiments, the iCAR comprises PD-1 (30) hinge domain (SEQ ID NO: 293). In some embodiments, the iCAR comprises PD-1 (26) hinge domain (SEQ ID NO: 294). In some embodiments, the iCAR comprises PD-1 (20) hinge domain (SEQ ID NO: 295). In some embodiments, the iCAR comprises a CD8 alpha transmembrane domain (SEQ ID NO:95). In some embodiments, the iCAR comprises a CD28 transmembrane domain (SEQ ID NO:96). In some embodiments, the iCAR comprises a PD-1 transmembrane domain (SEQ ID NO:97). In some embodiments, the iCAR comprises a LIR1 transmembrane domain (SEQ ID NO:98). In some embodiments, the iCAR comprises a CD33 transmembrane domain (SEQ ID NO:99). In some embodiments, the iCAR comprises a KIR2DL1 transmembrane domain (SEQ ID NO:100). In some embodiments, the iCAR comprises a PD-1 inhibitory domain (SEQ ID NO:101). In some embodiments, the iCAR comprises a KIR2DL1 inhibitory domain (SEQ ID NO:102). In some embodiments, the iCAR comprises a KIR2DL2 inhibitory domain (SEQ ID NO:103). In some embodiments, the iCAR comprises a KIR2DL3 inhibitory domain (SEQ ID NO:104). In some embodiments, the iCAR comprises a KIR2DL4 inhibitory domain (SEQ ID NO:105). In some embodiments, the iCAR comprises a KIR2DL5A inhibitory domain (SEQ ID NO:106). In some embodiments, the iCAR comprises a KIR3DL1 inhibitory domain (SEQ ID NO:107). In some embodiments, the iCAR comprises a KIR3DL2 inhibitory domain (SEQ ID NO:108). In some embodiments, the iCAR comprises a KIR3DL3 inhibitory domain (SEQ ID NO:109). In some embodiments, the iCAR comprises a LAIR1 inhibitory domain (SEQ ID NO:110). In some embodiments, the iCAR comprises a CD22 inhibitory domain (SEQ ID NO:111). In some embodiments, the iCAR comprises a CD33 inhibitory domain (SEQ ID NO:112). In some embodiments, the iCAR comprises a SIGLEC5 inhibitory domain (SEQ ID

NO:113). In some embodiments, the iCAR comprises a SIGLEC6 inhibitory domain (SEQ ID NO:114). In some embodiments, the iCAR comprises a SIGLEC7 inhibitory domain (SEQ ID NO:115). In some embodiments, the iCAR comprises a SIGLEC8 inhibitory domain (SEQ ID NO:116). In some embodiments, the iCAR comprises a SIGLEC9 inhibitory domain (SEQ ID NO:117). In some embodiments, the iCAR comprises a SIGLEC10 inhibitory domain (SEQ ID NO:118). In some embodiments, the iCAR comprises a SIGLEC11 inhibitory domain (SEQ ID NO:119). In some embodiments, the iCAR comprises a SIGLEC12 inhibitory domain (SEQ ID NO:120). In some embodiments, the iCAR comprises a PECAM1/CD31 inhibitory domain (SEQ ID NO:121). In some embodiments, the iCAR comprises a CD200R1 inhibitory domain (SEQ ID NO:122). In some embodiments, the iCAR comprises a FCRL1 inhibitory domain (SEQ ID NO:123). In some embodiments, the iCAR comprises a FCRL2 inhibitory domain (SEQ ID NO:124). In some embodiments, the iCAR comprises a FCRL3 inhibitory domain (SEQ ID NO:125). In some embodiments, the iCAR comprises a FCRL4 inhibitory domain (SEQ ID NO:126). In some embodiments, the iCAR comprises a FCRL5 inhibitory domain (SEQ ID NO:127). In some embodiments, the iCAR comprises a SLAMF1 inhibitory domain (SEQ ID NO:128). In some embodiments, the iCAR comprises a SLAMF5 inhibitory domain (SEQ ID NO:129). In some embodiments, the iCAR comprises a BTLA inhibitory domain (SEQ ID NO:130). In some embodiments, the iCAR comprises a LAG3 inhibitory domain (SEQ ID NO:131). In some embodiments, the iCAR comprises a 2B4 inhibitory domain (SEQ ID NO:132). In some embodiments, the iCAR comprises a CD160 inhibitory domain (SEQ ID NO:133). In some embodiments, the iCAR comprises a CEACAM1 inhibitory domain (SEQ ID NO:134). In some embodiments, the iCAR comprises a TIM3 inhibitory domain (SEQ ID NO:135). In some embodiments, the iCAR comprises a VISTA inhibitory domain (SEQ ID NO:136). In some embodiments, the iCAR comprises a TIGIT inhibitory domain (SEQ ID NO:137). In some embodiments, the iCAR comprises a SIRPalpha inhibitory domain (SEQ ID NO:138). In some embodiments, the iCAR comprises a FcγRIIB inhibitory domain (SEQ ID NO:139). In some embodiments, the iCAR comprises a CD5 inhibitory domain (SEQ ID NO:140). In some embodiments, the iCAR comprises a CD300a inhibitory domain (SEQ ID NO:141). In some embodiments, the iCAR comprises a CD300f inhibitory domain (SEQ ID NO:142). In some embodiments, the iCAR comprises a LIR1 inhibitory domain (SEQ ID NO:143). In some embodiments, the iCAR comprises a LIR2 inhibitory domain (SEQ ID NO:144). In some embodiments, the iCAR comprises a LIR3 inhibitory domain (SEQ ID NO:145). In some embodiments, the iCAR comprises a LIR5 inhibitory domain (SEQ ID NO:146). In some embodiments, the iCAR comprises a LIR8 inhibitory domain (SEQ ID

NO:147). In some embodiments, the iCAR comprises a Ly9 inhibitory domain (SEQ ID NO:148). In some embodiments, the iCAR comprises a 2xPD1(G4S) inhibitory domain (SEQ ID NO:149). In some embodiments, the iCAR comprises a 2xPD1(PD1) inhibitory domain (SEQ ID NO:150). In some embodiments, the iCAR comprises a PVRIg inhibitory domain (SEQ ID NO:151). In some embodiments, the iCAR comprises an AA2AR inhibitory domain (SEQ ID NO:152). In some embodiments, the iCAR comprises a signal peptide upstream of the iCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0438] In some embodiments, the iCAR has a set of components shown in Tables 9-10 and/or an amino acid sequence shown in Tables 11-12.

Table 9: iCAR constructs

Construct	scFv	VH SEQ ID NO	VL SEQ ID NO	Signal peptide	scFv Linker	Hinge	TM	Signal-ing
	BB7.2	38	37	CD8alpha	(G4S)x3	PD-1	PD-1	PD-1
MC0096 (VR96)	3PF12/C4	40	39	CD8alpha	(G4S)x3	PD-1	PD-1	PD-1
MC0274 (VR274)	3PF12/F12	42	41	CD8alpha	(G4S)x3	PD-1	PD-1	PD-1
MC0276 (VR276)	3PF12/B11	44	43	CD8alpha	(G4S)x3	PD-1	PD-1	PD-1
MC0097 (VR97)	W6/32	46	45	CD8alpha	(G4S)x3	PD-1	PD-1	PD-1
MC0098 (VR98)	BBM.1	48	47	CD8alpha	(G4S)x3	PD-1	PD-1	PD-1
MC0099 (VR99)	SN66E3.1	50	49	CD8alpha	(G4S)x3	PD-1	PD-1	PD-1
MC0100 (VR100)	Ha5C2.A2	52	51	CD8alpha	(G4S)x3	PD-1	PD-1	PD-1
MC0101 (VR101)	MWB1	54	53	CD8alpha	(G4S)x3	PD-1	PD-1	PD-1
MC0102 (VR102)	MWB1.1d	56	55	CD8alpha	(G4S)x3	PD-1	PD-1	PD-1
MC0372 (VR372)	Hz.BB7.2VH1-69_A18VK	58	57	CD8 alpha	(G4S)x3	CD8 alpha	CD8 alpha	41BBz
MC0373 (VR373)	Hz.BB7.2VH1-69 (27,30)_A18	60	59	CD8 alpha	(G4S)x3	CD8 alpha	CD8 alpha	41BBz
MC0374 (VR374)	Hz.BB7.2 VH1-69	62	61	CD8 alpha	(G4S)x3	CD8 alpha	CD8 alpha	41BBz

	(27,30,48) _ A18							
MC0375 (VR375)	Hz.BB7.2 VH1-69 (27,30,67)_ A18	64	63	CD8 alpha	(G4S)x3	CD8 alpha	CD8 alpha	41BBz
MC0376 (VR376)	Hz.BB7.2 VH1-69 (27,30,69) _A18	66	65	CD8 alpha	(G4S)x3	CD8 alpha	CD8 alpha	41BBz
MC0377 (VR377)	Hz.BB7.2 VH1-69 (27,30,67,6 9)_A18	68	67	CD8 alpha	(G4S)x3	CD8 alpha	CD8 alpha	41BBz
MC0378 (VR378)	Hz.BB7.2 VH1-3_A18	70	69	CD8 alpha	(G4S)x3	CD8al pha	CD8 alpha	41BBz
MC0379 (VR379)	Hz.BB7.2 VH1-3(48)_ A18	72	71	CD8 alpha	(G4S)x3	CD8 alpha	CD8 alpha	41BBz
MC0380 (VR380)	Hz.BB7.2 VH1-3(67)_A18	74	73	CD8 alpha	(G4S)x3	CD8 alpha	CD8 alpha	41BBz
MC0381 (VR381)	Hz.BB7.2 VH1-3(69)_A18	76	75	CD8 alpha	(G4S)x3	CD8 alpha	CD8 alpha	41BBz
MC0382 (VR382)	Hz.BB7.2 VH1-3(71)_A18	78	77	CD8 alpha	(G4S)x3	CD8 alpha	CD8 alpha	41BBz
MC0383 (VR383)	Hz.BB7.2 VH1-3(73)_A18	80	79	CD8 alpha	(G4S)x3	CD8 alpha	CD8 alpha	41BBz
MC0384 (VR384)	3PF12_274 _LIR1_HE R2_shRNA(A2)	40	41	CD8 alpha	(G4S)x3	PD-1	PD-1	LIR-1
MC0385 (VR385)	3PF12_276 _LIR1_HE R2_shRNA(A2)	44	43	CD8 alpha	(G4S)x3	PD-1	PD-1	LIR-1
MC0386 (VR386)	MWB1.1_H L_LIR1_H ER2_shRN A(A2)	56	55	CD8 alpha	(G4S)x3	PD-1	PD-1	LIR-1
MC0387 (VR387)	MWB1.1_L H_LIR1_H ER2_shRN A(A2)	56	55	CD8 alpha	(G4S)x3	PD-1	PD-1	LIR-1
MC0388 (VR388)	MWB1.2_H L_LIR1_H	164	163	CD8 alpha	(G4S)x3	PD-1	PD-1	LIR-1

	ER2_shRNA(A2)							
MC0389 (VR389)	MWB1.2_LH_LIR1_HER2_shRNA(A2)	164	163	CD8 alpha	(G4S)x3	Pd-1	PD-1	LIR-1
MC0390 (VR390)	SN66E3.1_HL_LIR1_HER2_shRNA(A2)	50	49	CD8 alpha	(G4S)x3	PD-1	PD-1	LIR-1
MC0391 (VR391)	SN66E3.1_LH_LIR1_HER2_shRNA(A2)	50	49	CD8 alpha	(G4S)x3	PD-1	PD-1	LIR-1
MC0446 (VR446)	SN66E3.2_HL_LIR1_HER2_	166	165	CD8 alpha	(G4S)x3	LIR1	LIR1	LIR-1
MC0447 (VR447)	SN66E3.2_LH_LIR1_HER2_	166	165	CD8 alpha	(G4S)x3	LIR1	LIR1	LIR-1
MC0448 (VR448)	SN66E3.3(HL)_LIR1(26)_HER2	284	283	CD8 alpha	(G4S)x3	LIR1	LIR1	LIR1
MC449 (VR449)	SN66E3.3(LH)_LIR1(26)_HER2	284	283	CD8 alpha	(G4S)x3	LIR1	LIR1	LIR1
MC0428 (VR428)	HzBB7.2.1_H69_LIR1_H	64	63	CD8 alpha	(G4S)x3	LIR1	LIR1	LIR-1
MC0421 (VR421)	HzBB7.2.2_H3_LIR1_)	72	71	CD8 alpha	(G4S)x3	LIR1	LIR1	LIR-1
(VR492)	Hz.BB7.2.2	72	71	CD8 alpha	(G4S)X3	LIR1	LIR1	LIR1 mut
(VR442)	Hz.BB7.2.2	72	71	CD8 alpha	(G4S)X3	LIR1	LIR1	LIR1
(VR443)	Hz.BB7.2.2	72	71	CD8 alpha	(G4S)X3	LIR1	LIR1	LIR1
(VR515)	Hz.BB7.2.2	72	71	CD8a alpha	(G4S)X3	LIR1	LIR1	LIR1
(VR516)	SN66E3.2	166	165	CD8a alpha	(G4S)X3	LIR1	LIR1	LIR1
(VR517)	SN66E3.3	284	283	CD8a alpha	(G4S)X3	LIR1	LIR1	LIR1
(VR506)	Hz.BB7.2.2	72	71	CD8a alpha	(G4S)X3	IgG4-LIR1	LIR1	LIR1

(VR507)	Hz.BB7.2.2	72	71	CD8a alpha	(G4S)X3	IgG4-LIR1	LIR1	LIR1
(VR508)	HzBB7.2.2	72	71	CD8a alpha	(G4S)X3	IgG4-LIR1	LIR1	LIR1

Table 10: iCAR constructs

Construct	Construct Name	Signal Peptide	scFv	scFv Linker	Hinge	TM	Signaling
MC0058 (VR58)	1xITIM	CD8alpha	BB7.2 VH VL	(G4S)x3	PD-1	PD-1	1xITIM PD-1
MC0059 (VR59)	2xITIM	CD8alpha	BB7.2 VH VL	(G4S)x3	PD-1	PD-1	2xITIM PD-1
MC0060 (VR60)	3xITIM	CD8alpha	BB7.2 VH VL	(G4S)x3	PD-1	PD-1	3xITIM PD-1
MC0061 (VR61)	4xITIM	CD8alpha	BB7.2 VH VL	(G4S)x3	PD-1	PD-1	4xITIM PD-1
MC0062 (VR62)	5xITIM	CD8alpha	BB7.2 VH VL	(G4S)x3	PD-1	PD-1	5xITIM PD-1
MC0063 (VR63)	1xITSM	CD8alpha	BB7.2 VH VL	(G4S)x3	PD-1	PD-1	1xITSM PD-1
MC0064 (VR64)	2xITSM	CD8alpha	BB7.2 VH VL	(G4S)x3	PD-1	PD-1	2xITSM PD-1
MC0065 (VR65)	3xITSM	CD8alpha	BB7.2 VH VL	(G4S)x3	PD-1	PD-1	3xITSM PD-1
MC0066 (VR66)	4xITSM	CD8alpha	BB7.2 VH VL	(G4S)x3	PD-1	PD-1	4xITSM PD-1
MC0067 (VR67)	5xITSM	CD8alpha	BB7.2 VH VL	(G4S)x3	PD-1	PD-1	5xITSM PD-1
MC0068 (VR68)	2xPD1(G4S)	CD8alpha	BB7.2 VH VL	(G4S)x3	PD-1	PD-1	2xPD-1 (G4S)x2
MC0069 (VR69)	2xPD1(PD1)	CD8alpha	BB7.2 VH VL	(G4S)x3	PD-1	PD-1	2xPD-1 (PD1 linker)

Table 11: iCAR constructs

Construct	scFv	SEQ ID NO	Amino acid sequence
MC0387 (VR387)	MWB1.1_ LH_LIR1_ HER2_shR NA(A2)	255	MALPVTALLLPLALLLHAARPQSALTQPPSASGSPG QSVTISCTGTSSDVGGYKYVSWYQHHPDKAPKLMI YEVNKRPSGVPDRFSGSKSDNTASLTVSGLQAEDEA DYYCSSYAGSNNWVFGGGTKLTVLGGGGSGGGGS GGGGSQVQLVESGGGVVQPGGSLRLSCAASGFTFST YGMHWVRQAPGKGLEWVASISYDGSNKYYADSGQ GRFTISRDTSKNSLYLQMNSLRAEDTAVYYCAIGIY GAYSFDYWGQGTLVTVSSTERRAEVPTAHPSPSPRP AGQFQTLVVGVVGGLLGSLVLLVWVLAVILRHRRQ GKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSP AADAQEENLYAAVKHTQPEDGVEMDTRSPHDEDP QAVTYAEVKHSRPRREMASPPSPLSGEFLDTKDRQA EEDRQMDTEAAASEAPQDVTYAQLHSLTLRREATE PPPSQEGPSPAVPSIYATLAIH
MC0389 (VR389)	MWB1.2_ LH_LIR1_ HER2_shR NA(A2)	256	MALPVTALLLPLALLLHAARPQSALTQPPSASGSPG QSVTISCTGTSSDVGGYKYVSWYQQHPGKAPKLMI YEVNKRPSGVPDRFSGSKSGNTASLTVSGLQAEDEA DYYCSSYAGSNNWVFGGGTKLTVLGGGGSGGGGS GGGGSQVQLVESGGGVVQPGGSLRLSCAASGFTFST YGMHWVRQAPGKGLEWVASISYDGSNKYYADSGQ GRFTISRDTSKNSLYLQMNSLRAEDTAVYYCAIGIY GAYSFDYWGQGTLVTVSSTERRAEVPTAHPSPSPRP AGQFQTLVVGVVGGLLGSLVLLVWVLAVILRHRRQ GKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSP AADAQEENLYAAVKHTQPEDGVEMDTRSPHDEDP QAVTYAEVKHSRPRREMASPPSPLSGEFLDTKDRQA EEDRQMDTEAAASEAPQDVTYAQLHSLTLRREATE PPPSQEGPSPAVPSIYATLAIH
MC0391 (VR391)	SN66E3.1_ LH_LIR1_ HER2_shR NA(A2)	257	MALPVTALLLPLALLLHAARPDIVMTQSPDSLAVSL GERATISCKSSQSVLYSSNNKNYLAWYQQKLGQPP KLLIYWASTRESGVPDRFSGSGSGTNFTLTISSLQAE NVAVYYCQQYYGTPFTFGGGTKVEIKGGGGSGGGG SGGGGSQVQLVQSGAEVKKPGASVKVSCKASGYTF TDYYLHWVRQAPGQGLEWMGWINPYTGGTNYAQ KFQGRVTMTRDASISTVYMELSGLTSDDTAVHFCA RAGASYYDFWSGWVFDYWGQGTLVTVSSTERRAE VPTAHPSPSPRPAGQFQTLVVGVVGGLLGSLVLLVW VLAVILRHRRQGKHWTSTQRKADFQHPAGAVGPEP TDRGLQWRSSPAADAQEENLYAAVKHTQPEDGVE MDTRSPHDEDPQAVTYAEVKHSRPRREMASPPSPLS GEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYAQL HSLTLRREATEPPPSQEGPSPAVPSIYATLAIH
MC0447 (VR447)	SN66E3.2 (LH)_LIR1 (30)_HER2	258	MALPVTALLLPLALLLHAARPDIVMTQSPDSLAVSL GERATISCKSSQSVLYSSNNKNYLAWYQQKPGQPPK LLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAED

			VAVYYCQQYYGTPFTFGGGTKVEIKGGGGSGGGGS GGGGSQVQLVQSGAEVKKPGASVKVSCKASGYTFT DYYLHWVRQAPGQGLEWMGWINPYTGGTNYAQK FQGRVTMTRDTSISTAYMELSGLTSDDTAVYYCAR AGASYYDFWSGWVFDYWGQGTLVTVSSGPTSTSGP EDQPLTPTGSDPQSGLGRHLGVVIGILVAVILLLLLL LLLFLILRHRRQGKHWTSTQRKADFQHPAGAVGPEP TDRGLQWRSSPAADAQEENLYAAVKHTQPEDGVE MDTRSPHDEDPQAVTYAEVKHSRPRREMASPPSPLS GEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYAQL HSLTLRREATEPPPSQEGPSPAVPSIYATLAIH
MC0449 (VR449)	SN66E3.3 (LH)_LIR1 (26)_HER2	305	MALPVTALLLPLALLLHAARPDIVMTQSPDSLAVSL GERATISCKSSQSVLYSSNNKNYLAWYQQKPGQPPK LLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAED VAVYYCQQYYGTPFTFGGGTKVEIKGGGGSGGGGS GGGGSQVQLVQSGAEVKKPGASVKVSCKASGYTFT DYYLHWVRQAPGQGLEWMGWINPYTGGTNYAQK FQGRVTMTRDTSISTAYMELSRLRSEDTAVYYCARA GASYYDFWSGWVFDYWGQGTLVTVSSTSGPEDQPL TPTGSDPQSGLGRHLGVVIGILVAVILLLLLLLLLFLI LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGL QWRSSPAADAQEENLYAAVKHTQPEDGVEMDTRSP HDEDPQAVTYAEVKHSRPRREMASPPSPLSGEFLDT KDRQAEEDRQMDTEAAASEAPQDVTYAQLHSLTLR REATEPPPSQEGPSPAVPSIYATLAIH
MC0428 (VR428)	HzBB7.2.1 _ _LIR1 (52)_HER2	259	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKP GSSVKVSCKASGYTFTSYHIQWVRQAPGQGLEWMG WIYPGDGSTQYNEKFKGRTTITADKSTSTAYMELSS LRSEDTAVYYCAREGTYYAMDYWGQGTLVTVSSG GGGSGGGGSGGGGSDVVMTQTPLSLSVTPGQPASIS CRSSQSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSN RFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCF QGSHVPRTFGGGTKVEIKHPSDPLELVVSGPSGGPSS PTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGVVIGIL VAVILLLLLLLLFLILRHRRQGKHWTSTQRKADFQ HPAGAVGPEPTDRGLQWRSSPAADAQEENLYAAVK HTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPRR EMASPPSPLSGEFLDTKDRQAEEDRQMDTEAAASEA PQDVTYAQLHSLTLRREATEPPPSQEGPSPAVPSIYA TLAIH
MC0421 (VR421)	HzBB7.2.2 _H3_LIR1 _HER2_	260	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKP GASVKVSCKASGYTFTSYHIQWVRQAPGQRLEWIG WIYPGDGSTQYNEKFKGRVTITRDTSASTAYMELSS LRSEDTAVYYCAREGTYYAMDYWGQGTLVTVSSG GGGSGGGGSGGGGSDVVMTQTPLSLSVTPGQPASIS CRSSQSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSN RFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCF

			QGSHVPRTFGGGTKVEIKHPSDPLELVVSGPSGGPSS PTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGVVIGIL VAVILLLLLLLLLFLILRHRRQGKHWTSTQRKADFQ HPAGAVGPEPTDRGLQWRSSPAADAQEENLYAAVK HTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPRR EMASPPSPLSGEFLDTKDRQAEEDRQMDTEAAASEA PQDVTYAQLHSLTLRREATEPPPSQEGPSPAVPSIYA TLAIH

Table 12: iCAR constructs

Construct	Construct Name	SEQ ID NO	full length iCAR sequence
MC0058 (VR58)	1xITIM	261	MALPVTALLLPLALLLHAARPEQKLISEEDLQVQLQQ SGPELVKPGASVKMSCKASGYTFTSYHIQWVKQRPG QGLEWIGWIYPGDGSTQYNEKFKGKTTLTADKSSST AYMLLSSLTSEDSAIYFCAREGTYYAMDYWGQGTS VTVSSGGGGSGGGGSGGGGSDVLMTQTPLSLPVSLG DQVSISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLI YKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGV YYCFQGSHVPRTFGGGTKLEIKTERRAEVPTAHPSPS PRPAGQFQTLVVGVVGGLLGSLVLLVWVLAVICSRA ARGTIGARRTGQPLKEDPSAVPVFSVDYGELVFPSG MGTSSPARRGSADGPRSAQPLRPEDGHCSWPL
MC0059 (VR59)	2xITIM	262	MALPVTALLLPLALLLHAARPEQKLISEEDLQVQLQQ SGPELVKPGASVKMSCKASGYTFTSYHIQWVKQRPG QGLEWIGWIYPGDGSTQYNEKFKGKTTLTADKSSST AYMLLSSLTSEDSAIYFCAREGTYYAMDYWGQGTS VTVSSGGGGSGGGGSGGGGSDVLMTQTPLSLPVSLG DQVSISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLI YKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGV YYCFQGSHVPRTFGGGTKLEIKTERRAEVPTAHPSPS PRPAGQFQTLVVGVVGGLLGSLVLLVWVLAVICSRA ARGTIGARRTGQPLKEDPSAVPVFSVDYGELDFQWR EKTPEPPVPCVPEQVDYGELVFPSGMGTSSPARRGSA DGPRSAQPLRPEDGHCSWPL
MC0060 (VR60)	3xITIM	263	MALPVTALLLPLALLLHAARPEQKLISEEDLQVQLQQ SGPELVKPGASVKMSCKASGYTFTSYHIQWVKQRPG QGLEWIGWIYPGDGSTQYNEKFKGKTTLTADKSSST AYMLLSSLTSEDSAIYFCAREGTYYAMDYWGQGTS VTVSSGGGGSGGGGSGGGGSDVLMTQTPLSLPVSLG DQVSISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLI YKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGV YYCFQGSHVPRTFGGGTKLEIKTERRAEVPTAHPSPS PRPAGQFQTLVVGVVGGLLGSLVLLVWVLAVICSRA ARGTIGARRTGQPLKEDPSAVPVFSVDYGELDFQWR EKTPEPPVPCVPEQVDYGELDFQWREKTPEPPVPCVP

			EQVDYGELVFPSGMGTSSPARRGSADGPRSAQPLRP EDGHCSWPL
MC0061 (VR61)	4xITIM	264	MALPVTALLLPLALLLHAARPEQKLISEEDLQVQLQQ SGPELVKPGASVKMSCKASGYTFTSYHIQWVKQRPG QGLEWIGWIYPGDGSTQYNEKFKGKTTLTADKSSST AYMLLSSLTSEDSAIYFCAREGTYYAMDYWGQGTS VTVSSGGGGSGGGGSGGGGSDVLMTQTPLSLPVSLG DQVSISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLI YKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGV YYCFQGSHVPRTFGGGTKLEIKTERRAEVPTAHPSPS PRPAGQFQTLVVGVVGGLLGSLVLLVWVLAVICSRA ARGTIGARRTGQPLKEDPSAVPVFSVDYGELDFQWR EKTPEPPVPCVPEQVDYGELDFQWREKTPEPPVPCVP EQVDYGELDFQWREKTPEPPVPCVPEQVDYGELVFP SGMGTSSPARRGSADGPRSAQPLRPEDGHCSWPL
MC0062 (VR62)	5xITIM	265	MALPVTALLLPLALLLHAARPEQKLISEEDLQVQLQQ SGPELVKPGASVKMSCKASGYTFTSYHIQWVKQRPG QGLEWIGWIYPGDGSTQYNEKFKGKTTLTADKSSST AYMLLSSLTSEDSAIYFCAREGTYYAMDYWGQGTS VTVSSGGGGSGGGGSGGGGSDVLMTQTPLSLPVSLG DQVSISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLI YKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGV YYCFQGSHVPRTFGGGTKLEIKTERRAEVPTAHPSPS PRPAGQFQTLVVGVVGGLLGSLVLLVWVLAVICSRA ARGTIGARRTGQPLKEDPSAVPVFSVDYGELDFQWR EKTPEPPVPCVPEQVDYGELDFQWREKTPEPPVPCVP EQVDYGELDFQWREKTPEPPVPCVPEQVDYGELDFQ WREKTPEPPVPCVPEQVDYGELVFPSGMGTSSPARR GSADGPRSAQPLRPEDGHCSWPL
MC0063 (VR63)	1xITSM	266	MALPVTALLLPLALLLHAARPEQKLISEEDLQVQLQQ SGPELVKPGASVKMSCKASGYTFTSYHIQWVKQRPG QGLEWIGWIYPGDGSTQYNEKFKGKTTLTADKSSST AYMLLSSLTSEDSAIYFCAREGTYYAMDYWGQGTS VTVSSGGGGSGGGGSGGGGSDVLMTQTPLSLPVSLG DQVSISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLI YKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGV YYCFQGSHVPRTFGGGTKLEIKTERRAEVPTAHPSPS PRPAGQFQTLVVGVVGGLLGSLVLLVWVLAVICSRA ARGTIGARRTGQPLKEDPSAVPVFSTEYATIVFPSGM GTSSPARRGSADGPRSAQPLRPEDGHCSWPL
MC0064 (VR64)	2xITSM	267	MALPVTALLLPLALLLHAARPEQKLISEEDLQVQLQQ SGPELVKPGASVKMSCKASGYTFTSYHIQWVKQRPG QGLEWIGWIYPGDGSTQYNEKFKGKTTLTADKSSST AYMLLSSLTSEDSAIYFCAREGTYYAMDYWGQGTS VTVSSGGGGSGGGGSGGGGSDVLMTQTPLSLPVSLG DQVSISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLI YKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGV YYCFQGSHVPRTFGGGTKLEIKTERRAEVPTAHPSPS PRPAGQFQTLVVGVVGGLLGSLVLLVWVLAVICSRA ARGTIGARRTGQPLKEDPSAVPVFSTEYATIDFQWRE

			KTPEPPVPCVPEQTEYATIVFPSGMGTSSPARRGSAD GPRSAQPLRPEDGHCSWPL
MC0065 (VR65)	3xITSM	268	MALPVTALLLPLALLLHAARPEQKLISEEDLQVQLQQ SGPELVKPGASVKMSCKASGYTFTSYHIQWVKQRPG QGLEWIGWIYPGDGSTQYNEKFKGKTTLTADKSSST AYMLLSSLTSEDSAIYFCAREGTYYAMDYWGQGTS VTVSSGGGGSGGGGSGGGGSDVLMTQTPLSLPVSLG DQVSISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLI YKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGV YYCFQGSHVPRTFGGGTKLEIKTERRAEVPTAHPSPS PRPAGQFQTLVVGVVGGLLGSLVLLVWVLAVICSRA ARGTIGARRTGQPLKEDPSAVPVFSTEYATIDFQWRE KTPEPPVPCVPEQTEYATIDFQWREKTPEPPVPCVPE QTEYATIVFPSGMGTSSPARRGSADGPRSAQPLRPED GHCSWPL
MC0066 (VR66)	4xITSM	269	MALPVTALLLPLALLLHAARPEQKLISEEDLQVQLQQ SGPELVKPGASVKMSCKASGYTFTSYHIQWVKQRPG QGLEWIGWIYPGDGSTQYNEKFKGKTTLTADKSSST AYMLLSSLTSEDSAIYFCAREGTYYAMDYWGQGTS VTVSSGGGGSGGGGSGGGGSDVLMTQTPLSLPVSLG DQVSISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLI YKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGV YYCFQGSHVPRTFGGGTKLEIKTERRAEVPTAHPSPS PRPAGQFQTLVVGVVGGLLGSLVLLVWVLAVICSRA ARGTIGARRTGQPLKEDPSAVPVFSTEYATIDFQWRE KTPEPPVPCVPEQTEYATIDFQWREKTPEPPVPCVPE QTEYATIDFQWREKTPEPPVPCVPEQTEYATIVFPSG MGTSSPARRGSADGPRSAQPLRPEDGHCSWPL
MC0067 (VR67)	5xITSM	270	MALPVTALLLPLALLLHAARPEQKLISEEDLQVQLQQ SGPELVKPGASVKMSCKASGYTFTSYHIQWVKQRPG QGLEWIGWIYPGDGSTQYNEKFKGKTTLTADKSSST AYMLLSSLTSEDSAIYFCAREGTYYAMDYWGQGTS VTVSSGGGGSGGGGSGGGGSDVLMTQTPLSLPVSLG DQVSISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLI YKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGV YYCFQGSHVPRTFGGGTKLEIKTERRAEVPTAHPSPS PRPAGQFQTLVVGVVGGLLGSLVLLVWVLAVICSRA ARGTIGARRTGQPLKEDPSAVPVFSTEYATIDFQWRE KTPEPPVPCVPEQTEYATIDFQWREKTPEPPVPCVPE QTEYATIDFQWREKTPEPPVPCVPEQTEYATIDFQWR EKTPEPPVPCVPEQTEYATIVFPSGMGTSSPARRGSA DGPRSAQPLRPEDGHCSWPL
MC0068 (VR68)	2xPD1(G4S)	271	MALPVTALLLPLALLLHAARPEQKLISEEDLQVQLQQ SGPELVKPGASVKMSCKASGYTFTSYHIQWVKQRPG QGLEWIGWIYPGDGSTQYNEKFKGKTTLTADKSSST AYMLLSSLTSEDSAIYFCAREGTYYAMDYWGQGTS VTVSSGGGGSGGGGSGGGGSDVLMTQTPLSLPVSLG DQVSISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLI YKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGV YYCFQGSHVPRTFGGGTKLEIKTERRAEVPTAHPSPS

			PRPAGQFQTLVVGVVGGLLGSLVLLVWVLAVICSRA ARGTIGARRTGQPLKEDPSAVPVFSVDYGELDFQWR EKTPEPPVPCVPEQTEYATIVFPSGMGTSSPARRGSA DGPRSAQPLRPEDGHCSWPLGGGGSGGGGSCSRAAR GTIGARRTGQPLKEDPSAVPVFSVDYGELDFQWREK TPEPPVPCVPEQTEYATIVFPSGMGTSSPARRGSADGP RSAQPLRPEDGHCSWPL
MC0069 (VR69)	2xPD1(PD1)	272	MALPVTALLLPLALLLHAARPEQKLISEEDLQVQLQQ SGPELVKPGASVKMSCKASGYTFTSYHIQWVKQRPG QGLEWIGWIYPGDGSTQYNEKFKGKTTLTADKSSST AYMLLSSLTSEDSAIYFCAREGTYYAMDYWGQGTS VTVSSGGGGSGGGGSGGGGSDVLMTQTPLSLPVSLG DQVSISCRSSQSIVHSNGNTYLEWYLQKPGQSPKLLI YKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGV YYCFQGSHVPRTFGGGTKLEIKTERRAEVPTAHPSPS PRPAGQFQTLVVGVVGGLLGSLVLLVWVLAVICSRA ARGTIGARRTGQPLKEDPSAVPVFSVDYGELDFQWR EKTPEPPVPCVPEQTEYATIDFQWREKTPEPPVPCVPE QVDYGELDFQWREKTPEPPVPCVPEQTEYATIVFPSG MGTSSPARRGSADGPRSAQPLRPEDGHCSWPL
MC0456 (VR456)	LIR1(ITIM 1)X4	327	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPG ASVKVSCKASGYTFTSYHIQWVRQAPGQRLEWIGWI YPGDGSTQYNEKFKGRVTITRDTSASTAYMELSSLRS EDTAVYYCAREGTYYAMDYWGQGTLVTVSSGGGG SGGGGSGGGGSDVVMTQTPLSLSVTPGQPASISCRSS QSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVP RTFGGGTKVEIKTERRAEVPTAHPSPSPRPAGQFQTL VVGVVGGLLGSLVLLVWVLAVILRHRRQGKHWTST QRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEE NLYAAVKHTQPEDGVEMDTRSPHDEDPQANLYAAV KHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDT EAAASEAPQDNLYAAVHSLTLRREATEPPPSQEGPSP AVPNLYAAVAIH
MC0457 (VR457)	LIR1(ITIM 2)X4	328	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPG ASVKVSCKASGYTFTSYHIQWVRQAPGQRLEWIGWI YPGDGSTQYNEKFKGRVTITRDTSASTAYMELSSLRS EDTAVYYCAREGTYYAMDYWGQGTLVTVSSGGGG SGGGGSGGGGSDVVMTQTPLSLSVTPGQPASISCRSS QSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVP RTFGGGTKVEIKTERRAEVPTAHPSPSPRPAGQFQTL VVGVVGGLLGSLVLLVWVLAVILRHRRQGKHWTST QRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEE VTYAEVKHTQPEDGVEMDTRSPHDEDPQAVTYAEV KHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDT EAAASEAPQDVTYAEVHSLTLRREATEPPPSQEGPSP AVPVTYAEVAIH
MC0458 (VR458)	LIR1(ITIM 3)X4	329	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPG ASVKVSCKASGYTFTSYHIQWVRQAPGQRLEWIGWI

			YPGDGSTQYNEKFKGRVTITRDTSASTAYMELSSLRS EDTAVYYCAREGTYYAMDYWGQGTLVTVSSGGGG SGGGGSGGGGSDVVMTQTPLSLSVTPGQPASISCRSS QSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVP RTFGGGTKVEIKTERRAEVPTAHPSPSPRPAGQFQTL VVGVVGGLLGSLVLLVWVLAVILRHRRQGKHWTST QRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEE VTYAQLKHTQPEDGVEMDTRSPHDEDPQAVTYAQL KHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDT EAAASEAPQDVTYAQLHSLTLRREATEPPPSQEGPSP AVPVTYAQLAIH
MC0459 (VR459)	LIR1(ITM4)X4	330	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPG ASVKVSCKASGYTFTSYHIQWVRQAPGQRLEWIGWI YPGDGSTQYNEKFKGRVTITRDTSASTAYMELSSLRS EDTAVYYCAREGTYYAMDYWGQGTLVTVSSGGGG SGGGGSGGGGSDVVMTQTPLSLSVTPGQPASISCRSS QSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVP RTFGGGTKVEIKTERRAEVPTAHPSPSPRPAGQFQTL VVGVVGGLLGSLVLLVWVLAVILRHRRQGKHWTST QRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEE SIYATLKHTQPEDGVEMDTRSPHDEDPQASIYATLKH SRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTEA AASEAPQDSIYATLHSLTLRREATEPPPSQEGPSPAVP SIYATLAIH
MC0460 (VR460)	LIR1ITIM(3-4)	331	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPG ASVKVSCKASGYTFTSYHIQWVRQAPGQRLEWIGWI YPGDGSTQYNEKFKGRVTITRDTSASTAYMELSSLRS EDTAVYYCAREGTYYAMDYWGQGTLVTVSSGGGG SGGGGSGGGGSDVVMTQTPLSLSVTPGQPASISCRSS QSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVP RTFGGGTKVEIKTERRAEVPTAHPSPSPRPAGQFQTL VVGVVGGLLGSLVLLVWVLAVILRHRRQGKHWTST QRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEE VTYAQLKHTQPEDGVEMDTRSPHDEDPQASIYATLK HSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTE AAASEAPQDVTYAQLHSLTLRREATEPPPSQEGPSPA VPSIYATLAIH
MC0461 (VR461)	PD-1ITSM LIR1 (ITIM3-4)	332	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPG ASVKVSCKASGYTFTSYHIQWVRQAPGQRLEWIGWI YPGDGSTQYNEKFKGRVTITRDTSASTAYMELSSLRS EDTAVYYCAREGTYYAMDYWGQGTLVTVSSGGGG SGGGGSGGGGSDVVMTQTPLSLSVTPGQPASISCRSS QSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVP RTFGGGTKVEIKTERRAEVPTAHPSPSPRPAGQFQTL VVGVVGGLLGSLVLLVWVLAVILRHRRQGKHWTST QRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEE

			TEYATIKHTQPEDGVEMDTRSPHDEDPQATEYATIKH SRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTEA AASEAPQDVTYAQLHSLTLRREATEPPPSQEGPSPAV PSIYATLAIH
MC0462 (VR462)	LIR1 (ITIM3-4) PD-1ITSMX2	333	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPG ASVKVSCKASGYTFTSYHIQWVRQAPGQRLEWIGWI YPGDGSTQYNEKFKGRVTITRDTSASTAYMELSSLRS EDTAVYYCAREGTYYAMDYWGQGTLVTVSSGGGG SGGGGSGGGGSDVVMTQTPLSLSVTPGQPASISCRSS QSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVP RTFGGGTKVEIKTERRAEVPTAHPSPSPRPAGQFQTL VVGVVGGLLGSLVLLVWVLAVILRHRRQGKHWTST QRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEE VTYAQLKHTQPEDGVEMDTRSPHDEDPQASIYATLK HSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTE AAASEAPQDTEYATIHSLTLRREATEPPPSQEGPSPAV PTEYATIAIH
MC0463 (VR463)	LIR1 ITIM3, PD-1 (ITSM)X2, LIR1 ITIM4	334	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPG ASVKVSCKASGYTFTSYHIQWVRQAPGQRLEWIGWI YPGDGSTQYNEKFKGRVTITRDTSASTAYMELSSLRS EDTAVYYCAREGTYYAMDYWGQGTLVTVSSGGGG SGGGGSGGGGSDVVMTQTPLSLSVTPGQPASISCRSS QSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVP RTFGGGTKVEIKTERRAEVPTAHPSPSPRPAGQFQTL VVGVVGGLLGSLVLLVWVLAVILRHRRQGKHWTST QRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEE VTYAQLKHTQPEDGVEMDTRSPHDEDPQATEYATIK HSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTE AAASEAPQDTEYATIHSLTLRREATEPPPSQEGPSPAV PSIYATLAIH
(VR492)		350	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPG ASVKVSCKASGYTFTSYHIQWVRQAPGQRLEWIGWI YPGDGSTQYNEKFKGRVTITRDTSASTAYMELSSLRS EDTAVYYCAREGTYYAMDYWGQGTLVTVSSGGGG SGGGGSGGGGSDVVMTQTPLSLSVTPGQPASISCRSS QSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVP RTFGGGTKVEIKHPSDPLELVVSGPSGGPSSPTTGPTS TSGPEDQPLTPTGSDPQSGLGRHLGVVIGILVAVILLL LLLLLLFLILRHRRQGKHWTSTQRKADFQHPAGAVG PEPTDRGLQWRSSPAADAQEENLFAAVKHTQPEDGV EMDTRSPHDEDPQAVTFAEVKHSRPRREMASPPSPLS GEFLDTKDRQAEEDRQMDTEAAASEAPQDVTFAQL HSLTLRREATEPPPSQEGPSPAVPSIFATLAIH
(VR442)		351	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPG ASVKVSCKASGYTFTSYHIQWVRQAPGQRLEWIGWI YPGDGSTQYNEKFKGRVTITRDTSASTAYMELSSLRS

			EDTAVYYCAREGTYYAMDYWGQGTLVTVSSGGGG SGGGGSGGGGSDVVMTQTPLSLSVTPGQPASISCRSS QSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVP RTFGGGTKVEIKPSSPTTGPTSTSGPEDQPLTPTGSDP QSGLGRHLGVVIGILVAVILLLLLLLLLFLILRHRRQG KHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPA ADAQEENLYAAVKHTQPEDGVEMDTRSPHDEDPQA VTYAEVKHSRPRREMASPPSPLSGEFLDTKDRQAEE DRQMDTEAAASEAPQDVTYAQLHSLTLRREATEPPP SQEGPSPAVPSIYATLAIH
(VR443)		352	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPG ASVKVSCKASGYTFTSYHIQWVRQAPGQRLEWIGWI YPGDGSTQYNEKFKGRVTITRDTSASTAYMELSSLRS EDTAVYYCAREGTYYAMDYWGQGTLVTVSSGGGG SGGGGSGGGGSDVVMTQTPLSLSVTPGQPASISCRSS QSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVP RTFGGGTKVEIKGPTSTSGPEDQPLTPTGSDPQSGLG RHLGVVIGILVAVILLLLLLLLLFLILRHRRQGKHWTS TQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQE ENLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAE VKHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMD TEAAASEAPQDVTYAQLHSLTLRREATEPPPSQEGPS PAVPSIYATLAIH
(VR515)		353	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPG ASVKVSCKASGYTFTSYHIQWVRQAPGQRLEWIGWI YPGDGSTQYNEKFKGRVTITRDTSASTAYMELSSLRS EDTAVYYCAREGTYYAMDYWGQGTLVTVSSGGGG SGGGGSGGGGSDVVMTQTPLSLSVTPGQPASISCRSS QSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVP RTFGGGTKVEIKGPTSTSGPEDQPLTPTGSDPQSGLG RHLGVVIGILVAVILLLLLLLLLFLILRHRRQGKHWTS TQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQE ENLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAE VKHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMD TEAAASEAPQDVTYAQLHSLTLRREATEPPPSQEGPS PAVPSIYATLAIH
(VR516)		354	MALPVTALLLPLALLLHAARPDIVMTQSPDSLAVSLG ERATISCKSSQSVLYSSNNKNYLAWYQQKPGQPPKL LIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVA VYYCQQYYGTPFTFGGGTKVEIKGGGGSGGGGSGG GGSQVQLVQSGAEVKKPGASVKVSCKASGYTFTDY YLHWVRQAPGQGLEWMGWINPYTGGTNYAQKFQG RVTMTRDTSISTAYMELSGLTSDDTAVYYCARAGAS YYDFWSGWVFDYWGQGTLVTVSSGPTSTSGPEDQP LTPTGSDPQSGLGRHLGVVIGILVAVILLLLLLLLLFLI

			LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGL QWRSSPAADAQEENLYAAVKHTQPEDGVEMDTRSP HDEDPQAVTYAEVKHSRPRREMASPPSPLSGEFLDT KDRQAEEDRQMDTEAAASEAPQDVTYAQLHSLTLR REATEPPPSQEGPSPAVPSIYATLAIH
(VR517)		355	MALPVTALLLPLALLLHAARPDIVMTQSPDSLAVSLG ERATISCKSSQSVLYSSNNKNYLAWYQQKPGQPPKL LIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVA VYYCQQYYGTPFTFGGGTKVEIKGGGGSGGGGSGG GGSQVQLVQSGAEVKKPGASVKVSCKASGYTFTDY YLHWVRQAPGQGLEWMGWINPYTGGTNYAQKFQG RVTMTRDTSISTAYMELSRLRSEDTAVYYCARAGAS YYDFWSGWVFDYWGQGTLVTVSSTSGPEDQPLTPT GSDPQSGLGRHLGVVIGILVAVILLLLLLLLLFLILRH RRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWR SSPAADAQEENLYAAVKHTQPEDGVEMDTRSPHDE DPQAVTYAEVKHSRPRREMASPPSPLSGEFLDTKDR QAEEDRQMDTEAAASEAPQDVTYAQLHSLTLRREAT EPPPSQEGPSPAVPSIYATLAIH
(VR506)		356	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPG ASVKVSCKASGYTFTSYHIQWVRQAPGQRLEWIGWI YPGDGSTQYNEKFKGRVTITRDTSASTAYMELSSLRS EDTAVYYCAREGTYYAMDYWGQGTLVTVSSGGGG SGGGGSGGGGSDVVMTQTPLSLSVTPGQPASISCRSS QSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVP RTFGGGTKVEIKESKYGPPCPPCPGPTSTSGPEDQPLT PTGSDPQSGLGRHLGVVIGILVAVILLLLLLLLLFLILR HRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQW RSSPAADAQEENLYAAVKHTQPEDGVEMDTRSPHD EDPQAVTYAEVKHSRPRREMASPPSPLSGEFLDTKDR QAEEDRQMDTEAAASEAPQDVTYAQLHSLTLRREAT EPPPSQEGPSPAVPSIYATLAIH
(VR507)		537	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPG ASVKVSCKASGYTFTSYHIQWVRQAPGQRLEWIGWI YPGDGSTQYNEKFKGRVTITRDTSASTAYMELSSLRS EDTAVYYCAREGTYYAMDYWGQGTLVTVSSGGGG SGGGGSGGGGSDVVMTQTPLSLSVTPGQPASISCRSS QSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVP RTFGGGTKVEIKESKYGPPCPPCPEDQPLTPTGSDPQS GLGRHLGVVIGILVAVILLLLLLLLLFLILRHRRQGKH WTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAAD AQEENLYAAVKHTQPEDGVEMDTRSPHDEDPQAVT YAEVKHSRPRREMASPPSPLSGEFLDTKDRQAEEDR QMDTEAAASEAPQDVTYAQLHSLTLRREATEPPPSQ EGPSPAVPSIYATLAIH

(VR508)		358	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPG ASVKVSCKASGYTFTSYHIQWVRQAPGQRLEWIGWI YPGDGSTQYNEKFKGRVTITRDTSASTAYMELSSLRS EDTAVYYCAREGTYYAMDYWGQGTLVTVSSGGGG SGGGGSGGGGSDVVMTQTPLSLSVTPGQPASISCRSS QSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVP RTFGGGTKVEIKESKYGPPCPPCPLTPTGSDPQSGLGR HLGVVIGILVAVILLLLLLLLLFLILRHRRQGKHWTST QRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEE NLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEV KHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDT EAAASEAPQDVTYAQLHSLTLRREATEPPPSQEGPSP AVPSIYATLAIH

[0439] In some embodiments, the iCAR comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:305, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:327, SEQ ID NO:328, SEQ ID NO:329, SEQ ID NO:330, SEQ ID NO:331, SEQ ID NO:332, SEQ ID NO:333, SEQ ID NO:334, SEQ ID NO:349, SEQ ID NO:350, SEQ ID NO:351, SEQ ID NO:352, SEQ ID NO:353, SEQ ID NO:354, SEQ ID NO: 356, SEQ ID NO: 357, and SEQ ID NO: 358.

7. iCAR portion/aCAR portion: linker

[0440] In some embodiments, the iCAR portion is covalently linked to the aCAR portion via a linker. In a certain embodiment, the linker is a gly-ser polypeptide linker, *i.e.*, a peptide that consists of glycine and serine residues. Exemplary gly-ser polypeptide linkers comprise the amino acid sequence $Ser(Gly_4Ser)_n$, as well as $(Gly_4Ser)_n$ and/or $(Gly_4Ser_3)_n$. In some embodiments, n=l. In some embodiments, n=2. In some embodiments, n=3, *i.e.*, $Ser(Gly_4Ser)_3$. In some embodiments, n=4, *i.e.*, $Ser(Gly_4Ser)_4$. In some embodiments, n=5. In some embodiments, n=6. In some embodiments, n=7. In some embodiments, n=8. In some embodiments, n=9. In some embodiments, n=10. Another exemplary gly-ser polypeptide linker comprises the amino acid sequence $Ser(Gly_4Ser)_n$. In some embodiments, n=l. In some embodiments, n=2. In some embodiments, n=3. In another embodiment, n=4. In some embodiments, n=5. In some embodiments, n=6. Another exemplary gly-ser polypeptide linker comprises $(Gly_4Ser)_n$. In some embodiments, n=l. In some embodiments, n=2. In some

embodiments, n=3. In some embodiments, n=4. In some embodiments, n=5. In some embodiments, n=6. Another exemplary gly-ser polypeptide linker comprises $(Gly_3Ser)_n$. In some embodiments, n=l. In some embodiments, n=2. In some embodiments, n=3. In some embodiments, n=4. In another embodiment, n=5. In yet another embodiment, n=6. Another exemplary gly-ser polypeptide linker comprises $(Gly_4Ser_3)_n$. In some embodiments, n=l. In some embodiments, n=2. In some embodiments, n=3. In some embodiments, n=4. In some embodiments, n=5. In some embodiments, n=6. Another exemplary gly-ser polypeptide linker comprises $(Gly_3Ser)_n$. In some embodiments, n=l. In some embodiments, n=2. In some embodiments, n=3. In some embodiments, n=4. In another embodiment, n=5. In yet another embodiment, n=6.

[0441] In some embodiments, the bicistronic construct comprises a linker that covalently connects the iCAR portion and the aCAR portion. In some embodiments, the bicistronic construct comprises a viral self-cleaving 2A peptide between the nucleic acid sequence encoding the iCAR portion and the nucleic acid sequence encoding the aCAR portion of the construct. In some embodiments, the viral self-cleaving 2A peptide includes T2A from *Thosea asigna* virus (TaV). In some embodiments, the iCAR portion is covalently linked to the aCAR portion via a linker. In some embodiments, the iCAR portion is covalently linked to the aCAR portion via a GSG . In some embodiments, the iCAR portion is covalently linked to the aCAR portion via a GGGGS linker (SEQ ID NO:153). In some embodiments, the iCAR portion is covalently linked to the aCAR portion via a GGGGSGGGGSGGGGS linker (SEQ ID NO:154). In some embodiments, the iCAR is covalently linked to the aCAR portion via a T2A linker (SEQ ID NO:155). In some embodiments, the iCAR is covalently linked to the aCAR portion via a F2A linker (SEQ ID NO:156). In some embodiments, the iCAR is covalently linked to the aCAR portion via a P2A linker (SEQ ID NO:157). In some embodiments, the iCAR is covalently linked to the aCAR portion via a E2A linker (SEQ ID NO:158). In some embodiments, the iCAR is covalently linked to the aCAR portion via a IRES long linker (SEQ ID NO:159). In some embodiments, the iCAR is covalently linked to the aCAR portion via a IRES short linker (SEQ ID NO:160).

Table 13: iCAR portion/aCAR portion linker sequences

Sequence Information	SEQ ID NO	Amino acid sequence
G_4S	153	GGGGS
$(G_4S)X3$	154	GGGGSGGGGSGGGGS

T2A	155	GSGEGRGSLLTCGDVEENPGP
F2A	156	GSGVKQTLNFDLLKLAGDVESNPGP
P2A	157	GSGATNFSLLKQAGDVEENPGP
E2A	158	GSGQCTNYALLKLAGDVESNPGP
Sequence Information	**SEQ ID NO**	**Nucleotide Sequence**
IRES long	159	CCCCCCCCCCTAACGTTACTGGCCGAAGCCGCTTGGA ATAAGGCCGGTGTGCGTTTGTCTATATGTTATTTTCCA CCATATTGCCGTCTTTTGGCAATGTGAGGGCCCGGAA ACCTGGCCCTGTCTTCTTGACGAGCATTCCTAGGGGT CTTTCCCCTCTCGCCAAAGGAATGCAAGGTCTGTTGA ATGTCGTGAAGGAAGCAGTTCCTCTGGAAGCTTCTTG AAGACAAACAACGTCTGTAGCGACCCTTTGCAGGCA GCGGAACCCCCCACCTGGCGACAGGTGCCTCTGCGGC CAAAAGCCACGTGTATAAGATACACCTGCAAAGGCG GCACAACCCCAGTGCCACGTTGTGAGTTGGATAGTTG TGGAAAGAGTCAAATGGCTCTCCTCAAGCGTATTCAA CAAGGGGCTGAAGGATGCCCAGAAGGTACCCCATTG TATGGGATCTGATCTGGGGCCTCGGTGCACATGCTTT ACATGTGTTTAGTCGAGGTTAAAAAAACGTCTAGGCC CCCCGAACCACGGGGACGTGGTTTTCCTTTGAAAAAC ACGATGATAATATG
IRES short	160	CCCCTCTCGCCAAAGGAATGCAAGGTCTGTTGAATGT CGTGAAGGAAGCAGTTCCTCTGGAAGCTTCTTGAAGA CAAACAACGTCTGTAGCGACCCTTTGCAGGCAGCGGA ACCCCCCACCTGGCGACAGGTGCCTCTGCGGCCAAAA GCCACGTGTATAAGATACACCTGCAAAGGCGGCACA ACCCCAGTGCCACGTTGTGAGTTGGATAGTTGTGGAA AGAGTCAAATGGCTCTCCTCAAGCGTATTCAACAAGG GGCTGAAGGATGCCCAGAAGGTACCCCATTGTATGG GATCTGATCTGGGGCCTCGGTGCACATGCTTTACATG TGTTTAGTCGAGGTTAAAAAAACGTCTAGGCCCCCCG AACCACGGGGACGTGGTTTTCCTTTGAAAAACACGAT GATAATATG

8. iCAR portion/aCAR portion: signal peptide

[0442] In some embodiments, the bicistronic construct comprises a signal peptide upstream of the iCAR and aCAR portions. In some embodiments, the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161). In some embodiments, the signal peptide is a GM-CSF signal peptide (SEQ ID NO: 162). In some embodiments, the signal peptide is a mIgK signal peptide (SEQ ID NO: 306).

Table 14: iCAR/aCAR signal peptide sequences

Sequence Information	SEQ ID NO	Amino acid sequence
CD8 alpha	161	MALPVTALLLPLALLLHAARP
GM-CSF	162	MLLLVTSLLLCELPHPAFLLIP
mIgK	306	MSVPTQVLGLLLLWLTDARC

9. aCAR portion: aCAR scFv

[0443] In some embodiments, the bicistronic construct comprises an aCAR portion comprising a single chain variable fragment (scFv) component. In some embodiments, the iCAR portion comprises an scFv component. In some embodiments, the scFv targets Her2, Mesothelin, or EGFR. In some embodiments, the scFv targets Her2. In some embodiments, the scFv targets Mesothelin. In some embodiments, the scFv targets EGFR. In some embodiments, the scFv is an scFv based on trastuzumab (anti-Her2 antibody, also referred to as HERCEPTIN®), pertuzumab (anti-Her2 antibody, also referred to as PERJETA®), another commercial anti-Her2 antibody including, but not limited to, FRP5, A21, XMT1517, XMT1518, XMT1519, FWP51, bioequivalents thereof, or biosimilars thereof. In some embodiments, the scFv has the VH and VL domains of trastuzumab, pertuzumab, FRP5, A21, XMT1517, XMT1518, XMT1519, FWP51, bioequivalents thereof, or biosimilars thereof. In some embodiments, the scFv is an scFv based on cetuximab (anti-EGFR antibody, also referred to as ERBITUX®), panitumumab (anti-EGFR antibody, also referred to as VECTIBIX®), another commercial anti-EGFR antibody including, but not limited to, Imgatuzumab, Nimotuzumab, Necitumumab, ICR62, Matuzumab, C10, Zalutumumab, P1X, P2X, P3X, EGFR-la1-VHH, bioequivalents thereof, or biosimilars thereof. In some embodiments, the scFv has the VH and VL domains of cetuximab, panitumumab, Imgatuzumab, Nimotuzumab, Necitumumab, ICR62, Matuzumab, C10, Zalutumumab, P1X, P2X, P3X, EGFR-la1-VHH, bioequivalents thereof, or biosimilars thereof. In some embodiments, the scFv is an scFv based on a commercial anti- Mesothelin antibody including, but not limited to, Amatuximab, P4, SS1, SD1, SD2, 1H7, 3C02, bioequivalents thereof, or biosimilars thereof. In some embodiments, the scFv has the VH and VL domains of Amatuximab, P4, SS1, SD1, SD2, 1H7, 3C02, bioequivalents thereof, or biosimilars thereof.

[0444] In some embodiments, the scFv targets Her2. In some embodiments, the Her2 scFv is based on the Vh and Vl from trastuzumab or pertuzumab. In some embodiments, the Her2 scFv is based on the Vh and Vl from trastuzumab. In some embodiments, the Her2 scFv is based on

the Vh and Vl from pertuzumab. The Vh and Vl chains for trastuzumab and pertuzumab are provided below in Tables 15 and 16. In some embodiments, the Her2 scFv is based on the Vh and Vl from FRP5. In some embodiments, the Her2 scFv is based on the Vh and Vl from A21. In some embodiments, the Her2 scFv is based on the Vh and Vl from XMT1517. In some embodiments, the Her2 scFv is based on the Vh and Vl from XMT1518. In some embodiments, the Her2 scFv is based on the Vh and Vl from XMT1519. In some embodiments, the Her2 scFv is based on the Vh and Vl from FWP51. In some embodiments, the Her2 scFv is based on the Vh and Vl from trastuzumab F9G.

Table 15: anti-Her2 sequences

Sequence Information	**SEQ ID NO**	**Amino acid sequence**
trastuzumab Variable heavy chain	170	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQA PGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKNTAY LQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVT VSS
trastuzumab Variable light chain	171	DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKP GKAPKLLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQPED FATYYCQQHYTTPPTFGQGTKVEIK
trastuzumab scFv	172	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQA PGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKNTAY LQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVT VSS**GSTSGSGKPGSGEGSTKG**DIQMTQSPSSLSASVGDRV TITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVP SRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQ GTKVEIK
Trastuzumab scFv: VL_whitlow linker_VH	451	DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKP GKAPKLLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQPED FATYYCQQHYTTPPTFGQGTKVEIKGSTSGSGKPGSGEGS TKGEVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWV RQAPGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKN TAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGT LVTVS
Trastuzumab scFv: VL_whitlow linker_VH	452	DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKP GKAPKLLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQPED FATYYCQQHYTTPPTFGQGTKVEIKGSTSGSGKPGSGEGS TKGEVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWV RQAPGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKN TAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGT LVTVSS
Trastuzumab F9G variable Heavy chain	307	DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKP GKAPKLLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQPED FATYYCQQHYTTPPTFGQGTKVEIK
Trastuzumab F9G variable Light chain	308	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQA PGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKNTAY

		LQMNSLRAEDTAVYYCSRWGGDGGYAMDYWGQGTLVT VSS
pertuzumab Variable heavy chain	173	EVQLVESGGGLVQPGGSLRLSCAASGFTFTDYTMDWVRQ APGKGLEWVADVNPNSGGSIYNQRFKGRFTLSVDRSKNT LYLQMNSLRAEDTAVYYCARNLGPSFYFDYWGQGTLVT VSS
pertuzumab Variable light chain	174	DIQMTQSPSSLSASVGDRVTITCKASQDVSIGVAWYQQKP GKAPKLLIYSASYRYTGVPSRFSGSGSGTDFTLTISSLQPED FATYYCQQYYIYPYTFGQGTKVEIK
pertuzumab scFv	175	DIQMTQSPSSLSASVGDRVTITCKASQDVSIGVAWYQQKP GKAPKLLIYSASYRYTGVPSRFSGSGSGTDFTLTISSLQPED FATYYCQQYYIYPYTFGQGTKVEIKGSTSGSGKPGSGEGS TKGEVQLVESGGGLVQPGGSLRLSCAASGFTFTDYTMDW VRQAPGKGLEWVADVNPNSGGSIYNQRFKGRFTLSVDRS KNTLYLQMNSLRAEDTAVYYCARNLGPSFYFDYWGQGT LVTVSS
FRP5 variable heavy vhain	176	QVQLQQSGPELKKPGETVKISCKASGYPFTNYGMNWVKQ APGQGLKWMGWINTSTGESTFADDFKGRFDFSLETSANT AYLQINNLKSEDMATYFCARWEVYHGYVPYWGQGTTVT VSS
FRP5 variable light vhain	177	DIQLTQSHKFLSTSVGDRVSITCKASQDVYNAVAWYQQK PGQSPKLLIYSASSRYTGVPSRFTGSGSGPDFTFTISSVQAE DLAVYFCQQHFRTPFTFGSGTKLEIK
A21 variable heavy vhain	178	EVQLQQSGPEVVKTGASVKISCKASGYSFTGYFINWVKKN SGKSPEWIGHISSSYATSTYNQKFKNKAAFTVDTSSSTAFM QLNSLTSEDSAVYYCVRSGNYEEYAMDYWGQGTSVTVSS
A21 variable light vhain	179	DIVLTQTPSSLPVSVGEKVTMTCKSSQTLLYSNNQKNYLA WYQQKPGQSPKLLISWAFTRKSGVPDRFTGSGSGTDFTLTI GSVKAEDLAVYYCQQYSNYPWTFGGGTKLEIK
XMT1517 variable heavy vhain	180	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQ APGKGLEWVAVIWYDGSNKYYADSVKGRFTISRDNSKNT LYLQMNSLRAEDTAVYYCAKEAPYYAKDYMDVWGKGT TVTVSS
XMT1517 variable light vhain	181	EIVLTQSPGTLSLSPGERATLSCRASQSVSSDYLAWYQQKP GQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPED FAVYYCQQYVSYWTFGGGTKVEIK
XMT1518 variable heavy vhain	182	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQ APGKGLEWVAGIWWDGSNEKYADSVKGRFTISRDNSKNT LYLQMNSLRAEDTAVYYCAKEAPYYAKDYMDVWGKGT TVTVSS
XMT1518 variable light vhain	183	EIVLTQSPGTLSLSPGERATLSCRASQSVSSDYLAWYQQKP GQAPRLLIYGASRRATGIPDRFSGSGSGTDFTLTISRLEPED FAVYYCQQYVSYWTFGGGTKVEIK
XMT1519 variable heavy vhain	184	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMNWVRQ APGKGLEWVSYISSSSSTIYYADSVKGRFTISRDNAKNSLY LQMNSLRAEDTAVYYCARGGHGYFDLWGRGTLVTVSS
XMT1519 variable light vhain	185	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKP GQAPRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPED FAVYYCQQYHHSPLTFGGGTKVEIK

FWP51 variable heavy vhain	186	QVQLQQSGAELVRPGTSVKLSCKASDYTFTSYWMNWVK QRPGQGLEWIGMIDPSDSETQYNQMFKDKAALTVDKSSN TAYMQLSSLTSEDSAVYYCAKGGASGDWYFDVWGQGTT VT
FWP51 variable light vhain	187	DIQLTQSPSSLSASLGGEVTITCKASQDIKKYIAWYQHKPG KSPRLLIHYTSVLQPGIPSRFSGSGSGRDYSFSIHNLEPEDIA TYYCLHYDYLYTFGGGTKLEI
FWP51 VL VH	188	MLLLVTSLLLCELPHPAFLLIPDYKDDDDKQVQLQQSGAE LVRPGTSVKLSCKASDYTFTSYWMNWVKQRPGQGLEWI GMIDPSDSETQYNQMFKDKAALTVDKSSNTAYMQLSSLT SEDSAVYYCAKGGASGDWYFDVWGQGTTVTGSTSGSGK PGSGEGSTKGDIQLTQSPSSLSASLGGEVTITCKASQDIKKY IAWYQHKPGKSPRLLIHYTSVLQPGIPSRFSGSGSGRDYSFS IHNLEPEDIATYYCLHYDYLYTFGGGTKLEI
Anti HER2 VHH	309	QVQLVQSGGGLVQAGGSLRLSCAASGRTFSSYAMAWFRQ APGKEREFVAAISWSGANIYVADSVKGRFTISRDNAKDTV YLQMNSLKPEDTAVYYCAVKLGFAPVEERQYDYWGQGT QVTVSS

[0445] In some embodiments, the scFv targets EGFR. In some embodiments, the EGFR scFv is based on the Vh and Vl from cetuximab, panitumumab, Imgatuzumab, Nimotuzumab, Necitumumab, ICR62, Matuzumab, C10, Zalutumumab, P1X, P2X, P3X, or EGFR-la1-VHH. In some embodiments, the EGFR scFv is based on the Vh and Vl from cetuximab. In some embodiments, the EGFR scFv is based on the Vh and Vl from panitumumab. In some embodiments, the EGFR scFv is based on the Vh and Vl from Imgatuzumab. In some embodiments, the EGFR scFv is based on the Vh and Vl from Nimotuzumab. In some embodiments, the EGFR scFv is based on the Vh and Vl from Nimotuzumab (K5). In some embodiments, the EGFR scFv is based on the Vh and Vl from Necitumumab. In some embodiments, the EGFR scFv is based on the Vh and Vl from ICR62. In some embodiments, the EGFR scFv is based on the Vh and Vl from Matuzumab. In some embodiments, the EGFR scFv is based on the Vh and Vl from C10. In some embodiments, the EGFR scFv is based on the Vh and Vl from Zalutumumab. In some embodiments, the EGFR scFv is based on the Vh and Vl from P1X. In some embodiments, the EGFR scFv is based on the Vh and Vl from P2X. In some embodiments, the EGFR scFv is based on the Vh and Vl from P3X. In some embodiments, the EGFR scFv is based on EGFR-la1-VHH. In some embodiments, the EGFR scFv is based on EGFR-VHH.

Table 16: anti-EGFR sequences

Sequence Information	**SEQ ID NO**	**Amino acid sequence**

cetuximab Variable heavy chain	189	QVQLKQSGPGLVQPSQSLSITCTVSGFSLTNYGVHWVRQ SPGKGLEWLGVIWSGGNTDYNTPFTSRLSINKDNSKSQV FFKMNSLQSNDTAIYYCARALTYYDYEFAYWGQGTLVT VS
cetuximab Variable light chain	190	DILLTQSPVILSVSPGERVSFSCRASQSIGTNIHWYQQRTN GSPRLLIKYASESISGIPSRFSGSGSGTDFTLSINSVESEDIA DYYCQQNNNWPTTFGAGTKLELK
cetuximab scFv (SEQ ID NO:)	191	QVQLKQSGPGLVQPSQSLSITCTVSGFSLTNYGVHWVRQ SPGKGLEWLGVIWSGGNTDYNTPFTSRLSINKDNSKSQV FFKMNSLQSNDTAIYYCARALTYYDYEFAYWGQGTLVT VSGSTSGSGKPGSGEGSTKGDILLTQSPVILSVSPGERVSF SCRASQSIGTNIHWYQQRTNGSPRLLIKYASESISGIPSRFS GSGSGTDFTLSINSVESEDIADYYCQQNNNWPTTFGAGT KLELK
panitumumab Variable heavy chain	192	QVQLQESGPGLVKPSETLSLTCTVSGGSVSSGDYYWTWI RQSPGKGLEWIGHIYYSGNTNYNPSLKSRLTISIDTSKTQF SLKLSSVTAADTAIYYCVRDRVTGAFDIWGQGTMVTVSS
panitumumab Variable light chain	193	DIQMTQSPSSLSASVGDRVTITCQASQDISNYLNWYQQKP GKAPKLLIYDASNLETGVPSRFSGSGSGTDFTFTISSLQPE DIATYFCQHFDHLPLAFGGGTKVEIK
panitumumab scFv	194	DIQMTQSPSSLSASVGDRVTITCQASQDISNYLNWYQQKP GKAPKLLIYDASNLETGVPSRFSGSGSGTDFTFTISSLQPE DIATYFCQHFDHLPLAFGGGTKVEIKGSTSGSGKPGSGEG STKGQVQLQESGPGLVKPSETLSLTCTVSGGSVSSGDYY WTWIRQSPGKGLEWIGHIYYSGNTNYNPSLKSRLTISIDT SKTQFSLKLSSVTAADTAIYYCVRDRVTGAFDIWGQGTM VTVSS
Imgatuzuma variable heavy chain	195	QVQLVQSGAEVKKPGSSVKVSCKASGFTFTDYKIHWVR QAPGQGLEWMGYFNPNSGYSTYAQKFQGRVTITADKST STAYMELSSLRSEDTAVYYCARLSPGGYYVMDAWGQGT TVTVSS
Imgatuzumab variable light chain	196	DIQMTQSPSSLSASVGDRVTITCRASQGINNYLNWYQQK PGKAPKRLIYNTNNLQTGVPSRFSGSGSGTEFTLTISSLQP EDFATYYCLQHNSFPTFGQGTKLEIK
Nimotuzumab variable heavy chain	197	QVQLQQSGAEVKKPGSSVKVSCKASGYTFTNYYIYWVR QAPGQGLEWIGGINPTSGGSNFNEKFKTRVTITVDESTNT AYMELSSLRSEDTAFYFCARQGLWFDSDGRGFDFWGQG STVTVSS
Nimotuzumab variable light chain	198	DIQMTQSPSSLSASVGDRVTITCRSSQNIVHSNGNTYLDW YQQTPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTFTIS SLQPEDIATYYCFQYSHVPWTFGQGTKLQIT
Nimotuzumab (K5) variable light chain	310	DIQMTQSPSSLSASVGDRVTITCRSSQNIVHSNGNTYLDW YQQTPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTFTIS SLQPEDIATYYCFQYSHVPWTFGQGTKLQIT
Nimotuzumab (K5) variable Heavy chain	311	QVQLQQSGAEVKKPGSSVKVSCKASGYTFTDYYIYWVR QAPGQGLEWIGGINPVTQRPVFNEKFKTRVTITVDESTNT AYMELSSLRSEDTAFYFCARQGLWFDSDGRGFDFWGQG STVTVSS

Necitumumab variable heavy chain	199	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGDYYWSWIR QPPGKGLEWIGYIYYSGSTDYNPSLKSRVTMSVDTSKNQ FSLKVNSVTAADTAVYYCARVSIFGVGTFDYWGQGTLV TVSS
Necitumumab variable light chain	200	EIVMTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKP GQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSLEPE DFAVYYCHQYGSTPLTFGGGTKAEIK
ICR62 variable heavy chain	201	QVNLLQSGAALVKPGASVKLSCKGSGFTFTDYKIHWVK QSHGKSLEWIGYFNPNSGYSTYNEKFKSKATLTADKSTD TAYMELTSLTSEDSATYYCTRLSPGGYYVMDAWGQGAS VTVSS
ICR62 variable light chain	202	DIQMTQSPSFLSASVGDRVTINCKASQNINNYLNWYQQK LGEAPKRLIYNTNNLQTGIPSRFSGSGSGTDYTLTISSLQP EDFATYFCLQHNSFPTFGAGTKLELK
ICR62 VL VH	203	MLLLVTSLLLCELPHPAFLLIPDIQMTQSPSFLSASVGDRV TINCKASQNINNYLNWYQQKLGEAPKRLIYNTNNLQTGI PSRFSGSGSGTDYTLTISSLQPEDFATYFCLQHNSFPTFGA GTKLELKGSTSGSGKPGSGEGSTKGQVNLLQSGAALVKP GASVKLSCKGSGFTFTDYKIHWVKQSHGKSLEWIGYFNP NSGYSTYNEKFKSKATLTADKSTDTAYMELTSLTSEDSA TYYCTRLSPGGYYVMDAWGQGASVTVSS
Matuzumab variable heavy chain	204	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSHWMHWV RQAPGQGLEWIGEFNPSNGRTNYNEKFKSKATMTVDTST NTAYMELSSLRSEDTAVYYCASRDYDYDGRYFDYWGQ GTLVTVSS
Matuzumab variable light chain	205	DIQMTQSPSSLSASVGDRVTITCSASSSVTYMYWYQQKP GKAPKLLIYDTSNLASGVPSRFSGSGSGTDYTFTISSLQPE DIATYYCQQWSSHIFTFGQGTKVEIK
C10 variable heavy chain	206	EVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAIGWVRQ APGQGLEWMGGIIPIFGIANYAQKFQGRVTITADESTSSA YMELSSLRSEDTAVYYCAREEGPYCSSTSCYAAFDIWGQ GTLVTLSS
C10 variable light chain	207	QSVLTQDPAVSVALGQTVKITCQGDSLRSYFASWYQQKP GQAPTLVMYARNDRPAGVPDRFSGSKSGTSASLSAISGL QPEDEAYYCAAWDDSLNGYLFGAGTKLTVL
Zalutumumab variable heavy chain	208	QVQLVESGGGVVQPGRSLRLSCAASGFTFSTYGMHWVR QAPGKGLEWVAVIWDDGSYKYYGDSVKGRFTISRDNSK NTLYLQMNSLRAEDTAVYYCARDGITMVRGVMKDYFD YWGQGTLVTVSS
Zalutumumab variable light chain	209	AIQLTQSPSSLSASVGDRVTITCRASQDISSALVWYQQKP GKAPKLLIYDASSLESGVPSRFSGSESGTDFTLTISSLQPED FATYYCQQFNSYPLTFGGGTKVEIK
P1X variable heavy chain	210	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQ APGQGLEWMGSIIPIFGTVNYAQKFQGRVTITADESTSTA YMELSSLRSEDTAVYYCARDPSVNLYWYFDLWGRGTLV TVSS
P1X variable light chain	211	DIQMTQSPSTLSASVGDRVTITCRASQSISSWWAWYQQK PGKAPKLLIYDASSLESGVPSRFSGSGSGTEFTLTISSLQPD DFATYYCQQYHAHPTTFGGGTKVEIK

P2X variable heavy chain	212	QVQLVQSGAEVKKPGSSVKVSCKASGGTFGSYAISWVR QAPGQGLEWMGSIIPIFGAANPAQKSQGRVTITADESTST AYMELSSLRSEDTAVYYCAKMGRGKVAFDIWGQGTMV TVSS
P2X variable light chain	213	DIVMTQSPDSLAVSLGERATINCKSSQSVLYSPNNKNYLA WYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTL TISSLQAEDVAVYYCQQYYGSPITFGGGTKVEIK
P3X variable heavy chain	214	QVQLVQSGAEVKKPGASVKVSCKASGYAFTSYGINWVR QAPGQGLEWMGWISAYNGNTYYAQKLRGRVTMTTDTS TSTAYMELRSLRSDDTAVYYCARDLGGYGSGSVPFDPW GQGTLVTVSS
P3X variable light chain	215	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQK PGQAPRLLIYGASTRATGIPARFSGSGSGTEFTLTISSLQSE DFAVYYCQDYRTWPRRVFGGGTKVEIK
EGFR-la1-VHH variable heavy chain	216	QVQLQESGGGLVQAGGSLLLSCAASGRTFSSYAMGWFR QAPGKEREFVAAINWSGGSTSYADSVKGRFTISRDNTKN TVYLQMNSLKPEDTAAFYCAATYNPYSRDHYFPRMTTE YDYWGQGTQVTVSS
EGFR-VHH variable heavy chain	312	EVQQASGGGLVQAGGSLRLSCAASGRTETTSAIAWFRQA PGKEREFVAQISASGLGINYSGTVKGRFTISRDADKTTVY LQMNSLTPEDTAVYYCAAGFHYIAAIRRTTDFHFWGPGT LVTVSS

[0446] In some embodiments, the scFv targets Mesothelin. In some embodiments, the Mesothelin scFv is based on the Vh and Vl from Amatuximab, P4, SS1, SD1, SD2, 1H7, or 3C02. In some embodiments, the Mesothelin scFv is based on the Vh and Vl from Amatuximab. In some embodiments, the Mesothelin scFv is based on the Vh and Vl from P4. In some embodiments, the Mesothelin scFv is based on the Vh and Vl from SS1. In some embodiments, the Mesothelin scFv is based on SD1. In some embodiments, the Mesothelin scFv is based on SD2. In some embodiments, the Mesothelin scFv is based on the Vh and Vl from 1H7. In some embodiments, the Mesothelin scFv is based on the Vh and Vl from 3C02.

Table 17: anti-Mesothelin sequences

Sequence Information	**SEQ ID NO**	**Amino acid sequence**
Amatuximab variable heavy chain	217	QVQLVQSGAEVKKPGASVKVSCKASGYSFTGYTMNWV RQAPGQGLEWMGLITPYNGASSYNQKFRGKATMTVDTS TSTVYMELSSLRSEDTAVYYCARGGYDGRGFDYWGQGT LVTVSS
Amatuximab variable light chain	218	DIQMTQSPSSLSASVGDRVTITCSASSSVSYMHWYQQKS GKAPKLLIYDTSKLASGVPSRFSGSGSGTDFTLTISSLQPE DFATYYCQQWSKHPLTFGQGTKLEIK
P4 variable heavy chain	219	QVQLQQSGPGLVTPSQTLSLTCAISGDSVSSNSATWNWIR QSPSRGLEWLGRTYYRSKWYNDYAVSVKSRMSINPDTS

		KNQFSLQLNSVTPEDTAVYYCARGMMTYYYGMDVWGQ GTTVTVSS
P4 variable light chain	220	QPVLTQSSSLSASPGASASLTCTLRSGINVGPYRIYWYQQ KPGSPPQYLLNYKSDSDKQQGSGVPSRFSGSKDASANAG VLLISGLRSEDEADYYCMIWHSSAAVFGGGTQLTVL
P4 VL VH	221	MLLLVTSLLLCELPHPAFLLIPQPVLTQSSSLSASPGASASL TCTLRSGINVGPYRIYWYQQKPGSPPQYLLNYKSDSDKQ QGSGVPSRFSGSKDASANAGVLLISGLRSEDEADYYCMI WHSSAAVFGGGTQLTVLGSTSGSGKPGSGEGSTKGQVQL QQSGPGLVTPSQTLSLTCAISGDSVSSNSATWNWIRQSPS RGLEWLGRTYYRSKWYNDYAVSVKSRMSINPDTSKNQF SLQLNSVTPEDTAVYYCARGMMTYYYGMDVWGQGTTV TVSS
SS1 variable heavy chain	222	QVQLQQSGPELEKPGASVKISCKASGYSFTGYTMNWVK QSHGKSLEWIGLITPYNGASSYNQKFRGKATLTVDKSSST AYMDLLSLTSEDSAVYFCARGGYDGRGFDYWGSGTPVT VSS
SS1 variable light chain	223	DIELTQSPAIMSASPGEKVTMTCSASSSVSYMHWYQQKS GTSPKRWIYDTSKLASGVPGRFSGSGSGNSYSLTISSVEAE DDATYYCQQWSKHPLTFGSGTKVEIK
SS1 VL VH	224	MLLLVTSLLLCELPHPDIELTQSPAIMSASPGEKVTMTCSA SSSVSYMHWYQQKSGTSPKRWIYDTSKLASGVPGRFSGS GSGNSYSLTISSVEAEDDATYYCQQWSKHPLTFGSGTKV EIKGSTSGSGKPGSGEGSTKGQVQLQQSGPELEKPGASVK ISCKASGYSFTGYTMNWVKQSHGKSLEWIGLITPYNGAS SYNQKFRGKATLTVDKSSSTAYMDLLSLTSEDSAVYFCA RGGYDGRGFDYWGSGTPVTVSS
SD1 VHH	225	QVQLVQSGGGLVQPGGSLRLSCAASDFDFAAYEMSWVR QSAPGQGLEWVAIISHDGIDKYYTDSVKGRFTISRDNSKN TLYLQMNTLRAEDTATYYCLRLGAVGQGTLVTVSSS
SD2 VHH	226	QVQLVQSGGGLVQPGGSLRLSCAASDFAFDDYEMSWVR QAPGKALEWIGDINHSGTTIYNPSLKSRVTISRDNSKNTL YLQMNTLRAEDTAIYYCARPHYGDYSDAFDIWGQGTMV TVSS
1H7 variable heavy chain	227	EVQLQQSGTVLARPGASVKMSCKASGYSFTNYRMNWV KQRPGQGLEWIGGIYPGNRDTTYNQKFKDKAKLTAVTSA NTAYMELSSLTNEDSAVYYCTRGVIGIYFDYWGQGTTLT VSS
1H7 variable light chain	228	DIVMTQSPASLAVSLGQRATISCKASQSVDYDGDSYMNW YQQKPGQPPKLLIYAASNLESGIPARFSGSGSGTDFTLNIH PVEEEDAATYYCQQNNEAPLTFGAGTKLELK
1H7 VL VH	229	MLLLVTSLLLCELPHPAFLLIPDIVMTQSPASLAVSLGQRA TISCKASQSVDYDGDSYMNWYQQKPGQPPKLLIYAASNL ESGIPARFSGSGSGTDFTLNIHPVEEEDAATYYCQQNNEA PLTFGAGTKLELKGSTSGSGKPGSGEGSTKGEVQLQQSGT VLARPGASVKMSCKASGYSFTNYRMNWVKQRPGQGLE WIGGIYPGNRDTTYNQKFKDKAKLTAVTSANTAYMELSS LTNEDSAVYYCTRGVIGIYFDYWGQGTTLTVSS
3C02 variable heavy chain	230	QVQLQQSGTVLARPGASVKMSCKASGYSFTNYRMYWV KQRPGQGLEWIGAIYPGNSDTTYKQKFKGKAKLTAVTSA

		STAYMELSSLTNEDSAVYYCTRGIRGSYFDVWGAGTTVT VSS
3C02 variable light chain	231	DIVMTQSPASLAVSLGQRATISCKASQSVDYDGDSYMNW YQQKPGQPPKLLIYAASNLESGIPARFSGSGSGTDFTLNIH PVEEEDAATYYCQQSNEDPYTFGGGTKLEIK
3C02 VL VH	232	MLLLVTSLLLCELPHPAFLLIPDIVMTQSPASLAVSLGQRA TISCKASQSVDYDGDSYMNWYQQKPGQPPKLLIYAASNL ESGIPARFSGSGSGTDFTLNIHPVEEEDAATYYCQQSNEDP YTFGGGTKLEIKGSTSGSGKPGSGEGSTKGQVQLQQSGT VLARPGASVKMSCKASGYSFTNYRMYWVKQRPGQGLE WIGAIYPGNSDTTYKQKFKGKAKLTAVTSASTAYMELSS LTNEDSAVYYCTRGIRGSYFDVWGAGTTVTVSS
M1 variable Ligh Chain	313	EIVLTQSPATLSLSPGERATISCRASQSVSSNFAWYQQRPG QAPRLLIYDASNRATGIPPRFSGSGSGTDFTLTISSLEPEDF AAYYCHQRSNWLYTFGQGTKVDIK
M1 variable Heavy Chain	314	QVQLQQSGAEVKKPGASVKVSCKASGYTFTGYYMHWV RQAPGQGLEWMGRINPNSGGTNYAQKFQGRVTMTRDTS ISTAYMELSRLRSEDTAVYYCARGRYYGMDVWGQGTM VTVSS
M5 Variable Light chain	315	DIVMTQSPSSLSASVGDRVTITCRASQSIRYYLSWYQQKP GKAPKLLIYTASILQNGVPSRFSGSGSGTDFTLTISSLQPED FATYYCLQTYTTPDFGPGTKVEIK
M5 Variable Heavy chain	316	QVQLVQSGAEVEKPGASVKVSCKASGYTFTDYYMHWV RQAPGQGLEWMGWINPNSGGTNYAQKFQGRVTMTRDT SISTAYMELSRLRSDDTAVYYCASGWDFDYWGQGTLVT VSS
VD9.V3 Variable light chain	317	DIQMTQSPSSLSASVGDRVTITCKSSQSVLYSSNQKNYLA WFQQKPGKAPKLLIYWASTRESGVPSRFSGSGSGTDFTLT ISSLQPEDFATYFCHQYLSSYTFGQGTKVEIK
VD9.V3 Variable Heavy chain	318	EVQLVESGGGLVQPGGSLRLSCAASGYTFTTYWMHWVR QAPGKGLEWVGYIRPSTGYTEYNQKFKDRFTISADTSKN TAYLQMNSLRAEDTAVYYCARSRWLLDYWGQGTLVTV SS

[0447] In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH.

[0448] In some embodiments, the aCAR scFv comprises a linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a GS based linker sequence, connecting the VH and VL to form the scFv. In some embodiments, the GS linker comprises GGGGS (SEQ ID NO:153). In some embodiments, the aCAR comprises a Whitlow linker sequence, e.g., GSTSGSGKPGSGEGSTKG (SEQ ID NO:82).

10. aCAR portion: Hinge and transmembrane domain

[0449] In some embodiments, the bicistronic construct comprises an aCAR portion comprising a hinge transmembrane (TM) domain component. In some embodiments, the aCAR portion

comprises a hinge TM domain. In some embodiments, the hinge TM domain comprises a hinge TM domain selected from the group consisting of a CD28 hinge TM domain and a CD8 hinge TM domain (including a CD8a hinge TM domain). In some embodiments, the hinge TM domain is a CD28 hinge TM domain. In some embodiments, the vector comprises a CD8 hinge TM domain. In some embodiments, the vector comprises a CD8a hinge TM domain. In some embodiments, the hinge domain comprises a hinge domain selected from the group consisting of a CD28 hinge domain and a CD8 hinge domain (including a CD8a hinge domain). In some embodiments, the hinge domain is a CD28 hinge domain. In some embodiments, the vector comprises a CD8 hinge domain. In some embodiments, the vector comprises a CD8a hinge domain. In some embodiments, the TM domain comprises a TM domain selected from the group consisting of a CD28 TM domain and a CD8 TM domain (including a CD8a TM domain). In some embodiments, the TM domain is a CD28 TM domain. In some embodiments, the vector comprises a CD8 TM domain. In some embodiments, the vector comprises a CD8a TM domain. In some embodiments, the hinge domain is a CD28 hinge domain of SEQ ID NO:85. In some embodiments, the vector comprises a CD8a hinge domain of SEQ ID NO:84. In some embodiments, the TM domain is a CD28 TM domain of SEQ ID NO:319. In some embodiments, the vector comprises a CD8a TM domain of SEQ ID NO:320.

Table 18: aCAR hinge and TM domain sequences

Sequence Information	**SEQ ID NO**	**Amino acid sequence**
CD28 hinge	85	IEVMYPPPYLDNEKSNGTIIHVKGKHLCPSP LFPGPSKP
CD28 TM	319	FWVLVVVGGVLACYSLLVTVAFIIFWV
CD8alpha hinge	84	TTTPAPRPPTPAPTIASQPLSLRPEACRPAAG GAVHTRGLDFACD
CD8alpha TM	320	IYIWAPLAGTCGVLLLSLVITLYC

11. aCAR portion: Co-stimulatory and activation signaling domain

[0450] In some embodiments, the bicistronic construct comprises an aCAR portion comprising co-stimulatory domain component. In some embodiments, the aCAR portion comprises a co-stimulatory domain. In some embodiments, the co-stimulatory domain is selected from the group consisting of CD137 (4-1BB) or CD28 or both 4-1BB and CD28 (28BB). In some embodiments, the co-stimulatory domain is a CD137 (4-1BB) co-stimulatory domain. In some embodiments, the co-stimulatory domain is a CD28 co-stimulatory domain. In some embodiments, the activation signaling domain is CD3z domain. In some embodiments, the co-stimulatory domain is a 28BB co-stimulatory domain. In some embodiments, the co-

stimulatory domain is 4-1BB (SEQ ID NO:233). In some embodiments, the co-stimulatory domain is CD28 (SEQ ID NO:234). In some embodiments, the activation signaling domain is CD3z (SEQ ID NO:235).

Table 19: aCAR co-stimulatory and activation signaling domain sequences

Sequence Information	SEQ ID NO	Amino acid sequence
4-1BB costim	233	KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEG GCEL
CD28 costim	234	RSKRSRLLHSDYMNMTPRRPGPTRKHYQPYAPPRDFA AY
CD3z activation signaling	235	RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLD KRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYS EIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQA LPPR

12. aCAR portion: Immunoreceptor Tyrosine-Based Activation Motif (ITAM)

[0451] In some embodiments, the aCAR portion comprises an Immunoreceptor Tyrosine-Based Activation Motif (ITAM). In some embodiments, the ITAM is a CD3 zeta domain. In some embodiments, the ITAM is a CD3 zeta domain of SEQ ID NO:236. In some embodiments, the ITAM is a CD3 zeta 3F domain of SEQ ID NO:237. In some embodiments, the ITAM is a CD3 zeta 4F domain of SEQ ID NO:238. In some embodiments, the ITAM is a CD3 zeta 4OF domain of SEQ ID NO:239.

Table 20: aCAR ITAM domain sequences

Sequence Information	SEQ ID NO	Amino acid sequence
CD3 zeta domain	236	RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLD KRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAY SEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQ ALPPR
CD3 Zeta 3F	237	RVKFSRSADAPAYQQGQNQLFNELNLGRREEYDVLD KRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAFS EIGMKGERRRGKGHDGLFQGLSTATKDTYDALHMQA LPPR
CD3 Zeta 4F	238	RVKFSRSADAPAYQQGQNQLFNELNLGRREEFDVLD KRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAFS EIGMKGERRRGKGHDGLFQGLSTATKDTYDALHMQA LPPR
CD3 Zeta 4OF	239	RVKFSRSADAPAYQQGQNQLFNELNLGRREEFDVLD KRRGRDPEMGGKPRRKNPQEGLFNELQKDKMAEAYS

		EIGMKGERRRGKGHDGLYQGLSTATKDTFDALHMQA LPPR

13. Exemplary aCARs

[0452] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of trastuzumab (SEQ ID NOs: 170 and 171). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z activation signaling domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0453] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of trastuzumab F9G (SEQ ID NOs: 307 and 308). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some

embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z activation signaling domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0454] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of pertuzumab (SEQ ID NOs: 173 and 174). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0455] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of FRP5 (SEQ ID NOs: 176 and 177). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3

linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0456] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of A21 (SEQ ID NOs: 178 and 179). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8

alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0457] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of XMT1517 (SEQ ID NOs: 180 and 181). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0458] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of XMT1518 (SEQ ID NOs: 182 and 183). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some

embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0459] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of XMT1519 (SEQ ID NOs: 184 and 185). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0460] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of FWP51 (SEQ ID NOs: 186 and 187). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82)

linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0461] In some embodiments, the aCAR comprises an scFv component comprising the anti-HER2 VHH (SEQ ID NO: 309). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239).

[0462] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of Cetuximab (SEQ ID NOs: 189 and 190). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation

of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0463] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of Panitumumab (SEQ ID NOs: 192 and 193). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR

comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0464] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of Imgatuzumab (SEQ ID NOs: 195 and 196). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0465] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of Nimotuzumab (SEQ ID NOs: 197 and 198). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some

embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0466] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of Nimotuzumab (K5) (SEQ ID NOs: 310 and 311). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0467] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of Necitumumab (SEQ ID NOs: 199 and 200). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form

the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0468] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of ICR62 (SEQ ID NOs: 201 and 202). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8

alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0469] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of Matuzumab (SEQ ID NOs: 204 and 205). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0470] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of C10 (SEQ ID NOs: 206 and 207). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some

embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0471] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of Zalutumumab (SEQ ID NOs: 208 and 209). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0472] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of P1X (SEQ ID NOs: 210 and 211). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82)

linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0473] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of P2X (SEQ ID NOs: 212 and 213). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0474] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of P3X (SEQ ID NOs: 214 and 215). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0475] In some embodiments, the aCAR comprises an scFv component comprising the VHH sequence of EGFR-la1-VHH (SEQ ID NO: 216). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some

embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0476] In some embodiments, the aCAR comprises an scFv component comprising the VHH sequence of EGFR-VHH (SEQ ID NO: 312). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0477] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of Amatuximab (SEQ ID NOs: 217 and 218). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some

embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0478] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of P4 (SEQ ID NOs: 219 and 220). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0479] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of SS1 (SEQ ID NOs: 222 and 223). In some embodiments, the orientation of

the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0480] In some embodiments, the aCAR comprises an scFv component comprising the VHH sequence of SD1 (SEQ ID NO: 225). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF

domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0481] In some embodiments, the aCAR comprises an scFv component comprising the VHH sequence of SD2 (SEQ ID NO: 226). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0482] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of 1H7 (SEQ ID NOs: 227 and 228). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some

embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0483] In some embodiments, the aCAR comprises an scFv component comprising the VL and VH sequences of 3C02 (SEQ ID NOs: 230 and 231). In some embodiments, the orientation of the aCAR VH and VL regions is VH-VL. In some embodiments, the orientation of the aCAR VH and VL regions is VL-VH. In some embodiments, the aCAR scFv comprises a (G4S)X3 linker (SEQ ID NO:81) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR scFv comprises a Whitlow linker (SEQ ID NO:82) linker that covalently connects the VH and the VL to form the aCAR scFv. In some embodiments, the aCAR comprises a CD8 alpha hinge TM domain (SEQ ID NO:84). In some embodiments, the aCAR comprises a CD28 hinge TM domain (SEQ ID NO:85). In some embodiments, the aCAR comprises a 4-1BB costimulatory domain (SEQ ID NO: 233). In some embodiments, the aCAR comprises a CD28 costimulatory domain (SEQ ID NO: 234). In some embodiments, the aCAR comprises a CD3z costimulatory domain (SEQ ID NO: 235). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta domain (SEQ ID NO: 236). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 3F domain (SEQ ID NO: 237). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4F domain (SEQ ID NO: 238). In some embodiments, the aCAR comprises an ITAM comprising a CD3 zeta 4OF domain (SEQ ID NO: 239). In some embodiments, the aCAR comprises a signal peptide upstream of the aCAR portion, wherein the signal peptide is a CD8 alpha signal peptide (SEQ ID NO: 161), a GM-CSF signal peptide (SEQ ID NO: 162), or a mIgK signal peptide (SEQ ID NO: 306).

[0484] In some embodiments, the aCAR has a set of components shown in Table 21.

Table 21: aCAR constructs

Construct	Signal Peptide	scFv	scFv Linker	Hinge	TM	Co-stimulatory	Signal-ing
Anti-EGFR							
MC0001 (VR1)	CD8 alpha	Imgatuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0002 (VR2)	CD8 alpha	Cextuximab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0003 (VR3)	CD8 alpha	Panitumumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0004 (VR4)	CD8 alpha	Nimotuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0005 (VR5)	CD8 alpha	Necitumumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0163 (VR163)	GM-CSF	ICR62 VH VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0164 (VR164)	GM-CSF	ICR62 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0165 (VR165)	GM-CSF	Matuzumab VH VL BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0166 (VR166)	GM-CSF	Matuzumab VL VH BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0167 (VR167)	GM-CSF	C10 VH VL BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0168 (VR168)	GM-CSF	C10 VL VH BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0169 (VR169)	GM-CSF	Zalutumumab VH VL BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0170 (VR170)	GM-CSF	Zalutumumab VL VH BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0171 (VR171)	GM-CSF	P1X VH VL BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0172 (VR172)	GM-CSF	P1X VL VH BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0173 (VR173)	GM-CSF	P2X VH VL BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0174 (VR174)	GM-CSF	P2X VL VH BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0175 (VR175)	GM-CSF	P3X VH VL BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0176 (VR176)	GM-CSF	P3X VL VH BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0177 (VR177)	GM-CSF	EGFR-la1-VHH BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	ICR62 VH_VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta

N/A	CD8 alpha	ICR62 VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	Matuzumab VH_VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	Matuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	C10 VH VL BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	C10 VL VH BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	Zalutumumab VH VL	whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0483 (VR483)	CD8 alpha	Zalutumumab VL_VH	whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	P1X VH VL BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	P1X VL VH BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	P2X VH VL BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	P2X VL VH BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	P3X VH VL BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	P3X VL VH BBz	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0484 (VR484)	CD8 alpha	EGFR-11a-VHH	whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0590	CD8 alpha	Panitumumab VL_VH	whitlow	CD8 alpha	CD8 alpha	CD28-41BB	CD3 zeta
MC0591	CD8 alpha	Panitumumab VL_VH	whitlow	CD8 alpha	CD28	CD28-41BB	CD3 zeta
MC0592	CD8 alpha	Zalutumumab VL_VH	whitlow	CD8 alpha	CD8 alpha	CD28-41BB	CD3 zeta
MC0593	CD8 alpha	Zalutumumab VL_VH	whitlow	CD8 alpha	CD28	CD28-41BB	CD3 zeta
MC0594	CD8 alpha	EGFR-11a-VHH	whitlow	CD8 alpha	CD8 alpha	CD28-41BB	CD3 zeta
MC0595	CD8 alpha	EGFR-11a-VHH	whitlow	CD8 alpha	CD28	CD28-41BB	CD3 zeta
Anti-HER2							
MC0006 (VR6)	CD8 alpha	Trastuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0007 (VR7)	CD8 alpha	Pertuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0008 (VR8)	CD8 alpha	FRP5 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0009 (VR9)	CD8 alpha	A21 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta

MC0178 (VR178)	GM-CSF	XMT1517 VH VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0179 (VR179)	GM-CSF	XMT1517 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0180 (VR180)	GM-CSF	XMT1518 VH VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0181 (VR181)	GM-CSF	XMT1518 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0182 (VR182)	GM-CSF	XMT1519 VH VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0183 (VR183)	GM-CSF	XMT1519 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0184 (VR184)	GM-CSF	FWP51 VH VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0185 (VR185)	GM-CSF	FWP51 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
(VR033)	CD8 alpha	Trastuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
(VR492)	CD8 alpha	Trastuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
(VR428)	CD8 alpha	Trastuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
(VR442)	CD8 alpha	Trastuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
(VR443)	CD8 alpha	Trastuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
(VR515)	CD8 alpha	Trastuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
(VR447)	CD8 alpha	Trastuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
(VR516)	CD8 alpha	Trastuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
(VR449)	CD8 alpha	Trastuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
(VR517)	CD8 alpha	Trastuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
(VR421)	CD8 alpha	Trastuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
(VR506)	CD8 alpha	Trastuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
(VR507)	CD8 alpha	Trastuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
(VR508)	CD8 alpha	Trastuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta

N/A	GM-CSF	Trastuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	GM-CSF	Pertuzumab VL_VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	GM-CSF	FRP5 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	GM-CSF	A21 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0178	CD8 alpha	XMT1517 VH VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0179	CD8 alpha	XMT1517 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0180	CD8 alpha	XMT1518 VH VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0181	CD8 alpha	XMT1518 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0182	CD8 alpha	XMT1519 VH VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A MC0183	CD8 alpha	XMT1519 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0184	CD8 alpha	FWP51 VH VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0185	CD8 alpha	FWP51 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0589	CD8 alpha	Trastuzumab VL VH	Whitlow	CD8 alpha	CD8 alpha	CD28-41BB	CD3 zeta
MC0589	CD3 zeta	Trastuzumab VL VH	Whitlow	CD8 alpha	CD28	CD28-41BB	CD3 zeta
Anti-Mesothelin							
MC0159 (VR159)	GM-CSF	Amatuximab VH VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0160 (VR160)	GM-CSF	Amatuximab VL VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0161 (VR161)	GM-CSF	P4 VH VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0162 (VR162)	GM-CSF	P4 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0186 (VR186)	GM-CSF	SS1 VH VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0187 (VR187)	GM-CSF	SS1 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0188 (VR188)	GM-CSF	SD1 VHH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0189 (VR189)	GM-CSF	SD2 VHH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0190 (VR190)	GM-CSF	1H07 VH VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta

MC0191 (VR191)	GM-CSF	1H07 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0192 (VR192)	GM-CSF	3C02 VH VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0193 (VR193)	GM-CSF	3C02 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	Amatuximab VH VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0485 (VR485)	CD8 alpha	Amatuximab VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	P4 VH VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0487 (VR487)	CD8 alpha	P4 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	SS1 VH VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0488 (VR488)	CD8 alpha	SS1 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	SD1 VHH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	SD2 VHH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	1H07 VH VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0490 (VR490)	CD8 alpha	1H07 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	3C02 VH VL	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
N/A	CD8 alpha	3C02 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0486 (VR486)	CD8 alpha	M1 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0498 (VR498)	CD8 alpha	M5 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0489 (VR489)	CD8 alpha	7D9.V3 VL VH	Whitlow	CD8 alpha	CD8 alpha	4-1BB	CD3 zeta
MC0596	CD8 alpha	M5	Whitlow	CD8 alpha	CD8 alpha	CD28-41BB	CD3z
MC0597	CD8 alpha	M5	whitlow	CD8 alpha	CD28	CD28-41BB	CD3z

14. Optional shRNA

[0485] In some embodiments, the bicistronic construct comprises an optional short hairpin RNA (shRNA). In some embodiments, the bicistronic construct comprises an HLA-A2 shRNA. In some embodiments, the bicistronic construct comprises an HLA-A2 shRNA having a sequence of SEQ ID NO:240. In some embodiments, the bicistronic construct comprises an

HLA-A2 shRNA having a sequence of SEQ ID NO:241. In some embodiments, the bicistronic construct comprises an HLA-beta2 shRNA. In some embodiments, the bicistronic construct comprises an HLA-beta2 shRNA having a sequence of SEQ ID NO:242. In some embodiments, the bicistronic construct comprises an HLA-A2 shRNA having both sequences of SEQ ID NO:240 and SEQ ID NO:242. In some embodiments, the bicistronic construct comprises an HLA-A2 shRNA having both sequences of SEQ ID NO:241 and SEQ ID NO:242.

Table 22: shRNA sequences

Sequence Information	**SEQ ID NO**	**Nucleic acid sequence**
HLA-A2-shRNA 1	240	GGATTACATCGCCCTGAAAGTTCAAGAGACTTTCAG GGCGATGTAATCCTTTTTT
HLA-A2-shRNA 2	241	CACCTGCCATGTGCAGCATGATTTGTGTAGTCATGC TGCACATGGCAGGTG
HLA-beta2-shRNA	242	GAATGGAGAGAGAATTGAATTCAAGAGATTCAATT CTCTCTCCATTC

15. Monocistronic constructs

[0486] In some embodiments, the iCAR and aCAR constructs are expressed by separate vectors, and the iCAR/aCAR pairs are co-expressed in cells. Methods of co-expressing multiple constructs in the same cell are well known in the art and include, *e.g.*, co-transfection of two or more expression vectors, integration of the constructs into the same or different loci within a cell, optionally followed by enrichment for co-expression.

iii. CAR-T BICISTRONIC iCAR/aCAR VECTOR CONSTRUCTION

[0487] In some embodiments, the bicistronic construct or co-transduction of monocistronic aCAR and iCAR constructs allows for the iCAR and the aCAR to be encoded by a single nucleic acid vector. In some embodiments, the present invention provides a vector comprising a nucleic acid molecule of the invention as defined in any one of the above embodiments, and at least one control element, such as a promoter, operably linked to the nucleic acid molecule.

[0488] In some embodiments, the vector is a lentiviral (LV) vector. In some embodiments, the LV vector is a commercially available LV vector. In some embodiments, the LV vector includes but is not limited to pLenti, pLVX-Puro, pLVX-IRES-Puro/Neo/Hygro, pLVx-EF1a-IRES (TAKARA), and/or pcLV-EF1a (Sirion). In some embodiments, the LV vector is pLVX-Puro. In some embodiments, the LV vector is pLVX-IRES-Puro/Neo/Hygro. In some

embodiments, the LV vector is pLVx-EF1a-IRES (TAKARA). In some embodiments, the LV vector is pcLV-EF1a (Sirion).

[0489] In some embodiments, the vector comprises an EF1 promoter. In some embodiments, the vector comprises a CMV promoter. In some embodiments, the vector comprises a PGK promoter.

[0490] In some embodiments, the nucleotide sequence of the vector comprises an internal ribosome entry site (IRES) between the nucleotide sequence encoding for the aCAR and the nucleotide sequence encoding for the iCAR. In general, the nucleotide sequence encoding for the aCAR and the nucleotide sequence encoding for the iCAR can be in any sequential order, but in particular embodiments, the nucleotide sequence encoding for the aCAR is downstream of the nucleotide sequence encoding for the iCAR.

[0491] In some embodiments, the nucleotide sequences encoding for the aCAR and the iCAR are encoded on a single vector. In some embodiments, the vector comprises an internal ribosome entry site (IRES) between the nucleotide sequence encoding for the aCAR and the nucleotide sequence encoding for the iCAR. In some embodiments, the nucleotide sequence encoding for the aCAR is downstream of the nucleotide sequence encoding for the iCAR. In some embodiments, the nucleotide sequence comprises a viral self-cleaving 2A peptide located between the nucleotide sequence encoding for the aCAR and the nucleotide sequence encoding for the iCAR. In some embodiments, the nucleotide sequence of the vector comprises a viral self-cleaving 2A peptide between the nucleotide sequence encoding for the aCAR and the nucleotide sequence encoding for the iCAR. In some embodiments, the viral self-cleaving 2A peptide includes is the T2A from *Thosea asigna* virus (TaV). In some embodiments, the vector comprises a nucleotide sequence encoding the constitutive aCAR linked via a flexible linker to said iCAR.

[0492] The immune cells may be transfected with the appropriate nucleic acid molecule described herein by *e.g.*, RNA transfection or by incorporation in a plasmid fit for replication and/or transcription in a eukaryotic cell or a viral vector. In some embodiments, the vector is selected from a retroviral or lentiviral vector.

[0493] Combinations of retroviral vector and an appropriate packaging line can also be used, where the capsid proteins will be functional for infecting human cells. Several amphotropic virus-producing cell lines are known, including PA12 (Miller, *et al.* (1985) *Mol. Cell. BioI.* 5:431-437); PA317 (Miller, *et al.* (1986) *Mol. Cell. Bioi.* 6:2895-2902); and CRIP (Danos, *et ai.* (1988) *Proc. Nati. Acad. Sci.* USA 85:6460-6464). Alternatively, non-amphotropic particles can be used, such as, particles pseudotyped with VSVG, RD 114 or GAL V envelope and in

some embodiments produced in a PG13 cell line. Cells can further be transduced by direct co-culture with producer cells, *e.g.*, by the method of Bregni, *et ai.* (1992) *Blood* 80: 1418-1422, or culturing with viral supernatant alone or concentrated vector stocks, *e.g.*, by the method of Xu, *et ai.* (1994) *Exp. Hemat.* 22:223-230; and Hughes, *et ai.* (1992) *J Clin. Invest.* 89: 1817.

[0494] In some embodiments, the iCAR and aCAR are encoded by different constructs, for example as separate monocistronic aCAR and iCAR constructs. In some embodiments, the iCAR and aCAR are encoded by a single construct, for example as separate monocistronic aCAR and iCAR constructs within a single expression vector.

[0495] In some embodiments, the iCAR and aCAR are encoded by the same expression vector. In some embodiments, the expression vector comprises a nucleic acid sequence that encodes a bicistronic iCAR/aCAR selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0496] In some embodiments, the expression vector comprises a bicistronic iCAR/aCAR nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0497] In some embodiments, the expression vector comprises a bicistronic iCAR/aCAR nucleic acid that encodes an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:276, SEQ ID NO:278, SEQ ID NO:280, SEQ ID NO:282, SEQ ID NO:322, SEQ ID NO:324, and SEQ ID NO:326.

[0498] In some embodiments, the nucleic acid sequence that encodes a bicistronic iCAR/aCAR exhibits 75%, 80%, 85%, 88%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ

ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0499] In some embodiments, the nucleic acid sequence that encodes a bicistronic iCAR/aCAR exhibits at least 75% sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0500] In some embodiments, the nucleic acid sequence that encodes a bicistronic iCAR/aCAR exhibits at least 80% sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0501] In some embodiments, the nucleic acid sequence that encodes a bicistronic iCAR/aCAR exhibits at least 85% sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0502] In some embodiments, the nucleic acid sequence that encodes a bicistronic iCAR/aCAR exhibits at least 90% sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0503] In some embodiments, the nucleic acid sequence that encodes a bicistronic iCAR/aCAR exhibits at least 91% sequence identity to a nucleic acid sequence selected from the group

consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0504] In some embodiments, the nucleic acid sequence that encodes a bicistronic iCAR/aCAR exhibits at least 92% sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0505] In some embodiments, the nucleic acid sequence that encodes a bicistronic iCAR/aCAR exhibits at least 93% sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0506] In some embodiments, the nucleic acid sequence that encodes a bicistronic iCAR/aCAR exhibits at least 94% sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0507] In some embodiments, the nucleic acid sequence that encodes a bicistronic iCAR/aCAR exhibits at least 95% sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0508] In some embodiments, the nucleic acid sequence that encodes a bicistronic iCAR/aCAR exhibits at least 96% sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0509] In some embodiments, the nucleic acid sequence that encodes a bicistronic iCAR/aCAR exhibits at least 97% sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0510] In some embodiments, the nucleic acid sequence that encodes a bicistronic iCAR/aCAR exhibits at least 98% sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0511] In some embodiments, the nucleic acid sequence that encodes a bicistronic iCAR/aCAR exhibits at least 99% sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0512] In some embodiments, the nucleic acid sequence that encodes a bicistronic iCAR/aCAR exhibits 100% sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33,

SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0513] As used herein, sequence identity can include the identity/similarity between two or more nucleic acid sequences, or two or more amino acid sequences, is expressed in terms of the identity or similarity between the sequences. Sequence identity can be measured in terms of percentage identity; the higher the percentage, the more identical the sequences are. Sequence similarity can be measured in terms of percentage similarity (which takes into account conservative amino acid substitutions); the higher the percentage, the more similar the sequences are. Homologs or orthologs of nucleic acid or amino acid sequences possess a relatively high degree of sequence identity/similarity when aligned using standard methods. Methods of alignment of sequences for comparison are well known in the art. Various programs and alignment algorithms are described in, for example but not limited to Smith & Waterman, *Adv. Appl. Math.* 2:482, 1981; Needleman & Wunsch, *J. Mol. Biol.* 48:443, 1970; Pearson & Lipman, *Proc. Natl. Acad. Sci.* USA 85:2444, 1988; Higgins & Sharp, Gene, 73:237-44, 1988; Higgins & Sharp, *CABIOS* 5:151-3, 1989; Corpet et al., Nuc. Acids Res. 16:10881-90, 1988; Huang et al. *Computer Appls. in the Biosciences* 8, 155-65, 1992; and Pearson et al., *Meth. Mol. Bio.* 24:307-31, 1994. Altschul et al., *J. Mol. Biol.* 215:403-10, 1990, presents a detailed consideration of sequence alignment methods and homology calculations. The NCBI Basic Local Alignment Search Tool (BLAST) (Altschul et al., J. Mol. Biol. 215:403-10, 1990) is available from several sources, including the National Center for Biological Information (NCBI, National Library of Medicine, Building 38A, Room 8N805, Bethesda, Md. 20894) and on the Internet, for use in connection with the sequence analysis programs blastp, blastn, blastx, tblastn and tblastx. Additional information can be found at the NCBI web site. For example, BLASTN can be used to compare nucleic acid sequences, while BLASTP can be used to compare amino acid sequences. To compare two nucleic acid sequences, the options can be set as follows: -i is set to a file containing the first nucleic acid sequence to be compared (such as C:\seq1.txt); --j is set to a file containing the second nucleic acid sequence to be compared (such as C:\seq2.txt); --p is set to blastn; --o is set to any desired file name (such as C:\output.txt); --q is set to --1; --r is set to 2; and all other options are left at their default setting. For example, the following command can be used to generate an output file containing a comparison between two sequences: C:\B12seq --i c:\seq1.txt --j c:\seq2.txt --p blastn --o c:\output.txt --q --1 --r 2.

iv. CONSTRUCTION OF EFFECTOR CELLS

[0514] In still another aspect, the present invention provides a method for preparing a safe effector immune cell comprising: (i) transfecting an effector immune cell directed to a tumor-associated antigen with a nucleic acid molecule comprising a nucleotide sequence encoding a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as defined herein above or transducing the cells with a vector or (ii) transfecting a naïve effector immune cell with a nucleic acid molecule comprising a nucleotide sequence encoding a bicistronic iCAR/aCAR construct as defined herein above; or transducing an effector immune cell with a vector as defined herein above. In some embodiments, the bicistronic iCAR/aCAR construct is encoded a single vector.

[0515] In still another aspect, the present invention provides a method for preparing a safe effector immune cell comprising: (i) transfecting a TCR-engineered effector immune cell directed to a tumor-associated antigen with a nucleic acid molecule comprising a nucleotide sequence encoding a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as defined herein above or transducing the cells with a vector or (ii) transfecting a naïve effector immune cell with a nucleic acid molecule comprising a nucleotide sequence encoding a bicistronic iCAR/aCAR construct as defined herein above; or transducing an effector immune cell with a vector as defined herein above. In some embodiments, the bicistronic iCAR/aCAR construct is encoded a single vector. In some embodiments, the bicistronic iCAR and aCAR constructs are encoded on different/separate vectors. In some embodiments, the monocistronic aCAR and iCAR constructs for co-transduction are encoded on a single vector. In some embodiments, the monocistronic aCAR and iCAR constructs for co-transduction are encoded on different/separate vectors.

[0516] In some embodiments, the immune cell for use in engineering includes but is not limited to a T-cell, a natural killer cell, or a cytokine-induced killer cell. In some embodiments, the immune cell for use in engineering includes but is not limited to a Jurkat T-cell, a Jurkat-NFAT T-cell, and/or a peripheral blood mononuclear cell (PBMC).

[0517] In some embodiments, the immune cell is modified such that is a safe effector immune cell. In yet another aspect, the present invention provides a safe effector immune cell obtained by the method of the present invention as described above. The safe effector immune cell may be a redirected T cell expressing an exogenous T cell receptor (TCR) and a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction, wherein the exogenous TCR is directed to a non-polymorphic cell surface epitope of an antigen

or a single allelic variant of a polymorphic cell surface epitope, wherein said epitope is a tumor-associated antigen or is shared at least by cells of related tumor and normal tissue, and a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction is as defined above; or the safe effector immune cell is a redirected effector immune cell such as a natural killer cell or a T cell expressing a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as defined above.

[0518] In some embodiments, the safe effector immune cell expresses on its surface an aCAR comprising an extracellular domain that specifically binds to a non-polymorphic cell surface epitope of an antigen and an iCAR comprising an extracellular domain that specifically binds a single allelic variant of a polymorphic cell surface epitope of a different antigen to which the extracellular domain of said aCAR binds. In some embodiments, the extracellular domain of the iCAR specifically binds a single allelic variant of a different polymorphic cell surface epitope are of the same antigen to which the extracellular domain of said aCAR binds; or the extracellular domain of the iCAR specifically binds a different single allelic variant of the same polymorphic cell surface epitope area to which the extracellular domain of said aCAR binds.

[0519] In some embodiments, the aCAR and the iCAR are present on the cell surface as separate proteins. In some embodiments, the expression level on the cell surface of the iCAR is greater than or equal to the expression level of the aCAR. In some embodiments, the extracellular domain of the iCAR expressed on the cell surface is directed against or specifically binds to a single allelic variant of an at least one extracellular polymorphic epitope.

[0520] In some embodiments, the extracellular domain of the iCAR expressed on the cell surface is directed against or specifically binds to a single allelic variant of HLA-A2. In some embodiments, the iCAR will be directed toward HLA-A2. In some embodiments, the aCAR with be directed toward EGFR. In some embodiments, the aCAR with be directed toward HER2. In some embodiments, the iCAR/aCAR set will be HLA-A2 and EGFR respectively. In some embodiments, the iCAR/aCAR set will be HLA-A2 and HER2 respectively.

[0521] In some embodiments, the safe effector immune cell comprises a bicistronic iCAR/aCAR nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0522] In some embodiments, the safe effector immune cell comprises and expression vector comprising a bicistronic iCAR/aCAR nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0523] In some embodiments, the safe effector immune cell comprises a bicistronic iCAR/aCAR nucleic acid that encodes an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:276, SEQ ID NO:278, SEQ ID NO:280, SEQ ID NO:282, SEQ ID NO:322, SEQ ID NO:324, and SEQ ID NO:326.

[0524] In some embodiments, the safe effector immune cell comprises expression vector comprises a bicistronic iCAR/aCAR nucleic acid that encodes an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:276, SEQ ID NO:278, SEQ ID NO:280, SEQ ID NO:282, SEQ ID NO:322, SEQ ID NO:324, and SEQ ID NO:326.

[0525] In some embodiments, EGFR is the aCAR target and HLA is the iCAR target. In some embodiments, HER2 is the aCAR target and HLA is the iCAR target. In some embodiments, the safe effector immune cells used for treating cancer as defined comprises an expression vector. In some embodiments, the iCAR and aCAR are encoded by a bicistronic nucleic acid based expression vector. In some embodiments, the expression vector comprises a nucleic acid sequence a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:3, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325. In some embodiments, the expression vector comprises a nucleic acid sequence that codes for an amino sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ

ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:276, SEQ ID NO:278, SEQ ID NO:280, SEQ ID NO:282, SEQ ID NO:322, SEQ ID NO:324, and SEQ ID NO:326.

[0526] In some embodiments, the safe effector immune cells used for treating cancer comprises an expression vector that comprises a bicistronic iCAR/aCAR nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0527] In some embodiments, the safe effector immune cells used for treating cancer comprises a bicistronic iCAR/aCAR nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325.

[0528] In some embodiments, the safe effector immune cells used for treating cancer as comprises a bicistronic iCAR/aCAR nucleic acid that encodes an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:276, SEQ ID NO:278, SEQ ID NO:280, SEQ ID NO:282, SEQ ID NO:322, SEQ ID NO:324, and SEQ ID NO:326.

[0529] In some embodiments, the safe effector immune cells used for treating cancer as comprises an expression vector that comprises a bicistronic iCAR/aCAR nucleic acid that encodes an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:276, SEQ ID NO:278, SEQ ID NO:280, SEQ ID NO:282, SEQ ID NO:322, SEQ ID NO:324, and SEQ ID NO:326.

A. ANTI-IDIOTYPIC ANTIBODIES

[0530] Provided herein are anti-idiotype antibodies that specifically recognize two anti-HLA-A2 specific scFvs, optionally wherein the anti-HLA-A2 specific scFvs are present in an iCAR, optionally wherein the iCAR is present in a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction. Accordingly, in some embodiments, the invention relates to an anti-idiotypic anti-HLA-A2 antibody. In some embodiments, the anti-idiotypic anti-HLA-A2 antibody comprises any of the FW1, CDRH1, FW2, CDRH2, FW3, CDRH3, and FW4 sequences shown in Table 23. In some embodiments, the anti-idiotypic anti-HLA-A2 antibody comprises the FW1, CDRH1, FW2, CDRH2, FW3, CDRH3, and FW4 sequences of SEQ ID NOs: 359, 360, 361, 362, 363, 364, and 365, respectively. In some embodiments, the anti-idiotypic anti-HLA-A2 antibody comprises the FW1, CDRH1, FW2, CDRH2, FW3, CDRH3, and FW4 sequences of SEQ ID NOs: 366, 367, 368, 369, 370, 372, and 372, respectively. In some embodiments, the anti-idiotypic anti-HLA-A2 antibody comprises the FW1, CDRH1, FW2, CDRH2, FW3, CDRH3, and FW4 sequences of SEQ ID NOs: 373, 374, 375, 376, 377, 378, and 379, respectively. In some embodiments, the anti-idiotypic anti-HLA-A2 antibody comprises the FW1, CDRH1, FW2, CDRH2, FW3, CDRH3, and FW4 sequences of SEQ ID NOs: 380, 381, 382, 383, 384, 385, and 386, respectively. In some embodiments, the anti-idiotypic anti-HLA-A2 antibody comprises the FW1, CDRH1, FW2, CDRH2, FW3, CDRH3, and FW4 sequences of SEQ ID NOs: 387, 388, 389, 390, 391, 392, and 393, respectively. In some embodiments, the anti-idiotypic anti-HLA-A2 antibody comprises the FW1, CDRH1, FW2, CDRH2, FW3, CDRH3, and FW4 sequences of SEQ ID NOs: 394, 395, 396, 397, 398, 399, and 400, respectively. In some embodiments, the anti-idiotypic anti-HLA-A2 antibody comprises the FW1, CDRH1, FW2, CDRH2, FW3, CDRH3, and FW4 sequences of SEQ ID NOs: 401, 402, 403, 404, 405, 406, and 407, respectively. In some embodiments, the anti-idiotypic anti-HLA-A2 antibody comprises the FW1, CDRH1, FW2, CDRH2, FW3, CDRH3, and FW4 sequences of SEQ ID NOs: 408, 409, 410, 411, 412, 413, and 414, respectively. In some embodiments, the anti-idiotypic anti-HLA-A2 antibody comprises the FW1, CDRH1, FW2, CDRH2, FW3, CDRH3, and FW4 sequences of SEQ ID NOs: 415, 416, 417, 418, 419, 420, and 421, respectively. In some embodiments, the anti-idiotypic anti-HLA-A2 antibody comprises the FW1, CDRH1, FW2, CDRH2, FW3, CDRH3, and FW4 sequences of SEQ ID NOs: 422, 423, 424, 425, 426, 427, and 428, respectively.

Table 23: anti HzBB7.2 anti-idiotype sequences

mAb	FW1 (SEQ ID NO)	CDRH1 (SEQ ID NO)	FW2 (SEQ ID NO)	CDRH2 (SEQ ID NO)	FW3 (SEQ ID NO)	CDRH3 (SEQ ID NO)	FW4 (SEQ ID NO)
Q3S1	EVQLQQSGPELVKPGSSVKISCKASGYTFT (359)	DYYMN (360)	WVKQSHGKSLEWIG (361)	DINPVNGATSYNQKFKG (362)	KATLTVDKSSSTDYMEIRGLTSEDSAVYYCVR (363)	KESKYGYFDV (364)	WGAGTTVTVSS (365)
Q7S1	DVQLQESGPGLVKPSQSLSVTCTVTGYSITS (366)	AYYWN (367)	WIRQFPGNKLEWMA (368)	NIHNSGSTNYNPSLKS (369)	RISITRDTSKNQFFLQLHSVTTEDTATYYCAR (370)	GEYDAAWFAY (371)	WGQGTLVTVSA (372)
Q11S3	EVQLHQSGPELVKPGASVRMSCKASGYTFT (373)	NYYMH (374)	WVKQSHGQSLEWIG (375)	YICPNSGDTNFTQKFKG (376)	KATLTVDKSSSTAYMELRSLTSEDSAVYYCAR (377)	GGYYYDGISFAY (378)	WGQGTLVAVSA (379)
Q14	EVQLHQSGPELVKPGASVKMSCKASGYTFT (380)	NYYIH (381)	WVKQSHGRTLEWIG (382)	YTYPNNGDNTYNQNFKG (383)	KATLTVDKSSSTAYMELRSLTSEDSAVYYCTR (384)	GAYYYDGTSFAY (385)	WGQGTLVTVSA (386)
Q30S1	QVQLQQPGAELVKPGASVKLSCRASGYSFT (387)	SYWMH (388)	WVKQRPGQGLEWIG (389)	EINPSNGGSNYNERFKS (390)	KATLTVDTSSNTAHMQLSSLTSEDSAVYYCAIF (391)	YEGRGDLYFDY (392)	WGQGTTLTVSS (393)
mAb	FW1	CDRL1	FW2	CDRL2	FW3	CDRL3	FW4
Q3S1	DVVMTQTPLTLSVTIGQPVSISC (394)	KSSQSLLDSDGKTYLS (395)	WLLQRPGQSPKRLIY (396)	LVSKLES (397)	GVPDRFTGSGSGTDFTLKISRVEAEDLGVYYC (398)	WQGTHFPQT (399)	FGGGTKLEIK (400)

Q7S1	DIVMSQSPSSLAVSAGEKVTMSC (401)	KSSQSLFNSRIRKNYLA (402)	WYQQKPGQSPKLLIY (403)	WASSRES (404)	GVPDRFTGSGSGTDFTLTISSVQAEDLAVYYC (405)	KQSYYLVT (406)	FGAGTKLELK (407)
Q11S3	DIVMSQSPSSLAVSVGERVTMSC (408)	KSSQSLFNSRTRKNDLA (409)	WYQQKPGQSPKLLIF (410)	WASTRES (411)	GVPDRFTGSGSGTDFTLTISGVQAEDLALYFC (412)	KQSYYLRT (413)	FGGGTKLEIK (414)
Q14	DIVMSQSPSSLAVSAGEKVTMSC (415)	KSSQSLFNSRIRKNDLA (416)	WYQQKPGQSPKLLIH (417)	WASTRES (418)	GVPDRFTGSGSGTDFTLTISSVQAEDLAVYYC (419)	KQSFYLRT (420)	FGGGTKLEFK (421)
Q30S1	DIVMTQSHKFLSTSVGDRVSITC (422)	KASQDVATTVA (423)	WYQQKPGQSPKLLIS (424)	WASTRHT (425)	GVPDRFTGSGSGTDFTLTISNVQSEDLADYFC (426)	QQYSRYPLT (427)	FGAGTKLELK (428)

[0531] In some embodiments, the anti-idiotypic anti-HLA-A2 antibody comprises any of the sets of H and L sequences shown in Table 24. In some embodiments, the anti-idiotypic anti-HLA-A2 antibody comprises the H and L sequences of SEQ ID NOs: 429-432. In some embodiments, the anti-idiotypic anti-HLA-A2 antibody comprises the H and L sequences of SEQ ID NOs: 433-436. In some embodiments, the anti-idiotypic anti-HLA-A2 antibody comprises the H and L sequences of SEQ ID NOs: 437-440. In some embodiments, the anti-idiotypic anti-HLA-A2 antibody comprises the H and L sequences of SEQ ID NOs: 441-444. In some embodiments, the anti-idiotypic anti-HLA-A2 antibody comprises the H and L sequences of SEQ ID NOs: 445-448.

Table 24. Anti-HzBB7 Hybridoma mAb Sequences

Q3S1 mAB	
H (SEQ ID NO: 429)	GAGGTCCAGCTGCAACAGTCTGGACCTGAGCTGGTGAAGCCTG GGTCTTCAGTGAAGATATCATGTAAGGCTTCTGGATACACATT CACTGACTACTACATGAACTGGGTGAAGCAGAGCCATGGAAA GAGCCTTGAGTGGATTGGAGATATTAATCCTGTCAATGGTGCT

	ACTAGCTACAACCAGAAGTTCAAGGGCAAGGCCACATTGACT GTAGACAAGTCCTCCAGCACAGACTACATGGAGATCCGCGGCC TGACATCTGAGGACTCTGCAGTCTATTACTGTGTAAGAAAAGA GAGTAAATACGGGTACTTCGATGTCTGGGGCGCAGGGACCAC GGTCACCGTCTCCTCA
H (SEQ ID NO: 430)	EVQLQQSGPELVKPGSSVKISCKASGYTFTDYYMNWVKQSHGKS LEWIGDINPVNGATSYNQKFKGKATLTVDKSSSTDYMEIRGLTSE DSAVYYCVRKESKYGYFDVWGAGTTVTVSS
L (SEQ ID NO: 431)	GACGTTGTGATGACCCAGACTCCACTCACTTTGTCGGTTACCAT TGGACAACCAGTCTCCATCTCTTGCAAGTCAAGTCAGAGCCTC TTAGATAGTGATGGAAAGACATATTTGAGTTGGTTGTTACAGA GGCCAGGCCAGTCTCCAAAGCGCCTAATCTATCTGGTGTCTAA ACTGGAGTCTGGAGTCCCTGACAGGTTCACTGGCAGTGGATCA GGGACAGATTTCACACTGAAAATCAGCAGAGTGGAGGCTGAG GATTTGGGAGTTTATTATTGCTGGCAAGGTACACATTTTCCTCA GACGTTCGGTGGAGGCACCAAGCTGGAAATCAAA
L (SEQ ID NO: 432)	DVVMTQTPLTLSVTIGQPVSISCKSSQSLLDSDGKTYLSWLLQRPG QSPKRLIYLVSKLESGVPDRFTGSGSGTDFTLKISRVEAEDLGVYY CWQGTHFPQTFGGGTKLEIK
Q7S1 mAB	
H (SEQ ID NO: 433)	GATGTGCAACTTCAGGAGTCAGGACCTGGCCTGGTGAAACCTT CTCAGTCTCTGTCCGTCACCTGCACTGTCACTGGGTACTCCATC ACCAGTGCTTATTACTGGAACTGGATCCGGCAGTTTCCAGGAA ACAAACTGGAGTGGATGGCCAACATACACAACAGTGGTAGCA CTAACTACAACCCTTCTCTCAAAAGTCGAATCTCTATCACTCGA GACACATCCAAGAACCAGTTCTTCCTGCAGTTGCATTCTGTGA CTACAGAGGACACAGCCACATATTACTGTGCAAGAGGGGAGT ATGACGCGGCCTGGTTTGCTTACTGGGGCCAAGGGACTCTGGT CACTGTCTCTGCA
H (SEQ ID NO: 434)	DVQLQESGPGLVKPSQSLSVTCTVTGYSITSAYYWNWIRQFPGNK LEWMANIHNSGSTNYNPSLKSRISITRDTSKNQFFLQLHSVTTEDT ATYYCARGEYDAAWFAYWGQGTLVTVSA
L (SEQ ID NO: 435)	GACATTGTGATGTCACAGTCTCCATCCTCCCTGGCTGTGTCCGC AGGAGAGAAGGTCACTATGAGCTGCAAATCCAGTCAGAGTCT GTTCAACAGTAGAATCCGAAAGAACTACTTGGCTTGGTACCAG CAGAAACCAGGGCAGTCTCCTAAACTGCTGATCTACTGGGCAT CCTCTAGGGAATCTGGGGTCCCTGATCGCTTCACAGGCAGTGG ATCTGGGACAGATTTCACTCTCACCATCAGCAGTGTGCAGGCT GAAGACCTGGCAGTTTATTACTGCAAGCAATCTTATTATCTGG TCACGTTCGGTGCTGGGACCAAGCTGGAGCTGAAA
L (SEQ ID NO: 436)	DIVMSQSPSSLAVSAGEKVTMSCKSSQSLFNSRIRKNYLAWYQQK PGQSPKLLIYWASSRESGVPDRFTGSGSGTDFTLTISSVQAEDLAV YYCKQSYYLVTFGAGTKLELK
Q11S3 mAB	
H (SEQ ID NO: 437)	GAGGTCCAGCTGCACCAGTCTGGACCTGAGCTGGTGAAGCCTG GGGCTTCAGTGAGGATGTCCTGCAAGGCTTCTGGATACACATT CACCAACTACTACATGCACTGGGTGAAGCAGAGCCATGGACA GAGCCTTGAATGGATTGGATATATTTGTCCTAATAGTGGTGAT ACTAACTTCACCCAGAAGTTCAAGGGCAAGGCCACATTGACTG

	TAGACAAGTCTTCCAGCACAGCCTACATGGAGCTCCGCAGCCT GACATCTGAGGATTCTGCAGTCTATTACTGTGCAAGAGGGGGT TATTATTACGATGGTATCTCTTTTGCTTACTGGGGCCAAGGGAC TCTGGTCGCTGTCTCTGCA
H (SEQ ID NO: 438)	EVQLHQSGPELVKPGASVRMSCKASGYTFTNYYMHWVKQSHGQ SLEWIGYICPNSGDTNFTQKFKGKATLTVDKSSSTAYMELRSLTSE DSAVYYCARGGYYYDGISFAYWGQGTLVAVSA
L (SEQ ID NO: 439)	GACATTGTGATGTCACAGTCTCCATCCTCCCTGGCTGTGTCAGT AGGAGAGAGGGTCACTATGAGCTGCAAATCCAGTCAGAGTCT GTTCAACAGTAGAACCCGAAAGAACGACTTGGCTTGGTACCAG CAGAAGCCAGGGCAGTCTCCTAAACTTCTGATCTTCTGGGCAT CCACTAGGGAATCTGGGGTCCCTGATCGCTTCACAGGCAGTGG ATCTGGGACAGATTTCACTCTCACCATCAGCGGTGTCCAGGCT GAAGACCTGGCACTTTATTTCTGCAAGCAATCTTATTATCTTCG GACGTTCGGTGGAGGCACCAAGCTGGAAATCAAA
L (SEQ ID NO: 440)	DIVMSQSPSSLAVSVGERVTMSCKSSQSLFNSRTRKNDLAWYQQ KPGQSPKLLIFWASTRESGVPDRFTGSGSGTDFTLTISGVQAEDLA LYFCKQSYYLRTFGGGTKLEIK
Q14 mAB	
H (SEQ ID NO: 441)	GAGGTCCAGCTGCACCAGTCTGGACCTGAGCTGGTGAAGCCTG GGGCTTCAGTGAAGATGTCCTGCAAGGCTTCTGGATACACATT CACTAACTACTACATACATTGGGTGAAGCAGAGCCATGGAAG GACCCTTGAGTGGATTGGATATACTTATCCTAACAATGGTGAT AATACTTACAACCAGAATTTCAAGGGCAAGGCCACTTTGACTG TAGACAAGTCCTCCAGCACAGCCTACATGGAGCTCCGCAGCCT GACATCTGAGGATTCTGCAGTCTATTACTGTACAAGAGGGGCT TATTACTACGATGGTACCTCTTTTGCTTACTGGGGCCAAGGGA CTCTGGTCACTGTCTCTGCA
H (SEQ ID NO: 442)	EVQLHQSGPELVKPGASVKMSCKASGYTFTNYYIHWVKQSHGRT LEWIGYTYPNNGDNTYNQNFKGKATLTVDKSSSTAYMELRSLTS EDSAVYYCTRGAYYYDGTSFAYWGQGTLVTVSA
L (SEQ ID NO: 443)	GACATTGTGATGTCACAGTCTCCATCCTCCCTGGCTGTGTCAGC AGGAGAGAAGGTCACTATGAGCTGCAAATCCAGTCAGAGTCT GTTCAACAGTAGAATCCGAAAGAACGACTTGGCTTGGTACCAG CAGAAACCAGGACAGTCTCCTAAATTGCTGATCCACTGGGCAT CTACTAGGGAATCTGGGGTCCCTGATCGCTTCACAGGCAGTGG ATCTGGGACAGATTTCACTCTCACCATCAGCAGTGTGCAGGCT GAAGACCTGGCAGTTTATTACTGCAAACAATCTTTTTATCTTCG GACGTTCGGTGGCGGCACCAAGCTGGAATTCAAA
L (SEQ ID NO: 444)	DIVMSQSPSSLAVSAGEKVTMSCKSSQSLFNSRIRKNDLAWYQQK PGQSPKLLIHWASTRESGVPDRFTGSGSGTDFTLTISSVQAEDLAV YYCKQSFYLRTFGGGTKLEFK
Q30S1 mAB	
H (SEQ ID NO: 445)	CAGGTCCAACTGCAGCAGCCTGGGGCTGAACTTGTGAAGCCTG GGGCTTCAGTGAAGTTGTCCTGCAGGGCTTCTGGCTACAGCTT CACCAGTTACTGGATGCACTGGGTGAAGCAGAGGCCTGGACA AGGCCTTGAGTGGATTGGAGAGATTAATCCTAGCAATGGTGGT TCTAACTACAATGAGAGGTTCAAGAGCAAGGCCACACTGACTG TAGACACGTCCTCCAACACAGCCCACATGCAACTCAGCAGCCT

	GACATCTGAGGACTCTGCGGTCTATTACTGTGCAATCTTCTACG AAGGTAGAGGGGACCTTTACTTTGACTACTGGGGCCAGGGCAC CACTCTCACAGTCTCCTCA
H (SEQ ID NO: 446)	QVQLQQPGAELVKPGASVKLSCRASGYSFTSYWMHWVKQRPGQ GLEWIGEINPSNGGSNYNERFKSKATLTVDTSSNTAHMQLSSLTS EDSAVYYCAIFYEGRGDLYFDYWGQGTTLTVSS
L (SEQ ID NO: 447)	GACATTGTGATGACCCAGTCTCACAAATTCTTGTCCACATCAG TGGGAGACAGGGTCAGCATCACCTGCAAGGCCAGTCAGGATG TGGCTACTACTGTTGCCTGGTATCAACAGAAACCAGGGCAATC TCCTAAACTACTGATTTCCTGGGCATCCACCCGGCACACTGGA GTCCCTGATCGCTTCACAGGCAGTGGATCTGGGACAGATTTCA CTCTCACCATTAGCAATGTGCAGTCTGAAGACTTGGCAGATTA TTTCTGTCAACAATATAGCAGGTATCCGCTCACGTTCGGTGCTG GGACCAAGCTGGAGCTGAAA
L (SEQ ID NO: 448)	DIVMTQSHKFLSTSVGDRVSITCKASQDVATTVAWYQQKPGQSP KLLISWASTRHTGVPDRFTGSGSGTDFTLTISNVQSEDLADYFCQQ YSRYPLTFGAGTKLELK

[0532] The present disclosure further relates to the use of the anti-idiotypic antibodies for the specific identification, detection, selection, depletion, and/or enrichment of cells expressing the anti-HLA-A2 scFv, optionally iCAR cells expressing the anti-HLA-A2 scFv, on the surface of T cells. In some embodiments, the anti-idiotypic antibodies are directly or indirectly labeled.

[0533] In some embodiments, the anti-idiotype antibodies are used to select, enrich, or deplete T cells from a cell population, wherein the T cells express an iCAR comprising an scFv comprising or derived from the sequence of BB7.2 or SN66E3.

[0534] In some embodiments, the anti-idiotype antibodies are used in affinity-based separation methods, including, but not limited to, affinity chromatography. In some embodiments, the anti-idiotype antibody is reversibly or irreversibly bound to or immobilized on a support or a stationary phase.

[0535] In some embodiments, the anti-idiotype antibodies are used in functional analyses of growth, activation, stimulation, cytokine release or other functional outcome of T cells expressing a CAR recognized by the antibodies. In some embodiments, the functional outcome is measured by marker up-regulation or cytokine release or production.

[0536] In some embodiments, the anti-idiotype antibodies are used in a method of analyzing proliferation response or iCAR down modulation in the presence of target cells or any other readout. In some embodiments, the anti-idiotype antibodies can be used for detection and/or quantification of iCAR on the cell surface, using different detection methods.

[0537] In some embodiments, the anti-idiotype antibodies are used in a method of analyzing modulation of a signal in a population of cells comprising CD4+ and/or CD8+ T cells.

[0538] In some assays, the methods for using the anti-idiotype antibodies can be achieved using a soluble or plate-bound form of the antibody or using the anti-idiotype antibodies coupled to beads.

[0539] In some embodiments, the disclosure relates to nucleic acids encoding the anti-idiotype antibodies, host cells comprising the nucleic acids, and methods of recombinant expression of the antibodies, optionally in mammalian expression systems (e.g., CHO recombinant cells) that express the antibodies or fragments thereof.

[0540] In some embodiments, the disclosure relates to CHO cell line development for the expression of the anti-idiotypes for producing GMP grade recombinant antibodies to be used through the process of manufacturing CAR T cells.

B. IN VITRO ASSAYS

[0541] In some embodiments, the bicistronic iCAR/aCAR constructs will be tested for activity effects, including effectiveness and ability to inhibit, using a variety of assays. In some embodiments, the bicistronic iCAR/aCAR constructs or monocistronic aCAR and iCAR constructs for co-transduction will be tested *in-vitro* and/or *in-vivo*. In some embodiments, the bicistronic iCAR/aCAR constructs or monocistronic aCAR and iCAR constructs for co-transduction will be tested *in-vitro*. In some embodiments, the bicistronic iCAR/aCAR constructs or monocistronic aCAR and iCAR constructs for co-transduction will be tested *in-vivo*. In some embodiments, the *in vitro* assays measure cytokine secretion and/or cytotoxicity effects. In some embodiments, the *in vivo* assays will evaluate the bicistronic iCAR/aCAR constructs or monocistronic aCAR and iCAR constructs for co-transduction inhibition and protection to on-target off tumor xenografts. In some embodiments, the *in vivo* assays will evaluate the bicistronic iCAR/aCAR constructs or monocistronic aCAR and iCAR constructs for co-transduction inhibition and protection to on-target off tumor tissue and/or viral organs.

i. Luciferase Cytotoxicity Assay

[0542] In some embodiments, bicistronic iCAR/aCAR constructs or monocistronic aCAR and iCAR constructs for co-transduction are evaluated using a luciferase cytotoxicity assay. Generally, for a luciferase cytotoxic assay, target tumor cells (which can be referred to as "T") are engineered to express firefly luciferase. In some embodiments, commercialy available ATCC cell lines are used. In some embodiments, H1703 cells were used. In some embodiments, H1650 cells were used. In some embodiments, H1792 cells were used. In some embodiments, H292 cells were used. The *in vitro* luciferase assay can be performed according to the Bright-Glo Luciferase assay (commercially available from Promega or BPS Biosciences

or other commercial vendors). Transduced effector (E) T cells (which have been transduced with bicistronic iCAR/aCAR constructs or mock/control construct) can be incubated for 18-48 hrs with recombinant target cells expressing the iCAR or aCAR target to be tested in different effector to target ratios. In some embodiments, the iCAR/aCAR pair comprises any of aCAR and/or iCAR with the components as described above. In some embodiments, the bicistronic iCAR/aCAR constructs described above are to be tested. In some embodiments, the bicistronic iCAR/aCAR comprises an amino acid sequence encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325. In some embodiments, the bicistronic iCAR/aCAR comprises an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:276, SEQ ID NO:278, SEQ ID NO:280, SEQ ID NO:282, SEQ ID NO:322, SEQ ID NO:324, and SEQ ID NO:326. Cell killing can be quantified indirectly by estimating the number of live cells with the Bright-Glo Luciferase system. Cell killing can also be measured using an IncuCyte cytotoxicity assay.

[0543] In some embodiments, the 'off-tumor' cytotoxicity can be manipulated by sorting transduced T cell populations according to iCAR/aCAR expression level or by selecting a sub population of recombinant target cells according to their target expression, including for example, expression of the gene product encoding for at least one extracellular polymorphic epitope. In some embodiments, the aCAR and iCAR target is any target with an extracellular domain. In some embodiments, the sorting is based on EGFR, HER2, or HLA-A2 expression level.

[0544] In some embodiments, the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction is examined to determine whether the iCAR transduced T cells can discriminate between the 'on-tumor' cells (*e.g.*, tumor cells) and 'off-tumor' cells (*e.g.*, non-tumor cells) *in vitro*. Generally, this is tested by examining the killing effect of transduced T cells incubated with a mix of 'on-tumor' and 'off-tumor' cells at a ratio of 1:1 to 1:10. In some embodiments, the ratio Target cells to Effector T cells (T:E ratio) is 1:0.02, 1:0.04, 1:0.06, 1:0.08, 1:0.1, 1:0.12, 1:0.12, 1:0.14, 1:0.16, 1:0.18, 1:2, 1:3, 1:4, 1:5,

1:6, 1:7, 1:8, 1:9, 1:10, 1:11, 1:12, 1:13, 1:14, 1:15, 1:16, 1:17, 1:18, 1:19, or 1:20. In some embodiments, the E:T ratio (Effector T cells to Target cells) is 0.02:1, 0.04:1, 0.06:1, 0.08:1, 0.1:1, 0.12:1, 0.12:1, 0.14:1, 0.16:1, 0.18:1, 2:1, 3:1, 4:1, 5:1:1, 6:1, 7:1, 8:1, 9:1, 10:1, 11:1, 12:1, 13:1, 14:1, 15:1, 16:1, 17:1, 18:1, 19:1, or 20:1. The on tumor recombinant cells can be distinguished from the 'off-tumor' recombinant cells by luciferase expression in embodiments where only one cell population will be engineered to express the luciferase gene at a time). Killing can be quantified after 24-48 hrs of co-incubation using the Bright-Glo Luciferase assay (Promega). Killing can also be quantified using an IncCyte cytotoxicity assay. In some embodiments, transduced cells were only used in the assay of transduction efficiency was greater than 10% and expression was observed for both aCAR and iCAR.

[0545] In some embodiments, the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction transduced T cells exhibit about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, and/or about 95% less off-tumor cell killing as compared to T cells transduced with aCAR (or other control) but not transduced with the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction. In some embodiments, the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction transduced T cells exhibit about 1-fold, about 2-fold, about 3-fold, about 4-fold, about 5-fold, or about 10-fold less off-tumor cell killing as compared to T cells transduced with aCAR (or other control) but not transduced with the bicistronic iCAR/aCAR construct.

ii. Caspase 3

[0546] In some embodiments, caspase 3-detection assays are employed to determine the level of apoptosis of the 'on-tumor' cells (*e.g.*, tumor cells) and 'off-tumor' cells (*e.g.*, non-tumor cells) *in vitro*. In some embodiments, caspase_3-detection of cytotoxic lymphocyte (CTL) induced apoptosis by an antibody to activated cleaved caspase 3 is examined.

[0547] Generally, one of the pathways by which CTLs kill target cells is by inducing apoptosis through the Fas ligand. The CASP3 protein is a member of the cysteine-aspartic acid protease (caspase) family. Typically, sequential activation of caspases plays a significant role in the execution-phase of cell apoptosis and as such, cleavage of pro-caspase 3 to caspase 3 results in conformational change and expression of catalytic activity. The cleaved activated form of caspase 3 can be recognized specifically by a monoclonal antibody.

[0548] In some embodiments, transduced T cells can be incubated with either 'on-tumor' (*e.g.*, mimicking tumor) and 'off-tumor' cells (*e.g.*, mimicking non-tumor) recombinant cells. In some embodiments, the 'on-tumor' (*e.g.*, tumor) and 'off-tumor' cells (*e.g.*, non-tumor)

recombinant cells have been previously labeled with CFSE ((5(6)-Carboxyfluorescein N-hydroxysuccinimidyl ester)) or other cell tracer dye (*e.g.*, CellTrace Violet). In some embodiments, co-incubation of target cells with effector cells occurs for about 1 hour to 6 about hours, about 2 hours to about 5 hours, or about 2 to about 4 hrs. In some embodiments, target cell apoptosis is quantified by flow cytometry. Cells can be permeabilized and fixed by an inside staining kit (Miltenyi or BD bioscience) and stained with an antibody for activated caspase 3 (BD bioscience).

[0549] In some embodiments, the bicistronic iCAR/aCAR construct transduced T cells induce about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, and/or about 95% less off-tumor cell apoptosis as compared to T cells transduced with the bicistronic iCAR/aCAR construct but not transduced with the iCAR (or other appropriate control). In some embodiments, the bicistronic iCAR/aCAR construct transduced T cells induce about 1-fold, about 2-fold, about 3-fold, about 4-fold, about 5-fold, or about 10-fold less off-tumor cell apoptosis as compared to T cells transduced with aCAR (or other control) but not transduced with the bicistronic iCAR/aCAR construct.

iii. Time-lapse microscopy

[0550] Time lapse microscopy of the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction transduced T cells can be employed in order to discern target binding. In some embodiments, target cells will be labeled with a reporter gene (for example but not limited to a fluorescent protein such as mCherry). In some embodiments, transduced T cells are incubated with either 'on-tumor' or 'off-tumor' cells for up to 5 days. In some embodiments, time lapse microscopy can be used to visualize killing. In some embodiments, flow cytometry analysis using viable cell number staining and CountBright™ beads (commercially available from Thermofisher/Invitrogen) for determining target cell number at end-point time will be conducted.

[0551] In some embodiments, in order to determine if the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction transduced T cells can discern targets *in vitro*, each recombinant target cells ('on-tumor' or 'off-tumor') is labeled with a different reporter protein (for example GFP and mCherry). In some embodiments, any report protein pair would work, so long as the reporter pair contains two reporters which are easily distinguishable. In some embodiments, transduced T cells (Effector cells) will be co-incubated with the recombinant cells (target cells) at a 1:1 ratio of E/T. In some embodiments, the ration of effector to target (E/T) includes but is not limited to 16:1, 15:1, 14:1, 13:1, 12:1, 11:1, 10:1,

9:1, 8:1, 6:1, 4:1, 2:1, or 1:1. In some embodiments, the cell fate is then examined by microscopy imaging.

iv. Cytokine expression intra cellular staining

[0552] Cytokine expression and/or release can be examined in order to determine T cells activation. In some embodiments, a bicistronic iCAR/aCAR construct transduced T cells are incubated with the recombinant target cells and cytokine production for one or more cytokines is quantified, for example, either by measuring cytokine secretion in cell culture supernatant according to or by flow cytometry analysis, or by Luminex and/or MSD . For the flow cytometry analysis, a Golgi stop can be employed to prevent the secretion of the cytokines. In some embodiments, following a 6 hour and 18 hour to 24 hour incubation of the transduced T cells with target cells, T cells will be permeabilized and fixed by an intracellular staining kit (Miltenyi) and stained with antibodies for the T cell markers (CD3 and CD8) and for one or more cytokines. In some embodiments, the cytokines include but are not limited to IL-2, INFγ, and/or TNFα. In some embodiments, the cytokines are secreted and include but are not limited to IL-2, INFγ, and/or TNFα. In some embodiments, the cytokines are intracellular and include but are not limited to IL-2, INFγ, and/or TNFα.

v. T cell degranulation assay measured by CD107a staining

[0553] Staining for CD107a can also be examined as a surrogate for cytolytic activity of the transduced T cells. Generally, degranulating of T cells can be identified by the surface expression of CD107a, a lysosomal associated membrane protein (LAMP-1), and surface expression of LAMP-1 has been shown to correlate with CD8 T cell cytotoxicity. Further, this molecule is located on the luminal side of lysosomes. Typically, upon activation, CD107a is transferred to the cell membrane surface of activated lymphocytes. Moreover, CD107a is expressed on the cell surface transiently and is rapidly re-internalized via the endocytic pathway. Therefore, while not being bound by theory, CD107a detection is maximized by antibody staining during cell stimulation and by the addition of monensin (for example, to prevent acidification and subsequent degradation of endocytosed CD107a antibody complexes).

[0554] In some embodiments, the bicistronic iCAR/aCAR construct transduced T cells are incubated with the target cells for about 6 hours to about 24 hours and CD107a expression on the CD8 T cells is examined. In some embodiments, the target cells expresso only one target protein recognized by aCAR (as in tumor cells) or target cells expressing both target proteins recognized by aCAR and iCAR (as in normal cells). In some embodiments, the bicistronic

iCAR/aCAR construct transduced T cells are incubated with the target cells for about 6 ours to about 24 hrs in the presence of monensin and CD107a expression on the CD8 T cells is followed by flow cytometry using conjugated antibodies against the T cell surface markers (for example, CD3 and CD8) and a conjugated antibody for CD107a.

vi. Quantitation of Secreted Cytokines by ELISA /Luminex

[0555] In some embodiments, following co-cultivation of bicistronic iCAR/aCAR construct transduced T-cells (Jurkat, or primary T- cells) expressing iCAR or aCAR or both aCAR and iCAR with modified target cells, expressing iCAR or aCAR or both aCAR and iCAR antigens on their cell surface, conditioned medium will be collected, and cytokine's concentration will be measured by cytokine ELISA or by Luminex xMAP Multiplex Assay technology (Luminex). In some embodiments, the cytokine is selected from the group consisting of IL-2, INFγ and/or TNF□. In some embodiments, the cytokine is selected from the group consisting of IL-2. In some embodiments, the cytokine is selected from the group consisting of INFγ. In some embodiments, the cytokine is selected from the group consisting of TNF□. In some embodiments, a decrease of about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, or about 99% is demonstrated with bicistronic iCAR/aCAR construct transduced cells.

vii. Cytokines Secretion Measured by Cytometric Bead Array (CBA) Assay

[0556] Cytometric Bead Array (CBA) is used to measure a variety of soluble and intracellular proteins, including cytokines, chemokines and growth factors. In some embodiments, T-cells (primary T-cells or Jurkat cells) transduced with aCAR or both aCAR and iCAR constructs (Effector cells) are stimulated with modified target cells expressing both iCAR and aCAR or aCAR or iCAR target antigens on their cell surface. In some embodiments, the effector to target ratio ranges from 20:1 up to 1:1. In some embodiments, the effector to target ratio ranges from 20:1, 19:1, 18:1, 17:1, 16:1, 15:1, 14:1, 13:1, 12:1, 11:1, 10:1, 9:1, 8:1, 7:1, 6:1, 5:1, 4:1, 3:1,2:1, or 1:1. In some embodiments, following several hours of co-incubation the effector cells produce and secrete cytokines which indicate their effector state. In some embodiments, the supernatant of the reaction is collected, and secreted IL-2, IFN-γ, and/or TNFα were measured and quantified by multiplex CBA assay.

[0557] In some embodiments, a decrease of about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%,

about 80%, about 85%, about 90%, about 95%, or about 99% is demonstrated with dual CAR (aCAR/iCAR) transduced cells were co-incubated with target cells expressing both target antigens as compared to IL-2, IFN-γ, and/or TNFα secretion resulted from co-incubation of the same effector cells with target cells expressing only one target. In some embodiments, a decrease of about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, or about 99% in IL-2 IFN-γ, and/or TNFα secretion was demonstrated when bicistronic iCAR/aCAR construct transduced cells were co-incubated with target cells expressing both target antigens as compared to IL-2 IFN-γ, and/or TNFα secretion resulted from co-incubation of the same effector cells with target cells expressing only one target. In some embodiments, a decrease of 86%.

C. IN VIVO ASSAYS

[0558] In some embodiments, the bicistronic iCAR/aCAR construct are tested for effectiveness *in vivo*. In some embodiments, NOD/SCID/γc- or similar mice are inoculated subcutaneously or orthotopically with tumor cells. In some embodiments, the tumor cells are EGFR and HER2 positive cells lines A549, A431, Fadu, SK-OV-3, U-87, MCF7, NCI-H460, NCI-H1703, NCI-H1650, NCI-H1975, NCI-H292 (ATCC cell lines) cells. In some embodiments, for establishment of and/or differentiation between 'on-target' cells and 'off-tumor' cells, A549, A431, Fadu, SK-OV-3, U-87, MCF7, NCI-H460 NCI-H1703, NCI-H1650, NCI-H1975, NCI-H292 can be engineered to be deficient or express the iCAR epitope, thereby representing the healthy cells. In some embodiments, the iCAR epitope comprises at least one extracellular polymorphic epitope. In some embodiments, the iCAR epitope is from HLA (including, for example, HLA-A2, HLA-A3, HLA-A, HLA-B, HLA-C, HLA-G, HLA-E, HLA-F, HLA-DPA1, HLA-DQA1, HLA-DQB1, HLA-DQB2, HLA-DRB1, or HLA-DRB5). In some embodiments, the iCAR epitope is from HLA-A2. Other cells that could be employed in these assays include but are not limited to Raji or any other recombinant cell lines. In some embodiments, such assays can be in a PDX (patient derived xenograft) model.

[0559] For the assay, mice will be divided into study groups; one cohort will be injected with the A549, A431, Fadu, SK-OV-3, U-87, MCF7, NCI-H460 NCI-H1703, NCI-H1650, NCI-H1975, and/or NCI-H292 cells not expressing the iCAR epitope, while the other will be injected with the corresponding A549, A431, Fadu, SK-OV-3, U-87, MCF7, NCI-H460 NCI-H1703, NCI-H1650, NCI-H1975, NCI-H292 cells expressing the iCAR epitope. Following staging, mice will be infused intravenously with T cells transduced with aCAR, aCAR/iCAR

and a control group of untransduced T cells or no T cells. Tumor burden will be measured by through measurement of the subcutaneous tumor volume.

[0560] According to one embodiment of the assay, in order to test whether the T cells expressing the bicistronic iCAR/aCAR constructs could discriminate between the target cells and off target cells *in vivo* within the same organism, mice are injected with a 1:1 mixture of the 'on-tumor'/'off-tumor A549, A431, Fadu, SK-OV-3, U-87, MCF7, NCI-H460 NCI-H1703, NCI-H1650, NCI-H1975, and/or NCI-H292 cells, followed by injection of transduced T cells expressing either the aCAR alone or both aCAR and iCAR (including as the bicistronic iCAR/aCAR constructs as described herein) after staging. With this embodiment, upon sacrifice of the mice the presence of the 'on-tumor' and 'off-tumor cells Will be evaluated by immunohistochemical staining

[0561] According to one embodiment of the assay, in order to test whether the T cells expressing the bicistronic iCAR/aCAR constructs could discriminate between the target cells and off target cells *in vivo* within the same organism, mice are injected with a 1:10 mixture of the 'on-tumor'/'off-tumor NALM-6, A549, A431, Fadu, SK-OV-3, U-87, MCF7, and/or NCI-H460 NCI-H1703, NCI-H1650, NCI-H1975, NCI-H292 cells, followed by injection of transduced T cells expressing either the aCAR alone or both aCAR and iCAR. With this embodiment, upon sacrifice of the mice the presence of the 'on-tumor' and 'off-tumor cells in the spleen and bone marrow will be analyzed by flow cytometry for iCAR and aCAR markers.

i. Tumor growth kinetics in human xenograft mouse models

[0562] In some embodiments, the tumor cells express either the iCAR target, aCAR target or both. In some embodiments, an aCAR tumor cell line could be the EGFR or HER2 positive cells lines A549, A431, Fadu, SK-OV-3 U-87, MCF7, and/or NCI-H460 (ATCC cell lines). In some embodiments, tumor cells that express both the aCAR and iCAR (i.e. 'off-tumor' cells) are NALM 6, A549, A431, Fadu, SK-OV-3, U-87, MCF7, MDA-MB-231, and/or NCI-H460 engineered to express the iCAR epitope (for example, HLA- A2) thereby representing the healthy cells. In some embodiments, NALM 6 and NALM 6-HLA-A2 can also be engineered to express a reporter gene (*e.g.*, firefly luciferase, GFP, mCherry), for easy detection. In some embodiments, A549 and A549-HLA-A2 can also be engineered to express a reporter gene (*e.g.*, firefly luciferase), for easy detection. In some embodiments, A431 and A431-HLA-A2 can also be engineered to express a reporter gene (*e.g.*, firefly luciferase), for easy detection. In some embodiments, Fadu and Fadu -HLA-A2 can also be engineered to express a reporter gene (*e.g.*, firefly luciferase), for easy detection. In some embodiments, SK-OV-3 and SK-OV-3-HLA-A2 can also be engineered to express a reporter gene (*e.g.*, firefly luciferase), for easy detection.

In some embodiments, NCI-H460 and NCI-H460-HLA-A2 can also be engineered to express a reporter gene (*e.g.*, firefly luciferase), for easy detection. In some embodiments, U-87 and U-87-HLA-A2 can also be engineered to express a reporter gene (*e.g.*, firefly luciferase), for easy detection. In some embodiments, MCF7 and MCF7-HLA-A2 can also be engineered to express a reporter gene (*e.g.*, firefly luciferase), for easy detection. In some embodiments, can also be engineered to express a reporter gene (*e.g.*, firefly luciferase), for easy detection. In some embodiments, NCI-H460 and NCI-H460 -HLA-A2 can also be engineered to express a reporter gene (*e.g.*, firefly luciferase), for easy detection.

[0563] In some embodiments, monitoring will be conducted by measuring tumor volume by mechanical means (caliper) and also by using in-vivo imaging systems (IVIS). In some embodiments, tumor burden can be quantified, and infiltrating T-cell populations can be analyzed by FACS.

D. TREATMENT METHODS

[0564] The present invention provides methods for the treatment of cancers by employing the bicistronic iCAR/aCAR constructs or monocistronic aCAR and iCAR constructs for co-transduction as described herein. The methods of treatment for cancer as described herein can employ exploiting loss of heterozygosity, or other genetic loss or allelic imbalance phenotypes found in human tumors, including, without limitation, loss of function or expression, resulting from mutations affecting one or more nucleotides (for example, without limitation, in HLA-1 genes) by means of CAR-T therapy, or by modifying other cells of the immune system.

[0565] In yet another aspect, the present invention provides a method of selecting a personalized biomarker for a subject having a tumor characterized by loss of heterozygosity, or other genetic loss or allelic imbalance phenotypes found in human tumors, the method comprising (i) obtaining a tumor biopsy from the subject; (ii) obtaining a sample of normal tissue from the subject, *e.g.*, PBMCs; (iii) identifying a single allelic variant of a polymorphic cell surface epitope that is not expressed by cells of the tumor due to loss of heterozygosity, or other genetic loss or allelic imbalance phenotypes found in human tumors, but that is expressed by the cells of the normal tissue, thereby identifying a personalized biomarker for the subject, and (iv) determining the appropriate bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as described herein for use in treatment.

[0566] In a further aspect, the present invention provides a method for treating cancer in a patient having a tumor characterized by loss of heterozygosity, or other genetic loss or allelic imbalance phenotypes found in human tumors, comprising administering to the patient an

effector immune cell as defined above, wherein the iCAR is directed to a single allelic variant encoding a polymorphic cell surface epitope absent from cells of the tumor due to loss of heterozygosity, or other genetic loss or allelic imbalance phenotypes found in human tumors but present at least on all cells of related mammalian normal tissue of the patient. In some embodiments, the effector immune cell comprises a bicistronic iCAR/aCAR construct as described herein.

[0567] In some embodiments, the treating results in reduced on-target, off-tumor reactivity, as compared with a treatment comprising administering to the cancer patient at least one population of immune effector cells expressing a bicistronic iCAR/aCAR construct as described herein.

[0568] In some embodiments, the safe effector immune cells used for treating cancer as defined above express on their surface an aCAR comprising an extracellular domain that specifically binds to a tumor-associated antigen or a non-polymorphic cell surface epitope of an antigen and an iCAR comprising an extracellular domain that specifically binds a single allelic variant of a polymorphic cell surface epitope of an antigen expressed at least in a tissue of origin of the tumor or of a housekeeping protein, which is a different antigen than that to which the extracellular domain of said aCAR binds. In some embodiments, the effector immune cell expresses the components of a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction as described herein.

[0569] In some embodiments, the safe effector immune cells used for treating cancer as defined above express on their surface an aCAR comprising an extracellular domain that specifically binds to a tumor-associated antigen or a non-polymorphic cell surface epitope of an antigen and an iCAR comprising an extracellular domain that specifically binds a single allelic variant of a polymorphic cell surface epitope of an antigen expressed at least in a tissue of origin of the tumor or of a housekeeping protein, such as an HLA genes (including for example, HLA-A, HLA-B, HLA-C, HLA-G, HLA-E, HLA-F, HLA-K, HLA-L, HLA-DM, HLA-DO, HLA-DP, HLA-DQ, or HLA-DR) which is a different antigen than that to which the extracellular domain of said aCAR binds.

[0570] In some embodiments, the safe effector immune cells used for treating cancer as defined above express on their surface an aCAR comprising an extracellular domain that specifically binds to a tumor-associated antigen or a non-polymorphic cell surface epitope of an antigen and an iCAR comprising an extracellular domain that specifically binds a single allelic variant of a polymorphic cell surface epitope of an antigen expressed at least in a tissue of origin of

the tumor, such as an HLA-A, which is a different antigen than that to which the extracellular domain of said aCAR binds.

[0571] In some embodiments, the safe effector immune cells used in the method of treating cancer are selected from T cells, natural killer cells or cytokine-induced killer cells. In some embodiments, the safe effector immune cell is autologous or universal (allogeneic) effector cells. In some embodiments, the iCAR used in any one of the methods of treating cancer defined above is directed to all tissues of the patient on which the target-antigen of the aCAR is present, wherein the target antigen of the aCAR is a non-polymorphic cell surface epitope of an antigen or a single allelic variant of a polymorphic cell surface epitope is present, and said epitope is a tumor-associated antigen or is shared at least by cells of related tumor and normal tissue.

[0572] In some embodiments, the cancer is selected from the group consisting of Acute Myeloid Leukemia [LAML], Adrenocortical carcinoma [ACC], Bladder Urothelial Carcinoma [BLCA], Brain Lower Grade Glioma [LGG], Breast invasive carcinoma [BRCA], Cervical squamous cell carcinoma and endocervical adenocarcinoma [CESC], Cholangiocarcinoma [CHOL], Colon adenocarcinoma [COAD], Esophageal carcinoma [ESCA], Glioblastoma multiforme [GBM], Head and Neck squamous cell carcinoma [HNSC], Kidney Chromophobe [KICH], Kidney renal clear cell carcinoma [KIRC], Kidney renal papillary cell carcinoma [KIRP], Liver hepatocellular carcinoma [LIHC], Lung adenocarcinoma [LUAD], Lung squamous cell carcinoma [LUSC], Lymphoid Neoplasm Diffuse Large B-cell Lymphoma [DLBC], Mesothelioma [MESO], Ovarian serous cystadenocarcinoma [OV], Pancreatic adenocarcinoma [PAAD], Pheochromocytoma and Paraganglioma [PCPG], Prostate adenocarcinoma [PRAD], Rectum adenocarcinoma [READ], Sarcoma [SARC], Skin Cutaneous Melanoma [SKCM], Stomach adenocarcinoma [STAD], Testicular Germ Cell Tumors [TGCT], Thymoma [THYM], Thyroid carcinoma [THCA], Uterine Carcinosarcoma [UCS], Uterine Corpus Endometrial Carcinoma [UCEC], Uveal Melanoma [UVM], Non-small cell lung carcinoma [NSCLC], and Small cell lung cancer [SCLC].

[0573] In some embodiments, the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction for use in the treatment of cancer is any bicistronic iCAR/aCAR construct described herein. In some embodiments, the bicistronic iCAR/aCAR construct used to treat the cancer, such as any one of the cancer types recited above, is directed against or specifically binds to a single allelic variant of an HLA genes (including for example, HLA-A, HLA-B, HLA-C, HLA-G, HLA-E, HLA-F, HLA-K, HLA-L, HLA-DM, HLA-DO, HLA-DP, HLA-DQ, or HLA-DR, HLA-B gene or HLA-C gene or against a single allelic

variant. In some embodiments, the treatment method employs administration of a safe effector cell comprising the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction. In some embodiments, the treatment method employs administration of a safe effector cell expressing the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction.

[0574] In some embodiments, the bicistronic iCAR/aCAR or monocistronic aCAR and iCAR constructs for co-transduction for use in the treatment of cancer comprises an amino acid sequence encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325. In some embodiments, the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction comprises an amino acid sequence encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO:275, SEQ ID NO:277, SEQ ID NO:279, SEQ ID NO:281, SEQ ID NO:321, SEQ ID NO:323, and SEQ ID NO:325. In some embodiments, the treatment method employs administration of a safe effector cell comprising the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction. In some embodiments, the treatment method employs administration of a safe effector cell expressing the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction.

[0575] In some embodiments, the bicistronic iCAR/aCAR for use in the treatment of cancer comprises an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:276, SEQ ID NO:278, SEQ ID NO:280, SEQ ID NO:282, SEQ ID NO:322, SEQ ID NO:324, and SEQ ID NO:326. In some embodiments, the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction comprises an amino acid sequence selected from the group consisting of SEQ ID NO:276, SEQ ID NO:278, SEQ ID NO:280, SEQ ID NO:282, SEQ ID NO:322, SEQ ID NO:324, and SEQ ID NO:326. In some embodiments, the treatment method employs administration of a safe effector cell comprising the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction. In some embodiments, the treatment method employs administration of a safe

effector cell expressing the bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction.

[0576] The compositions may be formulated for parenteral administration by injection, *e.g.*, by bolus injection or continuous infusion. Formulations for injection may be presented in unit dosage form, *e.g.*, in ampoules or in multidose containers, with an added pharmaceutically acceptable carrier and/or preservative. The compositions may take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents.

[0577] For purposes of clarity, and in no way limiting the scope of the teachings, unless otherwise indicated, all numbers expressing quantities, percentages or proportions, and other numerical values recited herein, should be interpreted as being preceded in all instances by the term "about." Accordingly, the numerical parameters recited in the present specification are approximations that may vary depending on the desired outcome. For example, each numerical parameter may be construed in light of the number of reported significant digits and by applying ordinary rounding techniques.

EXAMPLES

EXAMPLE 1. DEVELOPMENT AND TESTING OF BICISTRONIC INHIBITORY CHIMERIC ANTIGEN RECEPTOR (iCAR)/ACTIVATING CHIMERIC ANTIGEN RECEPTOR (aCAR) CONSTRUCTS

Introduction:

[0578] This example provides the results related to development and testing of bicistronic inhibitory chimeric antigen receptor (iCAR)/activating chimeric antigen receptor (aCAR) constructs in order to develop cancer therapeutics for use in safely target tumors that have lost genomic segments encoding cell-membrane proteins with polymorphic protein coding changes). Data provide in the example and figures include T-REP identification of new iCAR leads, new human HLA-A2 scFv constructs, and bicistronic LV transduction - FaDu/MCF7-Luc immune killing assay – including development of novel iCAR leads.

[0579] Bicistronic iCAR/aCAR constructs have been developed and preliminary testing performed in order to prepare and examine these constructs for use as cancer therapeutics. See, Figures 1-59 as well as Tables 1-22 for illustrative design and evaluation of examples of iCAR and aCAR constructs as described herein, as well as sequences thereof.

MATERIALS AND METHODS

mRNA transcription *in vitro*

[0580] Appropriate plasmids were linearized using SpeI or BamHI restriction enzymes. Linear plasmid was used to transcribe in-vitro mRNA using T7mScript Standard mRNA Production System (CELLSCRIPT, Madison, U.S.A.). The concentration and quality of the mRNA were assessed by spectrophotometry. Preparation was according to manufacturer's protocol.

PBMC Purification

[0581] Leukocyte enriched samples were acquired from The Sheba Medical Center blood bank, diluted with equal volumes of PBS and loaded on Ficoll-Paque PLUS (GE Healthcare) for density-based cell separation. Preparation was according to manufacturer's protocol. Mononuclear cells were collected from the plasma/Ficoll interface, washed several times and resuspended in Cryostor CS10 (Merck).

PBMC Culture and Transduction

[0582] PBMCs were thawed and seeded at a density of $1x10^6$ cells/ml in LymphoOne medium (Takara-Bio, Kusatsu, Japan) supplemented with 100 U/ml IL2 (Miltenyi Biotech, Bergisch Gladbach, Germany). The next day concentrated lentiviruses were added at an MOI of 5, 10, or 20 (according to prior calibrations). After 3 days cells were transferred to 24-well G-Rex plates (Wilson Wolf, Saint Paul, MN) containing LymphoOne medium supplemented with 1% human serum (Access Biologicals, Vista, CA) and 100 U/ml IL2. On day 7 post-thaw 100 U/ml IL2 was added, and on day 8 the medium was replaced. Functional assays were typically performed.

mRNA electroporation

[0583] On day 8 or 10 of PBMC's culture, $2x10^6$ cells were washed twice with OptiMEM medium (GibcoBRL, Grand Island, NY). The cells were resuspended in 100ul OptiMEM containing 1-10ug mRNA and electroporated in 2mm cuvette, using NepaGene21 electroporator (Nepa Gene Co., Ltd., Japan) at 200V, 2.5ms, one pulse or using ECM830 electroporator (BTX.Ltd., US) at 300V, 2ms, one pulse. The cells were resuspended in 5ml growth medium and transferred into 6well plates for further incubation.

IncuCyte Cytotoxicity Assay

[0584] Target cells expressing nuclear-GFP (nGFP) were seeded in black-walled 384-well plates with microclear bottom (Greiner Bio-One, Kremsmünster, Austria), $1.5x10^4$ cells per

well, in LymphoOne medium supplemented with 1% human serum. The next day, transduced or electroporated PBMCs were added to the wells at the desired E:T ratio. Annexin-V Red (Essen BioScience, Ann Arbor, MI) to detect apoptosis was added immediately before adding PBMCs). Plates were imaged for 3 days using the IncuCyte S3 (Essen BioScience) instrument at 37C, 5%CO_2. Percent killing was calculated as nGFP+ Annexin-V-Red+ cell count divided by total nGFP+ cell count.

ELISA

[0585] Target cells expressing nuclear-GFP (nGFP) were seeded in 96 well plates (Thermo, NU-167008), $5x10^3$ cells per well, in LymphoOne medium supplemented with 1% human serum. The next day, transduced or electroporated PBMCs were added to the wells at 5:1 E:T ratio. Cells are co-incubated for 15-18hrs at 37C, 5%CO_2. Following co-incubation, supernatant is harvested and transferred to non-binding 96-well plates (Greiner, #655901) at -200c. Supernatants are diluted 3 and 100-fold, ELISA performed as to manufactures instruction (Human IFN-gamma Quantikine, R&D, #SIF50) and quantified using Tecan plate reader.

Quantification of Antigen Expression by Flow Cytometry

[0586] The MESF/"Antibody Binding Capacity" (ABC) ratio of a particular antibody can be used to quantify the number of antigen sites per cell. To establish the MESF/ABC ratio of each antibody Lot, MFIs of stained SCQ beads were correlated to the MFIs of MESF standards. The slope of the curve constitutes the ratio of fluorochrome label in MESF units per antibody. The MESF/ABC of every antibody Lot was measured using mouse/human/rat Simple Cellular Quantum (SCQ) Beads and MESF standards purchased from Bangs laboratories. Each of the 4 populations of SCQ beads has a known Antibody Binding Capacity (ABC), typically in the range of several thousands to 500-800K, so by staining these beads with an antibody at near saturation, one can correlate the fluorescence measurement (MFI) on a flow cytometer to the amount of bound antibody (ABC). MESF standard beads are composed of 4-5 different bead populations labeled with a known amount of fluorochrome molecules. By running MESF beads on a flow cytometer, one can correlate an MFI measurement to MESF units and compare between data that was collected on multiple different occasions, PMT voltages and instruments. When using HLA-A2/NYESO1- PE tetramers to stain tag-less iCAR constructs, the MESF/ABC ratio was established by staining control Jurkat cell lines that express a tagged aCAR and iCAR at high and low levels, with both quantifiable Anti-Myc Tag antibody and HLA-A2/NYESO1- PE tetramers. For each staining 100-200K positive cells were washed

twice with 100ul of cold FACS buffer (2% FCS in PBS x1) by centrifugation, 300g for 5min at 4oC. For Flag tagged aCAR and Myc tagged iCAR quantification, the cells were stained with 50ul of APC (130-119-584, Miltenyi) and FITC (130-116-485, Miltenyi) labeled antibodies diluted 1/25 with FACS buffer. For un-tagged trastuzumab aCAR and Anti-HLA-A2 iCAR quantification, primary human Anti-Trastuzumab scFv69 (Ab00618-10.0, Absolute Antibody), HLA-A2/NYESO1- PE tetramers (TB-M105-1, MBL) and secondary Anti-human Fc APC (BLG-409306, biolegend) were diluted in FACS buffer, 1/25, 1/5 and 1/10 respectively. For target cell line antigen quantification, Anti-EGFR PE (FAB9577P-100, R&D), Anti-HER2 APC (130-106-696, Miltenyi) and Anti-HLA-A2 APC (17-9876-42, ebioscience) were diluted with FACS buffer, 1/2.5, 1/10 and 1/5 respectively. The cells were incubated at 4oC in the dark for 45-60min and washed thrice with 100ul cold FACS buffer as described previously. The cells were resuspended with 150ul of FACS buffer or PBS X1 containing 0.5-1 ug/ml DAPI (MBD0015-1, Merck-Sigma). The cells were analyzed by flow cytometry (BD FACS Celesta or MACSQuant Analyzer 10) collecting 10K– 50K double positive events from each sample. Next, without changing the PMT voltages on the instrument, 5-10K events of each population of relevant MESF standard beads (FITC 555P-5ML, APC 823-5ML, PE 827-5ML, Bangs), were collected. FlowJo software was used to gate and calculate MFIs (Geometric Mean Fluorescence) and MESF beads QuickCal files, provided by the manufacturer, were used to convert the MFIs in to MESF units. Next, the values were converted to ABC units Using the MESF/ABC curves of the specific antibody lots used.

DISCUSSION

FaDu/MCF7-Luc immune killing assay

[0587] Identification of novel iCAR using a nucGFP labeled target cells endpoint and bicistronic LV transduction.

[0588] The assay was useful regarding increasing the potency of iCAR inhibition (scFv avidity & activity) is necessary to decrease the iCAR/aCAR stoichiometry for efficient aCAR protection. Continued development and analysis related to dual differential expression in a lentiviral bicistronic format is ongoing and in progress.

[0589] Focused on HER2 (anti-Trastuzumab scFv) as an aCAR. Identified fully human or humanizied scFv's to target HLA-A2. Identified novel iDomains (LIR1, KIR2DL1, KIR2DL2, and/or BTLA).

Lentiviral dualCAR expression

[0590] Low transduction efficiency and variable differential expression.

[0591] iCAR constructs are identical, except for variations in the inhibitory domain.

[0592] aCAR constructs are also identical, except for variations in the scFv: Cetuximab or Panitumumab for EGFR and Trastuzumab or Pertuzumab for Her2.

[0593] All constructs are in iCAR/aCAR configuration with T2A cleavable linker.

[0594] IncuCyte Immune Cell Killing Assay: a cell imagining platform to monitor target killing and proliferation, and T-cell activation kinetics.

[0595] Quantum Bead Assay: a methodology to incorporate absolute aCAR & iCAR level, stoichiometry, and expression kinetics into screening and analysis.

[0596] IMPT001 GO: in vitro validation HLA-A2 scFv/PD-1 iCAR pairing with EGFR & HER2 scFv aCAR using mRNA co-electroporation of constructs into effector cells, using the Incucyte platform and FACS T-cell profiling IMPT001 go.

[0597] Lentiviral Technology: Design and evaluate the expression of mono- and dual lentiviral aCAR & iCAR to support IMPT001 and identify novel iCAR (64 constructs).

[0598] New Potent HLA-A2 scFv: Characterize a fully human HLA-A2 scFv alternative to murine BB7.2 as a lentiviral iCAR transduced into donor PBMC that appears to bind HLA-A tetramers more avidly.

[0599] FaDU/U87-Luc Immune Killing Assay: identification of novel iCAR using a Luciferase viability endpoint. LIR1 & KIR2DL1 iCARs identified.

Validation of an IncuCyte immune cell killing assay

[0600] Dependence of target cell killing & proliferation on E/T ratio.

[0601] Implemented an immune cell killing assay that simultaneously images the kinetics of target cell killing and proliferation, and T-cell activation.

[0602] The technology is applicable to diverse adherent cancer cell lines partially circumventing the time and cost associated with engineering isogenic cell lines.

[0603] The kinetic and endpoints are a quantitative metrics that will allow dual CAR ranking, *i.e.*, directly proportional to E/T ratio and aCAR and iCAR level.

[0604] The sensitivity (E/T EC50) of target cancer cell lines to EGFR and HER2 aCAR killing varies > 5-fold and does not correlate with EGFR expression level.

Cell-surface expression

[0605] Absolute iCAR/aCAR level and stoichiometry – Effector cells. Absolute iCAR/aCAR antigen level and stoichiometry – Target cells. *See*, for example, Figure 14.

[0606] A highly reproducible FACS based method has been implemented to quantify absolute CAR and target antigen levels)

[0607] The level of aCAR and iCAR expression obtained with mRNA co-electroporation are linearly dependent on mRNA amount.

[0608] Stoichiometric expression by co-electroporation is heavily iCAR biased (*e.g.*, iCAR/aCAR slope = 6.0 on the Jurkat experiment (*See*, for example, Figures 12-13).

An EGFR x HLA-A2 Dual CAR

[0609] Validation with mRNA co-electroporation studies.

[0610] Pairing of Cetuximab aCAR with a BB7.2 PD-1 iCAR was assessed by mRNA co-electroporation in HLA-A2 NEG and HLA-A2 POS adherent cancer cell-lines.

[0611] Killing of FaDu A2 NEG cells by dual CAR T-cells was obtained at low E/T ratios without apparent loss of aCAR activity, U87 A2 POS (EGFR aCAR sensitive) cancer cells were fully protected.

[0612] All HLA-A2 POS cancer cell lines tested inhibited T-cell activation (CD107a, IFNg) at low E/T regardless of HLA-A2 level (~10^5 to ~10^6 per cell) and target cell killing efficiency.

[0613] CAR quantification has not yet been performed, however HLA-A2 dependent protection is associated with excess iCAR exposure (>10-fold Cmax). *See*, for example, Figure 12A.

[0614] Pairing of Trastuzumab scFv aCAR with a BB7.2 scFv PD-1 iCAR was assessed by mRNA co-electroporation in HLA-A2 NEG and HLA-A2 POS adherent cancer cell-lines.

[0615] Killing of FaDu A2 NEG cells by dual CAR T-cells was obtained at E/T =10 without apparent loss of aCAR activity.

[0616] Protection of MDA-MB-231 A2 POS cancer cells appeared to depend on a 300-fold excess of iCAR over aCAR expression (Cmax).

[0617] In contrast, lower iCAR levels were sufficient to inhibit T-cell activation (CD107a, IFNg, TNFa) regardless of target cell killing efficiency.

Dual CAR lentiviral transduction

[0618] Absolute and stoichiometric expression in PBMCs.

[0619] iCAR constructs are identical, except for variations in the inhibitory domain.

[0620] aCAR constructs are also identical, except for variations in the scFv: Cetuximab or Panitumumab for EGFR and Trastuzumab or Pertuzumab for Her2.

[0621] All constructs are in iCAR/aCAR configuration with T2A cleavable linker.

[0622] The PBMC transduction efficiency (% gated double positive) of lentiviral bicistronic CARs was variable and most often too low (< 20%) for IncuCyte co-culture assays.

[0623] iCAR expression (proximal gene) could exceed aCAR expression (distal gene) by 5-10 fold but exceptions and failures were not uncommon.

Identification of HUMAN alternatives to BB7.2 HLA-A2 scFv

[0624] Mono-cistronic expression in PBMCs and HLA-A tetramer binding.

[0625] Binding to HLA-A2 tetramers was observed for BB7.2 (++), 3PF12 (+++), SN66E3 (+++), MBW1. Sequence Modifies (++). Binding to HLA-A2 tetramers was no observed for Ha5C2.A2 and murine BBM.1.

[0626] cMYC tag reports surface expression of iCARs.

[0627] HLA-A2 tetramer reports on HLA-A2 scFv binding.

[0628] Two fully human HLA-A2 scFv were identified as potential alternatives to BB7.2 (murine) that appear to bind HLA-A2 tetramer with higher avidity: 3PF12 and SN66E3.

FaDu/U87-Luc immune killing assay

[0629] Identification of novel iCAR using a Luciferase viability endpoint.

[0630] FaDu/U87-Luc Assay was developed and internal controls were validated. EGFR aCARs show robust specific killing of FaDu and U87 cells. HLA-A2 aCAR shows specific killing in U87 HLA-A2 POS cells.

[0631] Achieves high E/T ratios without assay interference (E/T = 64).

[0632] HLA-A2 dependent protection observed KIR2DL1 is consistent with T-REP (KIR2DL2) and Jurkat NFAT-Luc FA experiments (KIR2DL1 + KIR2DL2).

FaDu/MCF7-Luc immune killing assay

[0633] Identification of novel iCAR using a Luciferase viability endpoint.

[0634] FaDu/MCF7-Luc Assay was developed and internal controls were validated. HER2 aCARs show robust specific killing of FaDu and MCF7 cells. Achieves high E/T ratios without assay interference (E/T = 20).

[0635] HLA-A2 dependent protection observed with KIR2DL1 is consistent with T-REP (KIR2DL2) and Jurkat NFAT-Luc FA experiments (KIR2DL1 + KIR2DL2).

[0636] HLA-A2 dependent protection observed with LIR1 is consistent with Jurkat NFAT-Luc FA experiments.

Summary

[0637] The data provide herein supports *in vitro* validation of a humanizied BB7.2 iCAR scFv (*see*, for example, Fig. 59). This data confirmed that efficacy was observed for all constructs with a Hz BB7.2 version. This data also demonstrated that protection was observed for all constructs with a Hz BB7.2 version. VR428 and VR421 were identified as exemplary constructs.

[0638] Also provided by the data was *in vivo* validation of HzBB7.2 iCAR scFv (*see*, for example, Fig. 54 and Fig. 55). Both efficacy and protection were demonstrated in an *in vivo* study for low and high dose with VR428 administration. VR428 was identified as an exemplary construct.

[0639] Also provided by the data was *in vitro* validation of a fully human SN66E3.3 iCAR scFv (*see*, for example, Fig. 49). This data confirmed that efficacy was observed for all constructs with a fully human SN66E3 version. This data also demonstrated that protection was observed for all constructs with a fully human SN66E3 versions. VR447 and VR449 were identified as exemplary constructs.

EXAMPLE 2. GENERATION AND USE OF ANTI-IDIOTYPE BB7.2 ANTIBODIES

[0640] Background:

[0641] Enrichment of T cells expressing the bi cistronic iCAR/aCAR chimeric antigen receptors (CARs) described herein is based on the selection of cells expressing the iCAR inhibitory receptor comprising an scFv against the HLA-A2 antigen.

[0642] The target HLA-A2 specific iCAR is a single chain fragment that contains antibody variable regions joined by a flexible (G4S)X3 linker.

[0643] The antibodies described below specifically bind to the single chain variable fragment (scFv) derived from antibody BB7.2 contained in the extracellular portion of iCARs described herein.

[0644] The anti-idiotype antibodies recognize an epitope within all or part of the complementarity determining region (CDR) of the BB7.2 based on their ability to recognize both murine BB7.2 and humanized version of the BB7.2 scFv that only differ in their framework sequence, while they fail to bind a control antibody of the same human framework. Some of the anti-idiotype antibody may bind to the antigen binding domain of the iCAR based on their ability to compete with ligand binding.

[0645] Hybridoma generation and antibody screening:

[0646] Anti-Idiotype monoclonal antibodies in the form of murine antibodies were produced in mouse host, by inoculation with recombinant humanized BB7.2.1 scFv-His in immunization campaigns. In this regard four Swiss Inbred Mice were immunized with the extracellular domain (ECD) portion of iCAR containing anti-HLA-A2 scFv derived from the variable region sequence of humanized BB7.2.1, (SEQ ID.359) to provide hybridomas secreting high affinity, murine monoclonal anti idiotype antibody antibodies.

[0647] The immunogen (ECD region of the HzBB7.2 iCAR) has the following sequence:

MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGSSVKVSCKASGYTFTS
YHIQWVRQAPGQGLEWMGWIYPGDGSTQYNEKFKGRTTITADKSTSTAYME
LSSLRSEDTAVYYCAREGTYYAMDYWGQGTLVTVSSGGGGSGGGGSGGGG
SDVVMTQTPLSLSVTPGQPASISCRSSQSIVHSNGNTYLEWYLQKPGQSPQLLI
YKVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVPRTFGGG
TKVEIKGSHHHHHHHH (SEQ ID NO: 359)

[0648] The cDNA encoding HzBB7 scFv was cloned into a transient expression vector as a c-terminal His tagged protein which also contains an N-terminal T cell epitope. Expression constructs were transfected into HEK293 cells, and 600ml conditioned media was generated for each protein. Conditioned media was purified by Ni-NTA chromatography (Fig. 13). Immunogen purity of 80% was used for immunizations.

[0649] The Hz.BB7.2 sCFv fusion construct was expressed and purified from the supernatant of HEK 293 transfected cells. 10 μg of Hz.Bb7.2-His immunogen was emulsified with an equal volume of TITERMAX® Gold (CytRx Corporation) or alum adjuvant and used for the immunization of each mouse. The resulting emulsions were then injected into four Swiss Inbred Mice via the footpad route.

[0650] Sera isolated from immunized mice was examined by ELISA for binding ability to the recombinant soluble ECD moiety by detection with a secondary antibody, and by flow cytometry for binding ability to the iCAR expressed on the surface of Jurkat cells.

[0651] Sera-positive immunized mice were sacrificed, and draining lymph nodes (popliteal and inguinal, and medial iliac if enlarged) were dissected out and used as a source for antibody producing cells. A single cell suspension of B cells was fused with non-secreting P3×63Ag8.653 myeloma cells (ATCC #CRL-1580) at a ratio of 1:1 by electrofusion. After the fusion procedure, the cells were resuspended in hybridoma selection medium.

[0652] Hybridoma fusion clones were generated and further characterized by ELISA for binding to scFv, and positive clones were selected for secondary Flow cytometry screen.

Antibodies were evaluated for their ability to specifically bind to engineered Jurkat cells transduced with murine BB7.2 CAR, (VR370) and two different Hz.BB7.2 derived iCAR (VR375, and VR379). VR33 transduced Jurkat cells were used as a negative control in this assay, (Trastuzumab derived aCAR transduced control Jurkat cells).

[0653] Fig. 14 shows the binding specificity of purified Anti-HzBB7 anti idiotype antibody to surface of Jurkat cells expressing murine and humanized BB7.2 CAR vs trastuzumab CAR (NC VR33)

[0654] Binding to BB7.2 derived iCAR expressed on primary T cells:

[0655] Peripheral blood mononuclear cells were isolated from human subjects, cells were activated and transduced with a viral vector encoding BB7.2 iCAR constructs.

[0656] As shown in Fig. 15, four anti BB7.2 anti-idiotype antibodies detected T cells transduced with anti-HLA-A2 iCAR scFv containing variable regions derived from murine BB7.2 (CT0051), Hz.BB7.2.1 (CT0428) and Hz.BB7.2.2 (CT0421) in a concentration-dependent manner.

[0657] Q3, Q7, Q11 and Q30 antibodies detected positive iCAR expressing cells and not T cells expressing control CAR (CT0449). None of the candidate anti-idiotype antibodies to the BB7.2-derived antibody showed specific binding for cells expressing different anti-HLA-A2 CAR containing scFv derived from the SN66E3 antibody sequence (CT0449). Anti-idiotype antibody clones Q3, Q7, Q11, Q14 and Q30 were selected for further characterization.

[0658] Sequence identification:

[0659] Five of the distinct monoclonal antibodies that bound immobilized BB7.2 scFv or iCAR transduced Jurkat cells with apparently high affinity were selected for sequencing and further analysis.

[0660] The sequences of anti-BB7.2 clones Q3, Q7, Q11, Q14 and Q30 antibodies were determined. Total RNA was extracted from hybridoma cells containing hybridoma clones expressing anti-ID Q3, Q7, Q11, Q14 and Q30 and cDNA was extracted and sequenced.

[0661] As shown in a tabular fashion in Tables 23 and 24 above, sequence analysis of the light chain variable regions and heavy chain variable regions from selected monoclonal antibodies generated confirmed that many had novel complementarity determining regions and often displayed novel VDJ arrangements. Note that the complementarity determining regions set forth in Table 23 are defined as per Kabat et al., supra.

EXAMPLE 3. GENERATION OF ANTI-IDIOTYPE ANTIBODY AGAINST SN66E3-DERIVED ANTIBODY

[0662] This example shows anti-HLA-A2 scFv (shown in SEQ ID NO: 360 having VH domain and VL domain derived from SN66E3.2 The production of an anti-idiotype antibody that recognizes the binding domain (scFv) portion.

[0663] The immunogen (ECD region of the SN66E3 iCAR) has the following sequence:

MALPVTALLLPLALLLHAARPDIVMTQSPDSLAVSLGERATISCKSSQSVLYSS
NNKNYLAWYQQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQA
EDVAVYYCQQYYGTPFTFGGGTKVEIKGGGGSGGGGSGGGGSQVQLVQSGA
EVKKPGASVKVSCKASGYTFTDYYLHWVRQAPGQGLEWMGWINPYTGGTN
YAQKFQGRVTMTRDTSISTAYMELSRLRSEDTAVYYCARAGASYYDFWSGW
VFDYWGQGTLVTVSSHHHHHHHH (SEQ ID NO: 360)

[0664] Hybridoma generation and antibody screening:

[0665] Mice were immunized with a soluble protein containing the scFv portion of this iCAR. The soluble protein reagent used for immunization is shown in SEQ ID NO: 360. Sera isolated from immunized mice were examined by ELISA for the ability to bind to the scFv by detection with a secondary anti mouse Fc antibody.

[0666] Hybridoma fusion clones were generated, and 5 candidate clones were further characterized by flow cytometry. Hybridoma clones were screened for binding specificity using two different CAR derived from the sequence of SN66E3 that differ in 3 framework residues and their ability to cross react with both scFV expressed by VR447 and VR449.

EXAMPLE 4. REWIRING CAR T-CELLS FOR ABSOLUTE SOLID TUMOR SPECIFICITY AND SAFETY

Background

[0667] Translation of the success of CAR-T therapy to the treatment of cancer patients with solid tumors would address a large unmet need. On-Target' 'off-tumor' toxicity is a fundamental barrier to the effective dosing of solid tumors since CAR-T targets are shared between cancer and normal tissues. The dual CAR-T system described herein was developed such that it can distinguished tumor and normal cells with absolute specificity based on chromosomal loss-of-heterozygosity (LOH).

The iCAR Platform Targets loss-of heterozygosity (LOH)

[0668] The dual CAR-T cells incorporate an inhibitory CAR (iCAR) receptor that recognizes antigen LOH in cell-surface proteins and a conventional CAR (aCAR) that programs T-cell activation and killing. The expression of the HLA-A*02 iCAR target located on chromosome 6 and the HER2 aCAR target located on chromosome 17 (not shown) overlap in normal tissues. Normal cells are protected by iCAR antigen engagement which inhibits aCAR killing, whereas cancer cells are not protected by the iCAR since the antigen target is lost.

Summary

[0669] HLA-A2 LOH differentiates solid tumor from normal tissue with absolute and irreversible specificity. A dual CAR system that pairs an HLA-A2 specific iCAR and a HER2 targeted aCAR can recognize HLA-A2 loss in a lung cancer model that mimics LOH. This preclinical proof-of-concept supports clinical development the iCAR LOH targeting concept.

[0670] Reference: Bray, F. et al Global 2018 estimates of cancer mortality. A Cancer Journal for Clinicians, Volume: 68, Issue: 6, 394-424, 2018.

EXAMPLE 5. INCORPORATION OF INHIBITORY SIGNALING DOMAINS INTO CHIMERIC ANTIGEN RECEPTORS (iCAR) DESIGNED FOR SELF-REGULATION OF CANONICAL CAR-T TO TREAT SOLID TUMORS

Background

[0671] The system described in the present example directly addresses the challenge of increasing antigenic selectivity1of the therapeutic CARs to avoid damage to non-tumor tissues.

[0672] The approach is based on the identification of new inhibitory targets that when engaged by an inhibitory CAR inhibit the activation of the CAR-T-cells.

[0673] These inhibitory targets may comprise allelic variants of polymorphic cell surface epitopes, which are lost from tumor cells due to loss of heterozygosity (LOH) of the chromosomal region they reside in, while remaining expressed on normal tissue. Because of LOH, it is possible to distinguish the two alleles and target only the allele missing in the tumor cells[2-4].

[0674] The Dual CAR system is composed of an activating CAR (aCAR) and an inhibitory CAR (iCAR), where the iCARand aCARsignaling domains are referred to as iDomainand aDomainrespectively.

[0675] This exemplary approach for limiting T-cell responses exclusively to tumor cells, that express only the aCARtarget while protecting cells which express the iCARtarget, potentially

broadens the range of tumor related antigens which can be safely targeted by CAR T-cells in solid tumors.

Conclusion

[0676] The screen for iDomain.results in several highly potential iCARsthat can be paired with various aCARs

[0677] The Dual CAR-T cells are validated for both efficacy and protection, in several isogenic tumor models, both in-vitroand in-vivo.

References for Example 5:

[0678] 1. Rosenberg S. A, Finding suitable targets is the major obstacle to cancer gene therapy. *Cancer Gene Ther.*21, 45–47 (2014).

[0679] 2. Fedorov et al, PD-1-and CTLA-4-Based Inhibitory Chimeric Antigen Receptors (iCARs) Divert Off-Target Immunotherapy Responses. *Sci. Transl. Med.*5, 215ra172-215ra172 (2013).

[0680] 3. Tokatilanet al, Mesothelin-specific CAR-T cell therapy that incorporates an HLA-gated safety mechanism selectively kills tumor cells, Jour of Immunotherapy of Cancer, 2022;10:e003826. doi:10.1136/jitc-2021-003826.

[0681] 4. Hwang et al, Targeting loss of heterozygosity for cancer-specific immunotherapy. PNAS, 118, 2021.

[0682] 5. Parham et al, Partial purification and some properties of BB7.2 a cytotoxic monoclonal antibody with specificity for HLA-A2 and a variant of HLA-A28, Human Immunology, 1981.

[0683] All headings and section designations are used for clarity and reference purposes only and are not to be considered limiting in any way. For example, those of skill in the art will appreciate the usefulness of combining various aspects from different headings and sections as appropriate according to the spirit and scope of the invention described herein.

[0684] All references cited herein are hereby incorporated by reference herein in their entireties and for all purposes to the same extent as if each individual publication or patent or patent application was specifically and individually indicated to be incorporated by reference in its entirety for all purposes.

[0685] Many modifications and variations of this application can be made without departing from its spirit and scope, as will be apparent to those skilled in the art. The specific embodiments and examples described herein are offered by way of example only, and the

application is to be limited only by the terms of the appended claims, along with the full scope of equivalents to which the claims are entitled.

WHAT IS CLAIMED IS

1. A bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction comprising:
    i. an iCAR portion, wherein the iCAR portion comprises:
        a. an iCAR single chain variable fragment (scFv) component optionally in the VH-VL or VL-VH orientation;
        b. an iCAR hinge domain component;
        c. an iCAR transmembrane (TM) domain component;
        d. an iCAR inhibitory domain component; and
    ii. an aCAR portion, wherein the iCAR portion comprises:
        a. an aCAR single chain variable fragment (scFv) component optionally in the VH-VL or VL-VH orientation;
        b. an aCAR hinge domain component;
        c. an aCAR co-stimulatory domain component
        d. an aCAR activation signaling domain; and
    iii. a linker that connects the iCAR portion in (i) and the aCAR portion in (ii).

2. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 1, wherein the linker connecting the VH-VL or VL-VH in either orientation comprises one or more linkers selected from the group consisting of (G4S)X3 linker (SEQ ID NO:81), G4S (SEQ ID NO:153), (G4S)X3 (SEQ ID NO:154), and Whitlow linker (SEQ ID NO:82).

3. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 2, wherein the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is selected from the group consisting of HLA-A2, HLA-A3, HLA-A, HLA-B, HLA-C, HLA-G, HLA-E, HLA-F, HLA-DPA1, HLA-DQA1, HLA-DQB1, HLA-DQB2, HLA-DRB1, and HLA-DRB5.

4. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 3, wherein the iCAR scFv component targets an HLA antigen, wherein said HLA antigen is HLA-A2.

5. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 4, wherein the iCAR scFv comprises Hz BB7.2.1 of SEQ ID NO:287.

6. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 4, wherein the iCAR scFv consists essentially of Hz BB7.2.1 of SEQ ID NO:287.

7. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 4, wherein the iCAR scFv is Hz BB7.2.1 of SEQ ID NO:287.

8. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 4, wherein the iCAR scFv comprises or consists essentially of SN66E3.2 of SEQ ID NO:285.

9. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 4, wherein the iCAR scFv is SN66E3.2 of SEQ ID NO:285.

10. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 4, wherein the iCAR scFv is SN66E3.3 of SEQ ID NO:286.

11. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 7, wherein the iCAR hinge domain component comprises a LIR1 52 aa hinge (SEQ ID NO: 89)

12. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 7, wherein the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89).

13. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 9, wherein the iCAR hinge domain component comprises a LIR1 52 aa hinge (SEQ ID NO: 89).

14. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 9, wherein the iCAR hinge domain component is a LIR1 52 aa hinge (SEQ ID NO: 89).

15. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 12, wherein the iCAR TM domain component is a LIR1 TM domain (SEQ ID NO:98).

16. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 14, wherein the iCAR TM domain component is a LIR1 TM domain (SEQ lD NO:98).

17. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 15, wherein the iCAR inhibitory domain component is a LIR1 inhibitory domain (SEQ ID NO:143).

18. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 17, wherein the iCAR inhibitory domain component is a LIR1 inhibitory domain (SEQ ID NO:143).

19. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 16, wherein the aCAR single chain variable fragment (scFv) component targets Her2.

20. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 18, wherein the aCAR single chain variable fragment (scFv) component targets Her2

21. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 19, wherein the aCAR scFv comprises the VH and VL from trastuzumab (SEQ ID NOs:170 and 171, respectively).

22. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 20, wherein the aCAR scFv comprises the VH and VL from trastuzumab (SEQ ID NOs:170 and 171, respectively).

23. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 19, wherein the aCAR scFv comprises SEQ ID NO: 451.

24. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 19, wherein the aCAR scFv comprises SEQ ID NO: 452.

25. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 19, wherein the aCAR scFv consists of SEQ ID NO: 451.

26. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 19, wherein the aCAR scFv consists of SEQ ID NO: 452.

27. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 20, wherein the aCAR scFv comprises SEQ ID NO: 451.

28. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 20, wherein the aCAR scFv comprises SEQ ID NO: 452.

29. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 20, wherein the aCAR scFv consists of SEQ ID NO: 451.

30. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 20, wherein the aCAR scFv consists of SEQ ID NO: 452.

31. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 19, wherein the aCAR scFv comprises or consists of SEQ ID NO:172.

32. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 26, wherein the hinge TM domain component comprises a CD8 alpha hinge domain (SEQ ID NO:84).

33. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 26, wherein the hinge TM domain component is a CD8 alpha hinge domain (SEQ ID NO:84).

34. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 30, wherein the hinge TM domain component comprises a CD8 alpha hinge domain (SEQ ID NO:84).

35. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 30, wherein the hinge TM domain component is a CD8 alpha hinge domain (SEQ ID NO:84).

36. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 33, wherein the co-stimulatory domain component is a CD137 (4-1BB) co-stimulatory domain (SEQ ID NO:233).

37. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 35, wherein the co-stimulatory domain component is a CD137 (4-1BB) co-stimulatory domain (SEQ ID NO:233).

38. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 36, wherein the ITAM is a CD3 zeta domain (SEQ ID NO:236).

39. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 37, wherein the ITAM is a CD3 zeta domain (SEQ ID NO:236).

40. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 38, wherein the bicistronic iCAR/aCAR construct comprises an amino acid sequence encoded by the nucleic acid sequence of SEQ ID NO:277.

41. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 38, wherein the nucleic acid sequence that encodes said bicistronic iCAR/aCAR has at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the nucleic acid sequence of SEQ ID NO:277.

42. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 38, wherein the nucleic acid sequence that encodes said bicistronic iCAR/aCAR has at least 98% identity to the nucleic acid sequence of SEQ ID NO:277.

43. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 38, wherein the nucleic acid sequence that encodes said bicistronic iCAR/aCAR has at least 99% identity to the nucleic acid sequence of SEQ ID NO:277.

44. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 39, wherein the bicistronic iCAR/aCAR construct comprises an amino acid sequence encoded by the nucleic acid sequence of SEQ ID NO:279.

45. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 39, wherein the nucleic acid sequence that encodes said bicistronic iCAR/aCAR has at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to the nucleic acid sequence of SEQ ID NO:279.

46. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 39, wherein the nucleic acid sequence that encodes said bicistronic iCAR/aCAR has at least 98% identity to the nucleic acid sequence of SEQ ID NO:279.

47. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 39, wherein the nucleic acid sequence that encodes said bicistronic iCAR/aCAR has at least 99% identity to the nucleic acid sequence of SEQ ID NO:279.

48. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 38, wherein said bicistronic iCAR/aCAR construct comprises or consists of a nucleic acid sequence that encodes SEQ ID NO:278.

49. The bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 39, wherein said bicistronic iCAR/aCAR construct comprises or consists of a nucleic acid sequence that encodes SEQ ID NO:280.

50. A bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR construct for co-transduction comprising:
    i. an iCAR portion, wherein the iCAR portion comprises:
        f. a CD8a Leader Sequence having the sequence of MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);
        g. an iCAR single chain variable fragment (scFv) component having the sequence of SN66E3.2 scFv: DIVMTQSPDSLAVSLGERATISCKSSQSVLYSSNNKNYLAWYQQKPGQPP KLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYGTP FTFGGGTKVEIKGGGGSGGGGSGGGGSQVQLVQSGAEVKKPGASVKVSC KASGYTFTDYYLHWVRQAPGQGLEWMGWINPYTGGTNYAQKFQGRVT MTRDTSISTAYMELSGLTSDDTAVYYCARAGASYYDFWSGWVFDYWGQ GTLVTVSS (SEQ ID NO: 285);
        h. an iCAR hinge domain component having the sequence of LIR1 Hinge (52): PSDPLELVVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGV (SEQ ID NO: 89);
        i. an iCAR transmembrane (TM) domain component having the sequence of LIR1 TM: VIGILVAVILLLLLLLLLFLI (SEQ ID NO: 98);
        j. an iCAR inhibitory domain component having the sequence of LIR1 Inhibitory domain: LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEE NLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPRREMASPPS

PLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYAQLHSLTLRREATEP PPSQEGPSPAVPSIYATLAIH (SEQ ID NO: 143); and

ii. an aCAR portion, wherein the aCAR portion comprises:
   g. a CD8a Leader Sequence: MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);
   h. an aCAR scFv component having the sequence of Trastuzumab scFv : VL_whitlow linker_VH: DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYS ASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGT KVEIKGSTSGSGKPGSGEGSTKGEVQLVESGGGLVQPGGSLRLSCAASGF NIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKN TAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSS (SEQ ID NO: 452);
   i. an aCAR hinge domain component having the sequence of CD8a: Hinge: TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO: 84);
   j. CD8a: TM: IYIWAPLAGTCGVLLLSLVITLYC (SEQ ID NO: 95);
   k. an aCAR co-stimulatory domain component having the sequence of 41BB costim: KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL (SEQ ID NO: 233);
   l. an aCAR activation signaling domain having the sequence of CD3 zeta: RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGK PRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTA TKDTYDALHMQALPPR (SEQ ID NO: 236); and

iii. an IRES long sequence that connects the iCAR portion in (i) and the aCAR portion in (ii), wherein the IRES has the sequence of SEQ ID NO: 159.

51. A bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR construct for co-transduction consisting of:

i. an iCAR portion, wherein the iCAR portion consists of:
   f. a CD8a Leader Sequence having the sequence of MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);
   g. an iCAR single chain variable fragment (scFv) component having the sequence of SN66E3.2 scFv: DIVMTQSPDSLAVSLGERATISCKSSQSVLYSSNNKNYLAWYQQKPGQPP

KLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYGTP
FTFGGGTKVEIKGGGGSGGGGSGGGGSQVQLVQSGAEVKKPGASVKVSC
KASGYTFTDYYLHWVRQAPGQGLEWMGWINPYTGGTNYAQKFQGRVT
MTRDTSISTAYMELSGLTSDDTAVYYCARAGASYYDFWSGWVFDYWGQ
GTLVTVSS (SEQ ID NO: 285);

h. an iCAR hinge domain component having the sequence of LIR1 Hinge (52): HPSDPLELVVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGV (SEQ ID NO: 89);

i. an iCAR transmembrane (TM) domain component having the sequence of LIR1 TM: VIGILVAVILLLLLLLLLFLI (SEQ ID NO: 98);

j. an iCAR inhibitory domain component having the sequence of LIR1 Inhibitory domain:
LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEE
NLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPRREMASPPS
PLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYAQLHSLTLRREATEP
PPSQEGPSPAVPSIYATLAIH (SEQ ID NO: 143); and

ii. an aCAR portion, wherein the aCAR portion consists of:

g. a CD8a Leader Sequence: MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);

h. an aCAR scFv component having the sequence of Trastuzumab scFv :
VL_whitlow linker_VH:
DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYS
ASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGT
KVEIKGSTSGSGKPGSGEGSTKGEVQLVESGGGLVQPGGSLRLSCAASGF
NIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKN
TAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSS (SEQ
ID NO: 452);

i. an aCAR hinge domain component having the sequence of CD8a: Hinge:
TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID
NO: 84);

j. CD8a: TM: IYIWAPLAGTCGVLLLSLVITLYC (SEQ ID NO: 95);

k. an aCAR co-stimulatory domain component having the sequence of 41BB costim:
KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL (SEQ ID NO:
233);

l. an aCAR activation signaling domain having the sequence of CD3 zeta: RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGK PRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTA TKDTYDALHMQALPPR (SEQ ID NO: 236); and

iii. an IRES long sequence that connects the iCAR portion in (i) and the aCAR portion in (ii), wherein the IRES has the sequence of SEQ ID NO: 159.

52. A bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR construct for co-transduction comprising:

i. an iCAR portion, wherein the iCAR portion comprises:

f. a CD8a Leader Sequence having the sequence of MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);

g. an iCAR single chain variable fragment (scFv) component having the sequence of Hz BB7.2.1 scFv: QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYHIQWVRQAPGQGLEWM GWIYPGDGSTQYNEKFKGRTTITADKSTSTAYMELSSLRSEDTAVYYCAR EGTYYAMDYWGQGTLVTVSSGGGGSGGGGSGGGGSDVVMTQTPLSLSV TPGQPASISCRSSQSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGVP DRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVPRTFGGGTKVEIK (SEQ ID NO: 287);

h. an iCAR hinge domain component having the sequence of LIR1 Hinge (52): HPSDPLELVVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGV (SEQ ID NO: 89);

i. an iCAR transmembrane (TM) domain component having the sequence of LIR1 TM: VIGILVAVILLLLLLLLLFLI (SEQ ID NO: 98);

j. an iCAR inhibitory domain component having the sequence of LIR1 Inhibitory domain: LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEE NLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPRREMASPPS PLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYAQLHSLTLRREATEP PPSQEGPSPAVPSIYATLAIH (SEQ ID NO: 143); and

ii. an aCAR portion, wherein the aCAR portion comprises:

g. a CD8a Leader Sequence: MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);

h. an aCAR scFv component having the sequence of Trastuzumab scFv : VL_whitlow linker_VH: DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYS ASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGT KVEIKGSTSGSGKPGSGEGSTKGEVQLVESGGGLVQPGGSLRLSCAASGF NIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKN TAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSS (SEQ ID NO: 452);

i. an aCAR hinge domain component having the sequence of CD8a: Hinge: TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO: 84);

j. CD8a: TM: IYIWAPLAGTCGVLLLSLVITLYC (SEQ ID NO: 95);

k. an aCAR co-stimulatory domain component having the sequence of 41BB costim: KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL (SEQ ID NO: 233);

l. an aCAR activation signaling domain having the sequence of CD3 zeta: RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGK PRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTA TKDTYDALHMQALPPR (SEQ ID NO: 236); and

iii. an IRES long sequence that connects the iCAR portion in (i) and the aCAR portion in (ii), wherein the IRES has the sequence of SEQ ID NO: 159.

53. A bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR construct for co-transduction, consisting of:

i. an iCAR portion, wherein the iCAR portion consists of:

f. a CD8a Leader Sequence having the sequence of MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);

g. an iCAR single chain variable fragment (scFv) component having the sequence of Hz BB7.2.1 scFv: QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYHIQWVRQAPGQGLEWM GWIYPGDGSTQYNEKFKGRTTITADKSTSTAYMELSSLRSEDTAVYYCAR EGTYYAMDYWGQGTLVTVSSGGGGSGGGGSGGGGSDVVMTQTPLSLSV TPGQPASISCRSSQSIVHSNGNTYLEWYLQKPGQSPQLLIYKVSNRFSGVP

DRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVPRTFGGGTKVEIK (SEQ ID NO: 287);

h. an iCAR hinge domain component having the sequence of LIR1 Hinge (52): HPSDPLELVVSGPSGGPSSPTTGPTSTSGPEDQPLTPTGSDPQSGLGRHLGV (SEQ ID NO: 89);

i. an iCAR transmembrane (TM) domain component having the sequence of LIR1 TM: VIGILVAVILLLLLLLLLFLI (SEQ ID NO: 98);

j. an iCAR inhibitory domain component having the sequence of LIR1 Inhibitory domain: LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEE NLYAAVKHTQPEDGVEMDTRSPHDEDPQAVTYAEVKHSRPRREMASPPS PLSGEFLDTKDRQAEEDRQMDTEAAASEAPQDVTYAQLHSLTLRREATEP PPSQEGPSPAVPSIYATLAIH (SEQ ID NO: 143); and

ii. an aCAR portion, wherein the aCAR portion consists of:

g. a CD8a Leader Sequence: MALPVTALLLPLALLLHAARP (SEQ ID NO: 161);

h. an aCAR scFv component having the sequence of Trastuzumab scFv : VL_whitlow linker_VH: DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYS ASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGT KVEIKGSTSGSGKPGSGEGSTKGEVQLVESGGGLVQPGGSLRLSCAASGF NIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKN TAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSS (SEQ ID NO: 452);

i. an aCAR hinge domain component having the sequence of CD8a: Hinge: TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO: 84);

j. CD8a: TM: IYIWAPLAGTCGVLLLSLVITLYC (SEQ ID NO: 95);

k. an aCAR co-stimulatory domain component having the sequence of 41BB costim: KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL (SEQ ID NO: 233);

l. an aCAR activation signaling domain having the sequence of CD3 zeta: RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGK PRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTA TKDTYDALHMQALPPR (SEQ ID NO: 236); and

iii. an IRES long sequence that connects the iCAR portion in (i) and the aCAR portion in (ii), wherein the IRES has the sequence of SEQ ID NO: 159.

54. A nucleic acid composition comprising a nucleic acid that encodes a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 48.

55. A nucleic acid composition comprising a nucleic acid that encodes a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 49.

56. A nucleic acid composition comprising a nucleic acid that encodes a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 50.

57. A nucleic acid composition comprising a nucleic acid that encodes a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 51.

58. A nucleic acid composition comprising a nucleic acid that encodes a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 52.

59. A nucleic acid composition comprising a nucleic acid that encodes a bicistronic iCAR/aCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 53.

60. A vector comprising a nucleic acid sequence encoding for a bicistronic iCAR/iCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 56.

61. A vector comprising a nucleic acid sequence encoding for a bicistronic iCAR/iCAR construct or monocistronic aCAR and iCAR constructs for co-transduction according to claim 58.

62. A vector composition comprising the nucleic acid composition of claim 60.

63. A vector composition comprising the nucleic acid composition of claim 61.

64. A safe effector cell comprising a nucleic acid or nucleic acid composition according to claim 56.

65. A safe effector cell comprising a nucleic acid or nucleic acid composition according to claim 58.

66. A method for treating cancer in a patient having a tumor characterized by LOH, the method comprising administering to the patient a safe effector immune cell according to claim 64.

67. A method for treating cancer in a patient having a tumor characterized by LOH, the method comprising administering to the patient a safe effector immune cell according to claim 65.

68. A method for treating cancer in a patient having a tumor characterized by loss of heterozygosity (LOH), or other genetic loss or allelic imbalance phenotypes including, without limitation, loss of function or expression, resulting from mutations affecting one or more nucleotides, comprising administering to the patient a safe effector immune cell according to claim 66.

69. A method for treating cancer in a patient having a tumor characterized by loss of heterozygosity (LOH), or other genetic loss or allelic imbalance phenotypes including, without limitation, loss of function or expression, resulting from mutations affecting one or more nucleotides, comprising administering to the patient a safe effector immune cell according to claim 67.

70. The method of any one of claim 68 or claim 69, wherein the cancer is selected from the group consisting of Acute Myeloid Leukemia [LAML], Adrenocortical carcinoma [ACC], Bladder Urothelial Carcinoma [BLCA], Brain Lower Grade Glioma [LGG], Breast invasive carcinoma [BRCA], Cervical squamous cell carcinoma and endocervical DB2/ 42811099.1 Attorney Docket No.: 120575-5016-PR 291 adenocarcinoma [CESC], Cholangiocarcinoma [CHOL], Colon adenocarcinoma [COAD], Esophageal carcinoma [ESCA], Glioblastoma multiforme [GBM], Head and Neck squamous cell carcinoma [HNSC], Kidney Chromophobe [KICH], Kidney renal clear cell carcinoma [KIRC], Kidney renal papillary cell carcinoma [KIRP], Liver hepatocellular carcinoma [LIHC], Lung adenocarcinoma [LUAD], Lung squamous cell carcinoma [LUSC], Lymphoid Neoplasm Diffuse Large B-cell

Lymphoma [DLBC], Mesothelioma [MESO], Ovarian serous cystadenocarcinoma [OV], Pancreatic adenocarcinoma [PAAD], Pheochromocytoma and Paraganglioma [PCPG], Prostate adenocarcinoma [PRAD], Rectum adenocarcinoma [READ], Sarcoma [SARC], Skin Cutaneous Melanoma [SKCM], Stomach adenocarcinoma [STAD], Testicular Germ Cell Tumors [TGCT], Thymoma [THYM], Thyroid carcinoma [THCA], Uterine Carcinosarcoma [UCS], Uterine Corpus Endometrial Carcinoma [UCEC], Uveal Melanoma [UVM], Non-small cell lung carcinoma [NSCLC], and Small cell lung cancer [SCLC].

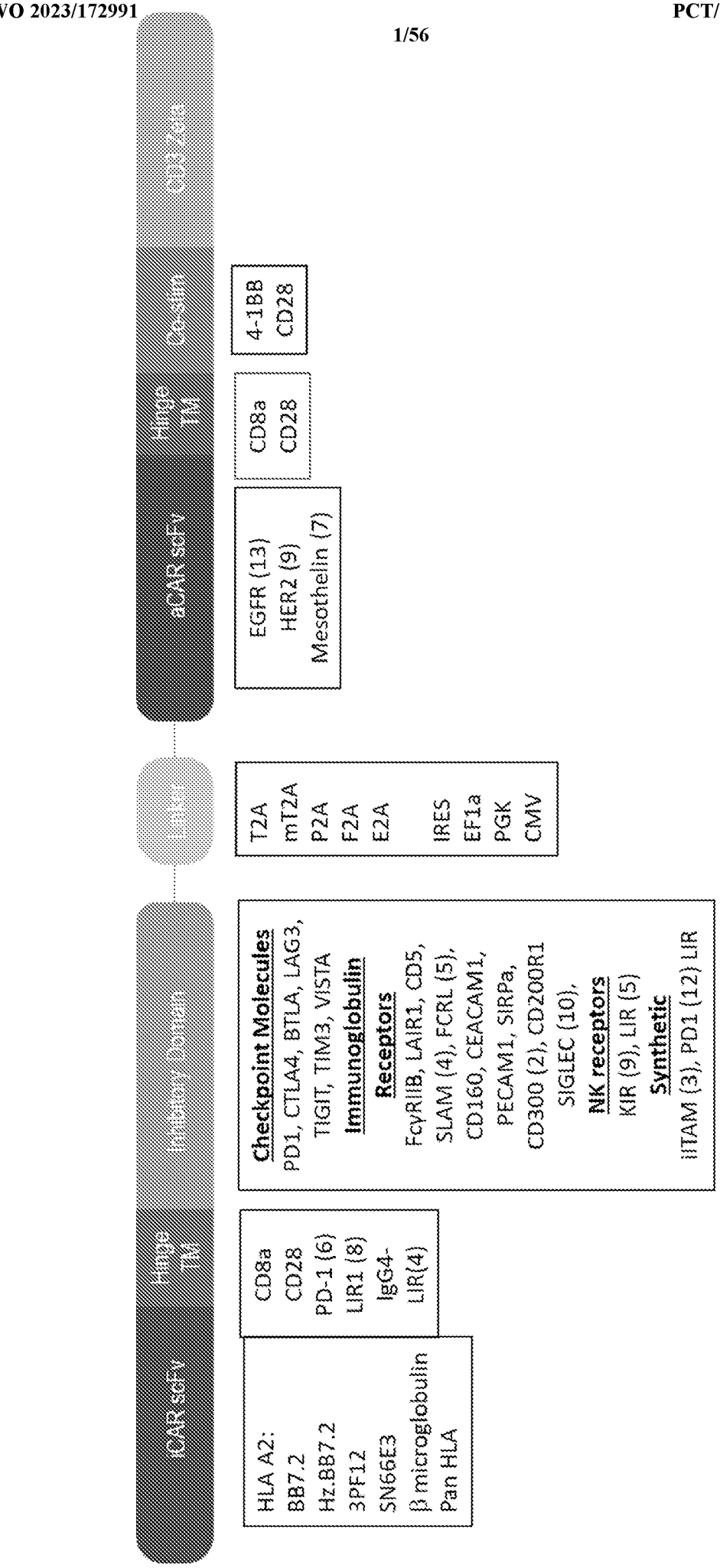

iCAR scFv
Hinge TM
Inhibitory Domain
HLA A2:
BB7.2
Hz.BB7.2
3PF12
SN66E3
β microglobulin
Pan HLA
CD8a
CD28
PD-1 (6)
LIR1 (8)
IgG4-
LIR(4)
Checkpoint Molecules
PD1, CTLA4, BTLA, LAG3,
TIGIT, TIM3, VISTA
Immunoglobulin
Receptors
FcγRIIB, LAIR1, CD5,
SLAM (4), FCRL (5),
CD160, CEACAM1,
PECAM1, SIRPa,
CD300 (2), CD200R1
SIGLEC (10),
NK receptors
KIR (9), LIR (5)
Synthetic
iITAM (3), PD1 (12) LIR
T2A
mT2A
P2A
F2A
E2A
IRES
EF1a
PGK
CMV
dCAR scFv
Hinge TM
Co-stim
CD3ζ/Fcεr
EGFR (13)
HER2 (9)
Mesothelin (7)
CD8a
CD28
4-1BB
CD28

FIG. 1

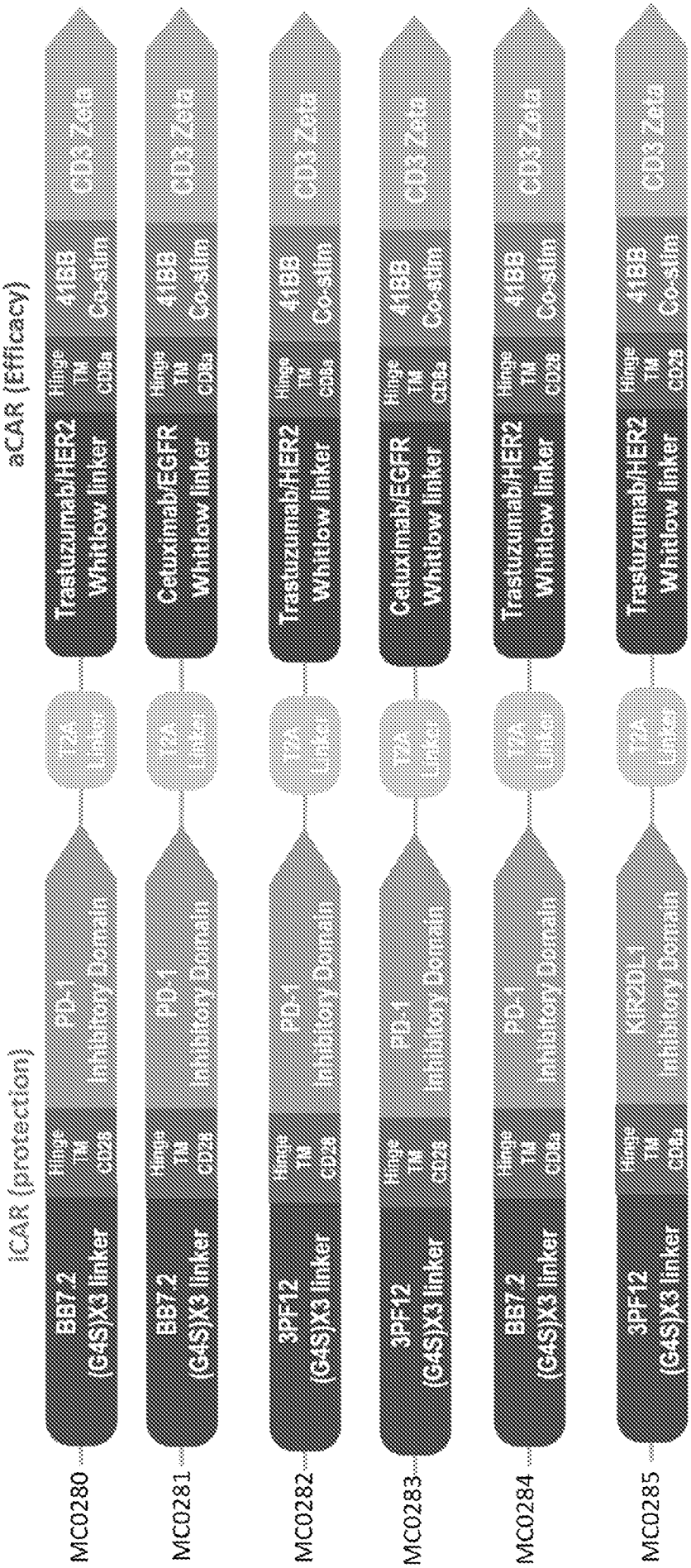

iCAR (protection)
aCAR (Efficacy)
MC0280
MC0281
MC0282
MC0283
MC0284
MC0285
BB7.2 (G4S)X3 linker
3PF12 (G4S)X3 linker
Hinge
TM
cd28
PD-1 Inhibitory Domain
KIR2DL1 Inhibitory Domain
T2A Linker
Trastuzumab/HER2 Whitlow linker
Cetuximab/EGFR Whitlow linker
4-1BB Co-Stim
CD3 Zeta

FIG. 2A

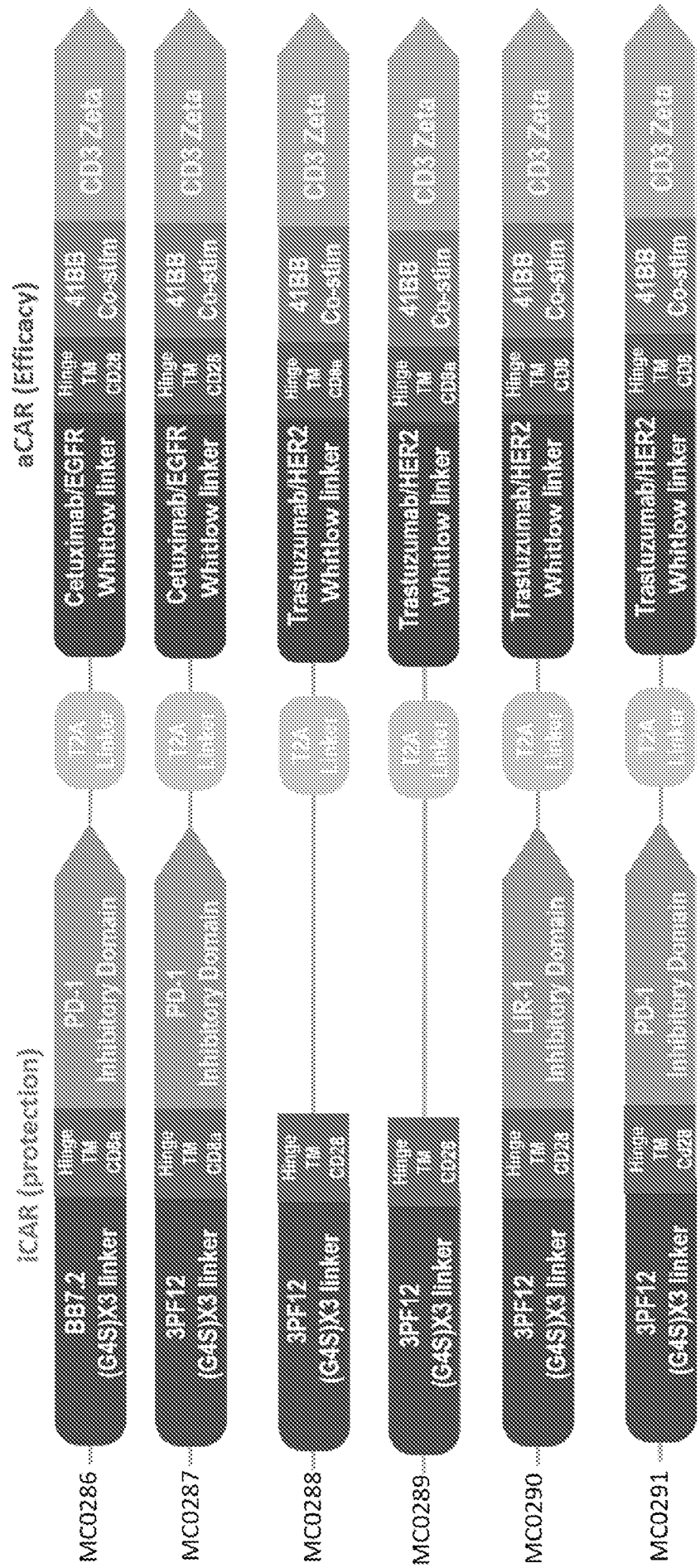

iCAR (protection)
aCAR (Efficacy)
MC0286
MC0287
MC0288
MC0289
MC0290
MC0291
BB7.2 (G4S)X3 linker
3PF12 (G4S)X3 linker
PD-1 Inhibitory Domain
LIR-1 Inhibitory Domain
Hinge TM cd28
Hinge TM cd8a
Cetuximab/EGFR Whitlow linker
Trastuzumab/HER2 Whitlow linker
41BB Co-stim
CD3 Zeta
T2A Linker

FIG. 2B

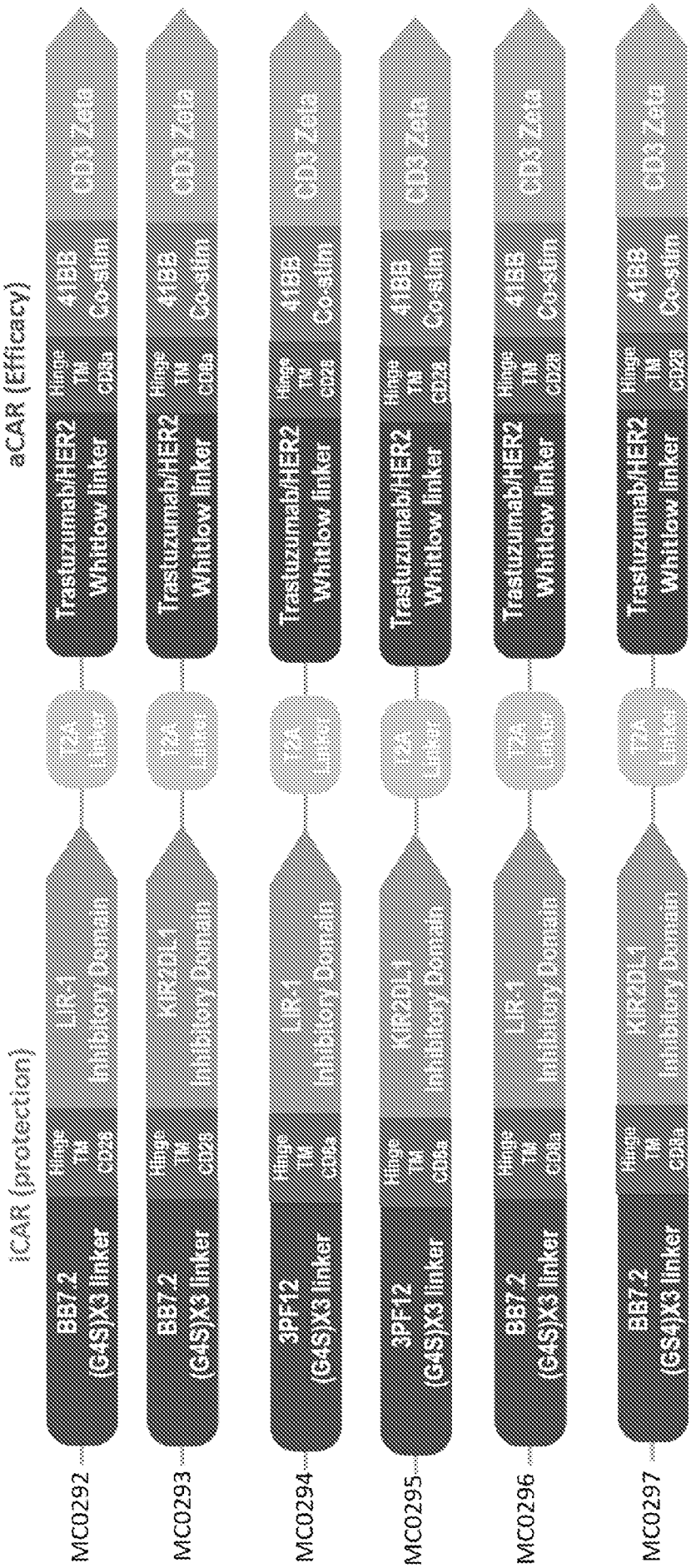

iCAR (protection)
aCAR (Efficacy)
MC0292
MC0293
MC0294
MC0295
MC0296
MC0297
BB7.2 (G4S)X3 linker
3PF12 (G4S)X3 linker
KIR2DL1 Inhibitory Domain
LIR1 Inhibitory Domain
Hinge TM cd28
Hinge TM cd8a
P2A Linker
Trastuzumab/HER2 Whitlow linker
Hinge TM cd28
Hinge TM cd8a
4-1BB Co-stim
CD3 Zeta

FIG. 2C

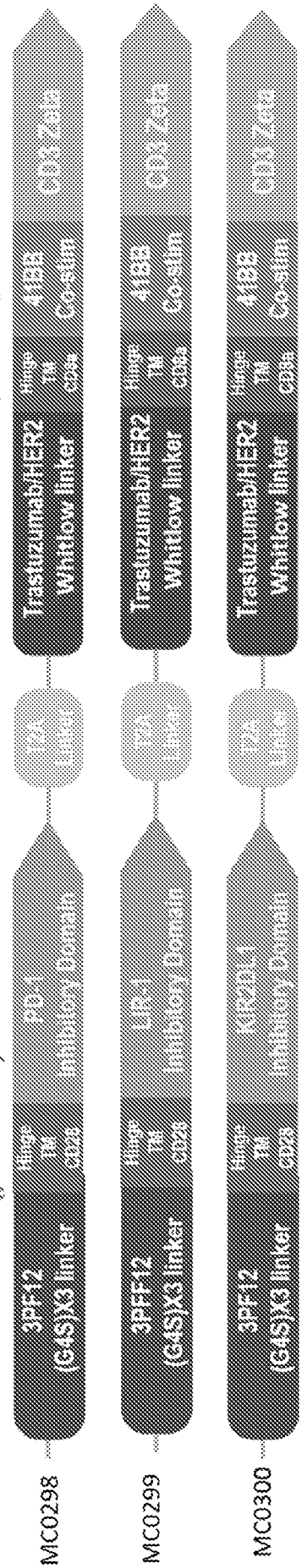

iCAR (protection)
aCAR (Efficacy)
MC0298
3PF12 (G4S)X3 linker
Hinge TM cos
PD-1 Inhibitory Domain
T2A Linker
Trastuzumab/HER2 Whitlow linker
Hinge TM cos
4-1BB Co-stim
CD3 Zeta
MC0299
3PFF12 (G4S)X3 linker
Hinge TM cos
LIR-1 Inhibitory Domain
T2A Linker
Trastuzumab/HER2 Whitlow linker
Hinge TM cos
4-1BB Co-stim
CD3 Zeta
MC0300
3PF12 (G4S)X3 linker
Hinge TM cos
KIR2DL1 Inhibitory Domain
T2A Linker
Trastuzumab/HER2 Whitlow linker
Hinge TM cos
4-1BB Co-stim
CD3 Zeta

FIG. 2D

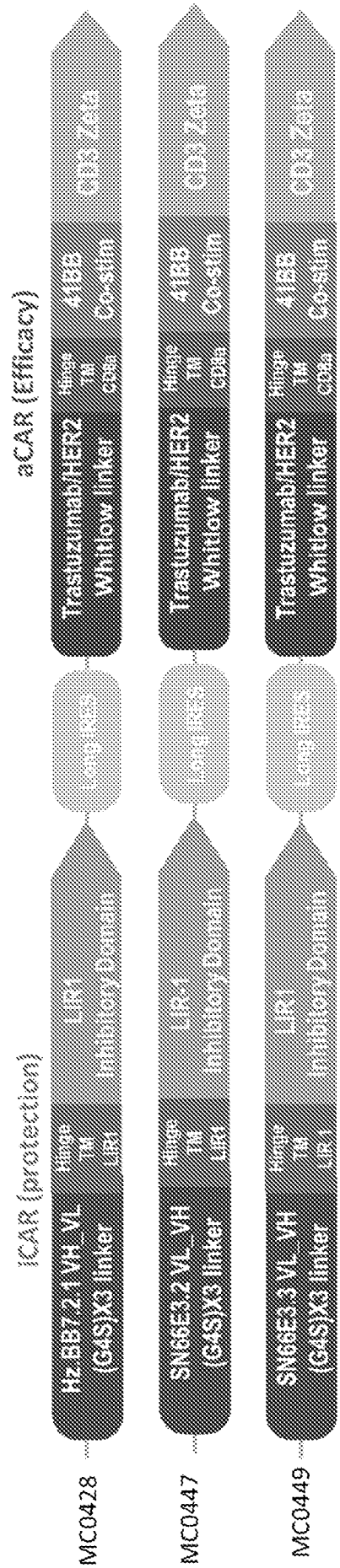

iCAR (protection)
aCAR (Efficacy)
MC0428
Hz BBT.2.1 VH_VL (G4S)X3 linker
Hinge TM cos
LIR1 Inhibitory Domain
T2A Linker
Trastuzumab/HER2 Whitlow linker
Hinge TM cos
4-1BB Co-stim
CD3 Zeta
MC0447
SN66E3.2 VL_VH (G4S)X3 linker
Hinge TM Lin1
LIR1 Inhibitory Domain
T2A Linker
Trastuzumab/HER2 Whitlow linker
Hinge TM cos
4-1BB Co-stim
CD3 Zeta
MC0449
SN66E3.3 VL_VH (G4S)X3 linker
Hinge TM LR1
LIR1 Inhibitory Domain
T2A Linker
Trastuzumab/HER2 Whitlow linker
Hinge TM cos
4-1BB Co-stim
CD3 Zeta

FIG. 2E

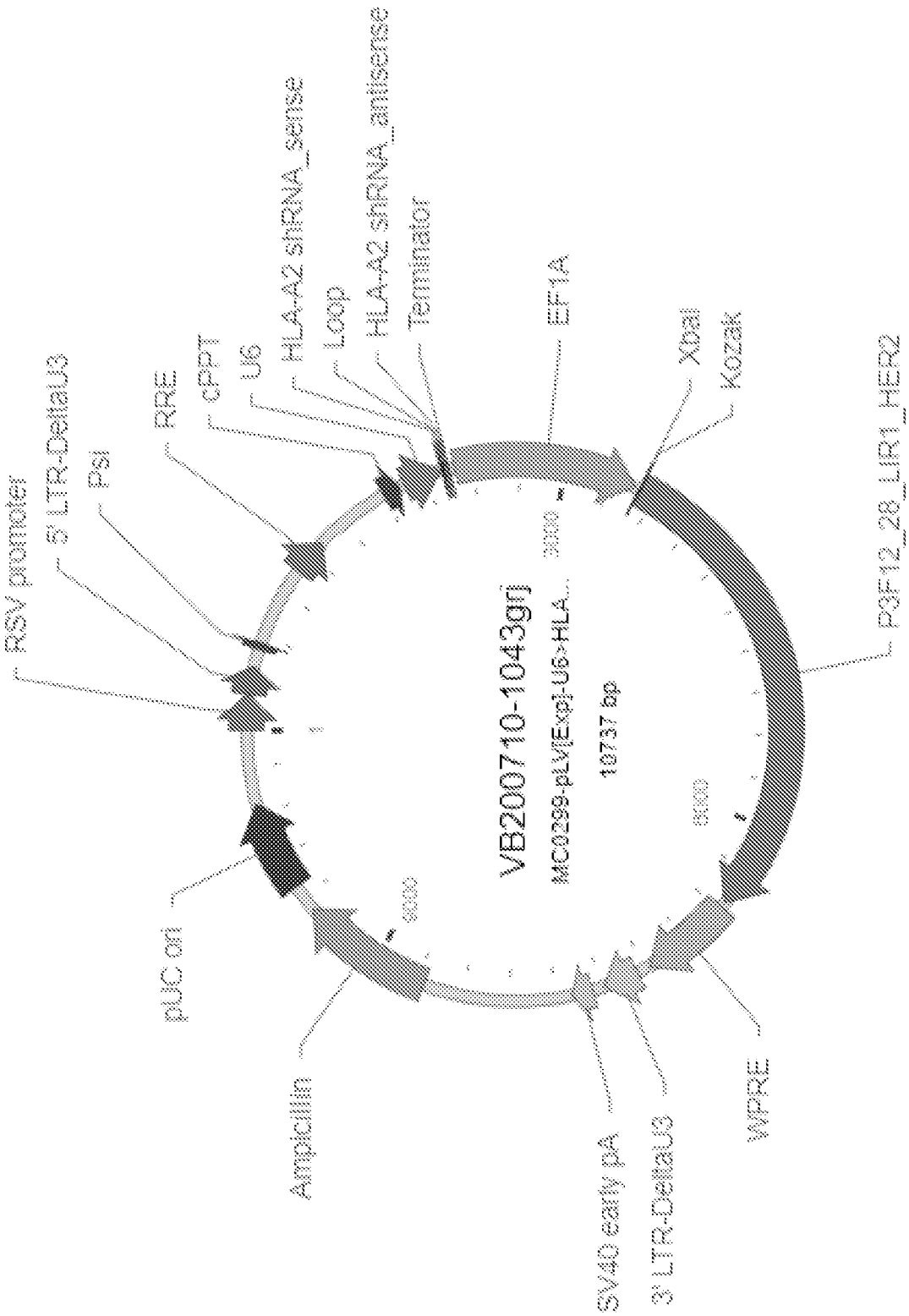

VB200710-1043gri
MC0299-pLV[Exp]-U6>HLA...
10737 bp
RSV promoter
5' LTR-DeltaU3
Psi
RRE
cPPT
U6
HLA-A2 shRNA_sense
Loop
HLA-A2 shRNA_antisense
Terminator
EF1A
XbaI
Kozak
P3F12_28_LIR1_HER2
WPRE
3' LTR-DeltaU3
SV40 early pA
Ampicillin
pUC ori
2000
4000
6000
8000

FIG. 2F

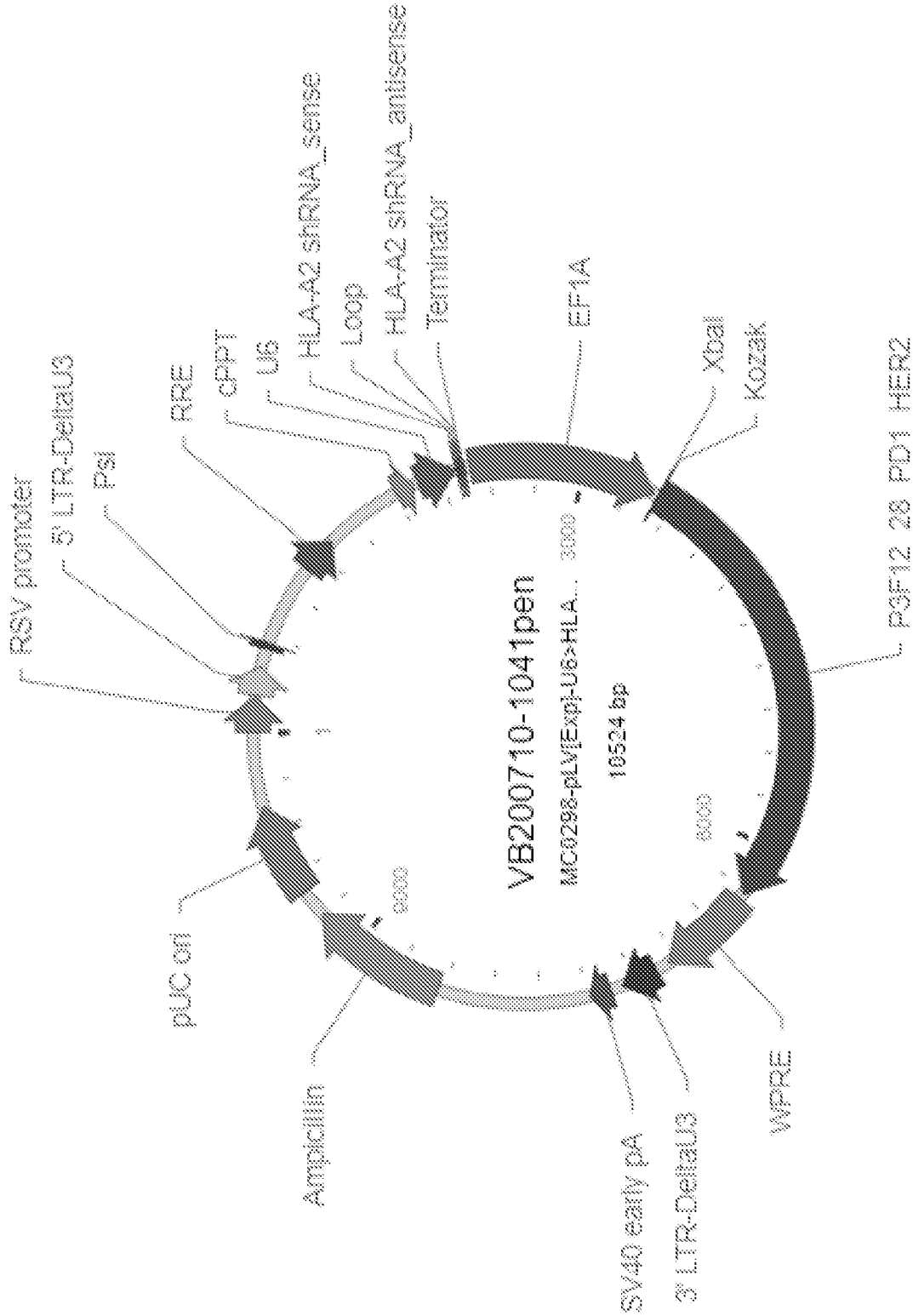

VB200710-1041pen
MC0298-pLV[Exp]-U6>HLA...
10524 bp
RSV promoter
5' LTR-DeltaU3
Psi
RRE
cPPT
U6
HLA-A2 shRNA_sense
Loop
HLA-A2 shRNA_antisense
Terminator
EF1A
XbaI
Kozak
P3F12_28_PD1_HER2
WPRE
3' LTR-DeltaU3
SV40 early pA
Ampicillin
pUC ori

FIG. 2G

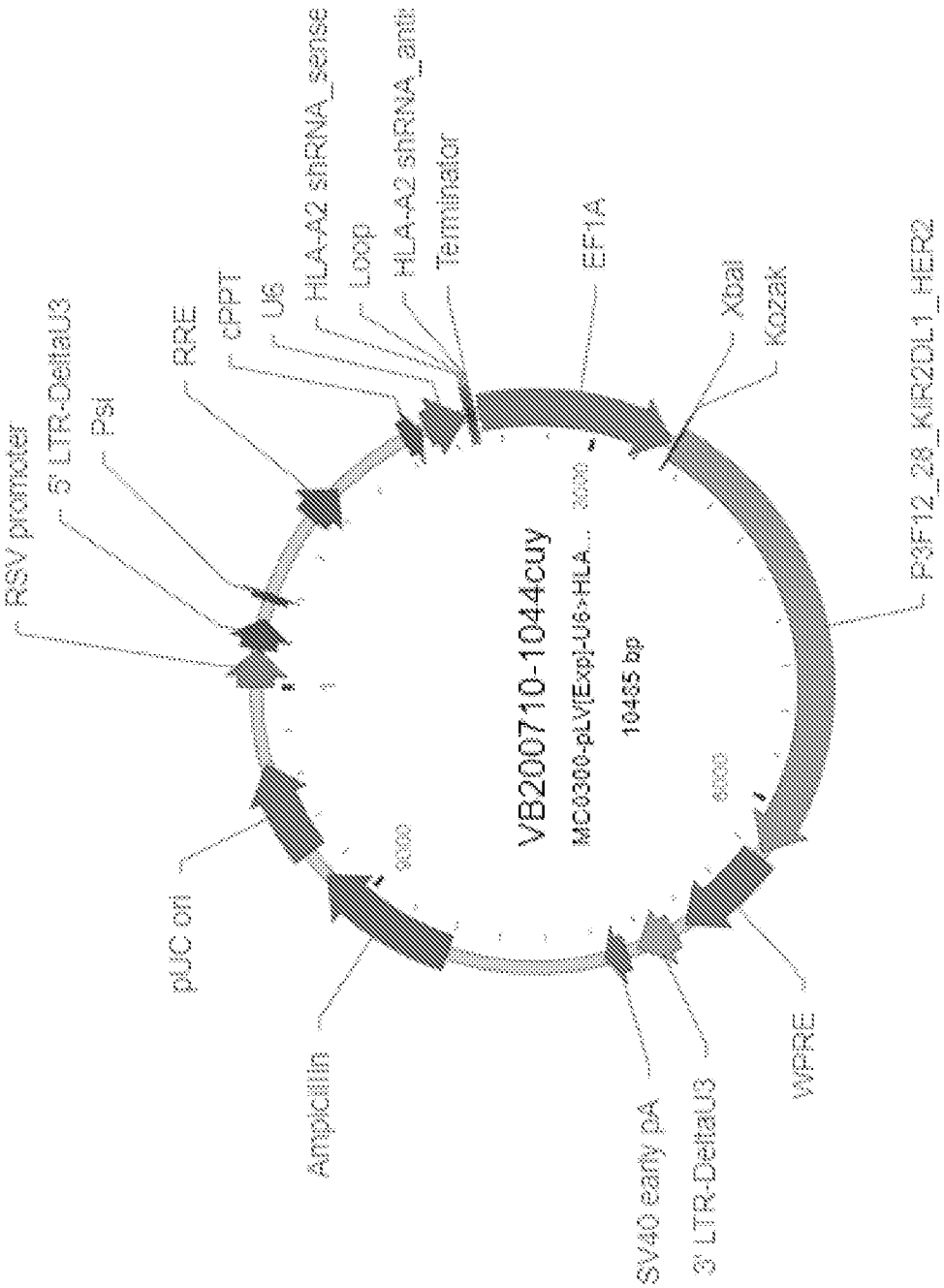

VB200710-1044cuy
MD0310-pLVIEXpl-U6>HLA...
10485 bp
RSV promoter
5' LTR-DeltaU3
Psi
RRE
cPPT
U6
HLA-A2 shRNA_sense
Loop
HLA-A2 shRNA_anti
Terminator
EF1A
XbaI
Kozak
P3F12_28_KIR2DL1_HER2
WPRE
3' LTR-DeltaU3
SV40 early pA
Ampicillin
pUC ori

FIG. 2H

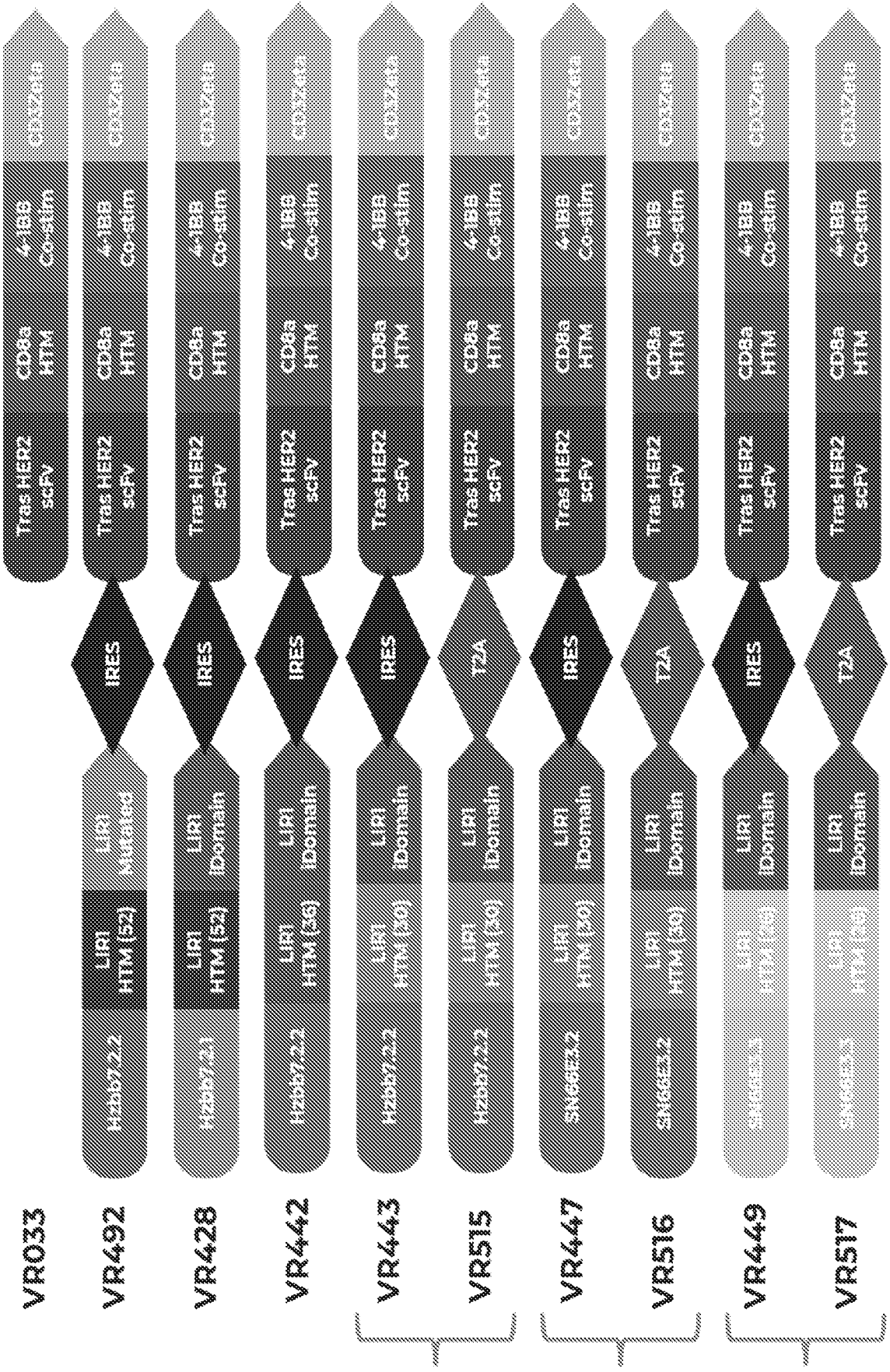

VR033
VR492
VR428
VR442
VR443
VR515
VR447
VR516
VR449
VR517
Tras HER2 scFv
CD8a HTM
4-1BB Co-stim
CD3ζ sig
IRES
T2A
LIR1 HTM (52)
LIR1 HTM (36)
LIR1 HTM (30)
LIR1 Mutated
LIR1 Domain
H2d17.2.2
H2d17.2.1
SNH82.2.2
SNH82.2.1

FIG. 3A

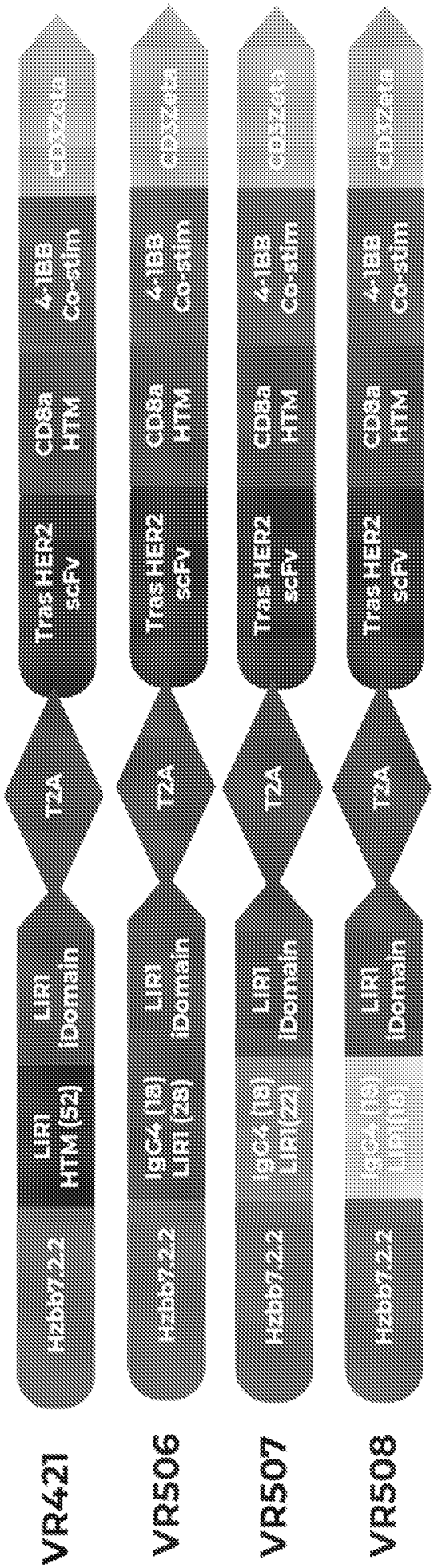

VR421
VR506
VR507
VR508
Hzaby7.2.2
LiR1 HTM (S2)
LiR1 iDomain
IgG4 (S)
LiR1 (S)
IgG4 (S)
LiR1(Z2)
IgG4 (S)
LiR1 (S)
T2A
Tras HER2 scFV
CD8a HTM
4-1BB Co-stim
CD3Zeta

FIG. 3B

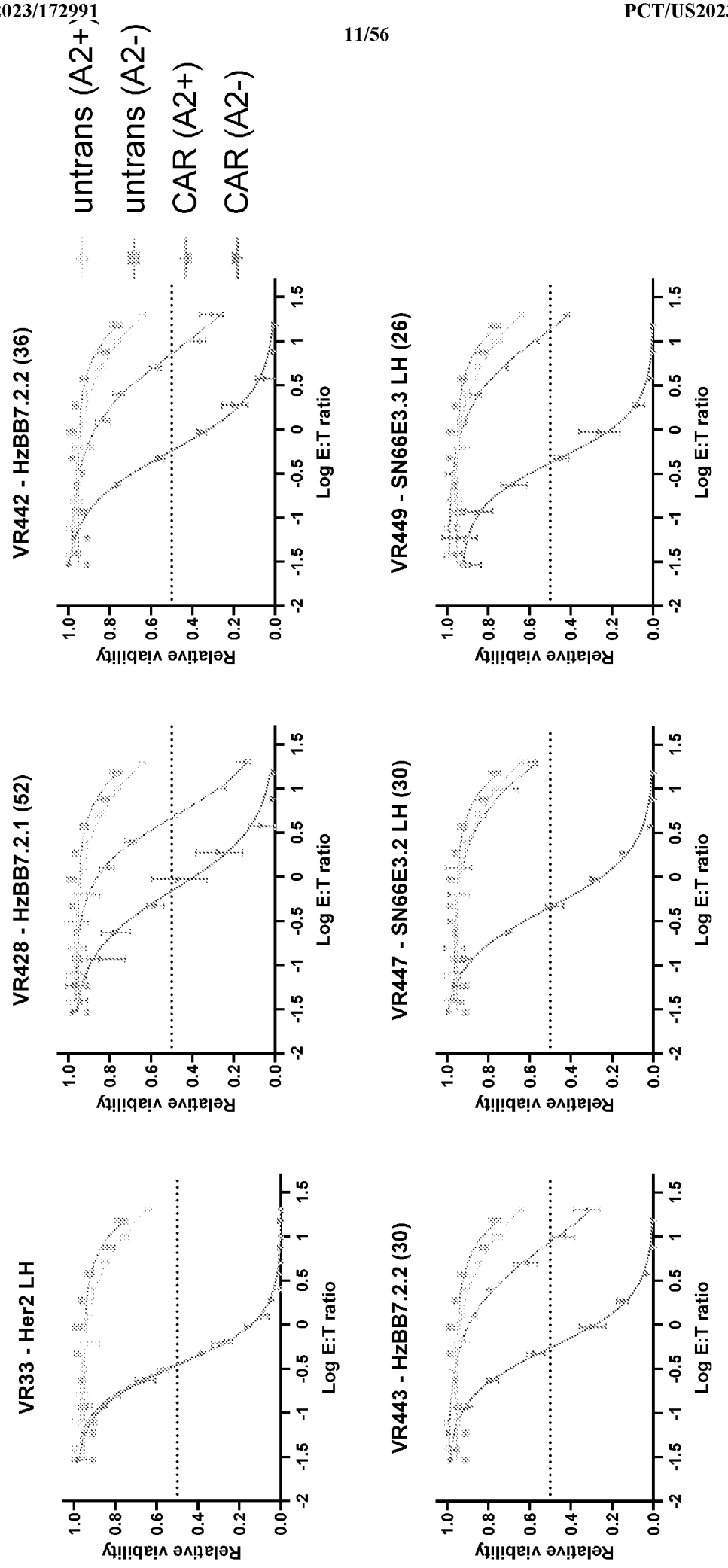

untrans (A2+)
untrans (A2-)
CAR (A2+)
CAR (A2-)
VR33 - Her2 LH
VR428 - HzBB7.2.1 (52)
VR442 - HzBB7.2.2 (36)
VR443 - HzBB7.2.2 (30)
VR447 - SN66E3.2 LH (30)
VR449 - SN66E3.3 LH (26)
Relative viability
Log E:T ratio
1.0
0.8
0.6
0.4
0.2
0.0
-2
-1.5
-1
-0.5
0
0.5
1
1.5

FIG. 4A

Const	Protection H1703 (A2+) EC50	Efficacy H1703(A2-) EC50	EC50 ratio
untrans	43.35	40.53	1.07
VR033	0.36	0.35	1.02
VR428	4.95	0.71	6.96
VR442	7.39	0.56	13.28
VR443	8.74	0.55	15.93
VR447	**27.34**	**0.44**	**61.76**
VR449	**13.90**	**0.46**	**30.51**

FIG. 4B

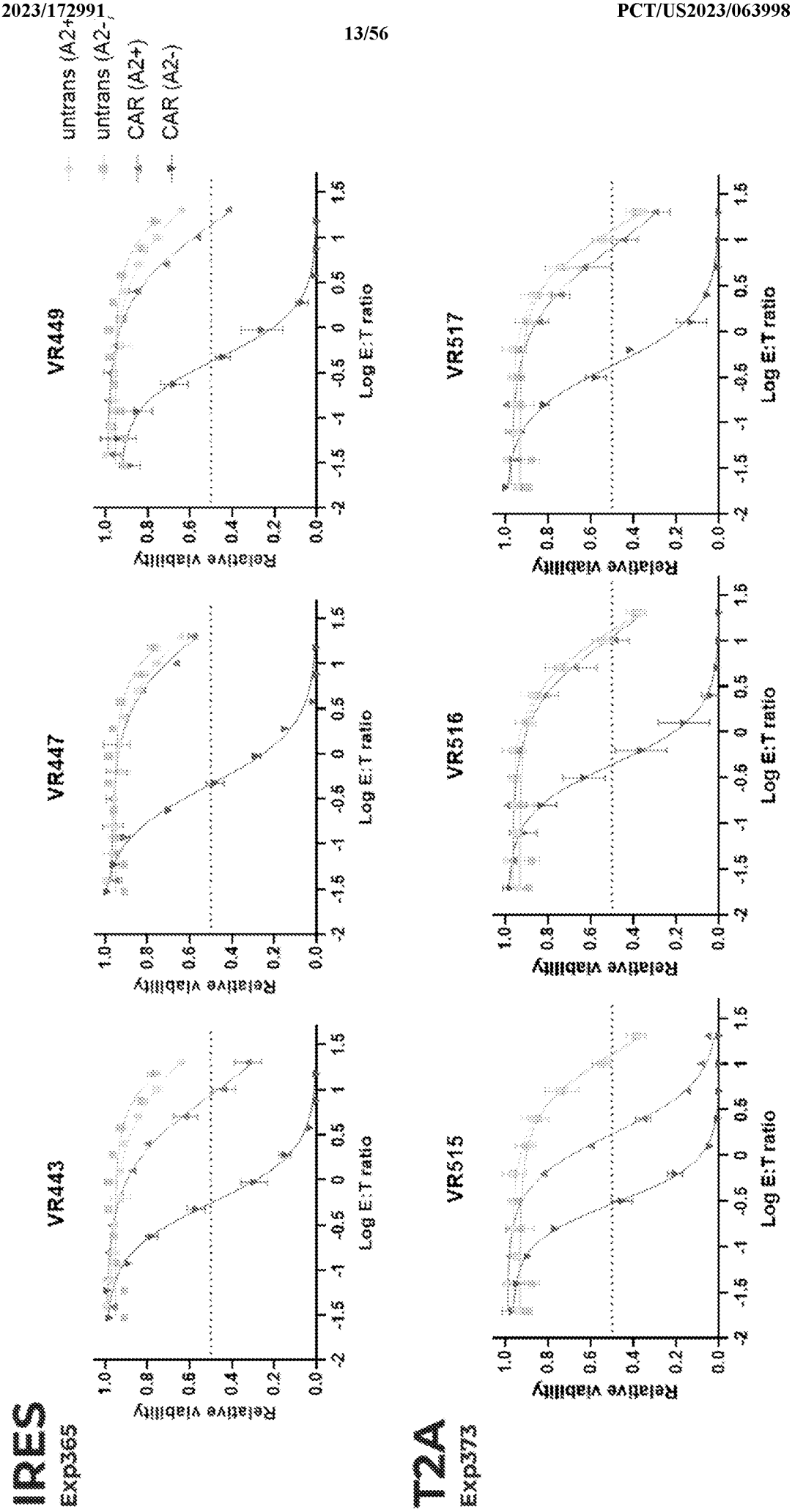

IRES
Exp365
T2A
Exp373
VR443
VR447
VR449
VR515
VR516
VR517
untrans (A2+)
untrans (A2-)
CAR (A2+)
CAR (A2-)
Relative viability
Log E:T ratio

FIG. 5A

Construct	Protection H1703 (A2+) EC50	Efficacy H1703(A2-) EC50	EC50 ratio
VR443 Hz2BB7.2-IRES	8.74	0.55	15.93
VR447 SN66E3.2-IRES	27.34	0.44	61.76
VR449 SN66E3.3-IRES	13.90	0.46	30.51
VR515 Hz2BB7.2-T2A	1.67	0.30	5.48
VR516 SN66E3.2-T2A	11.28	0.44	25.67
VR517 SN66E3.3-T2A	8.51	0.43	19.75

FIG. 5B

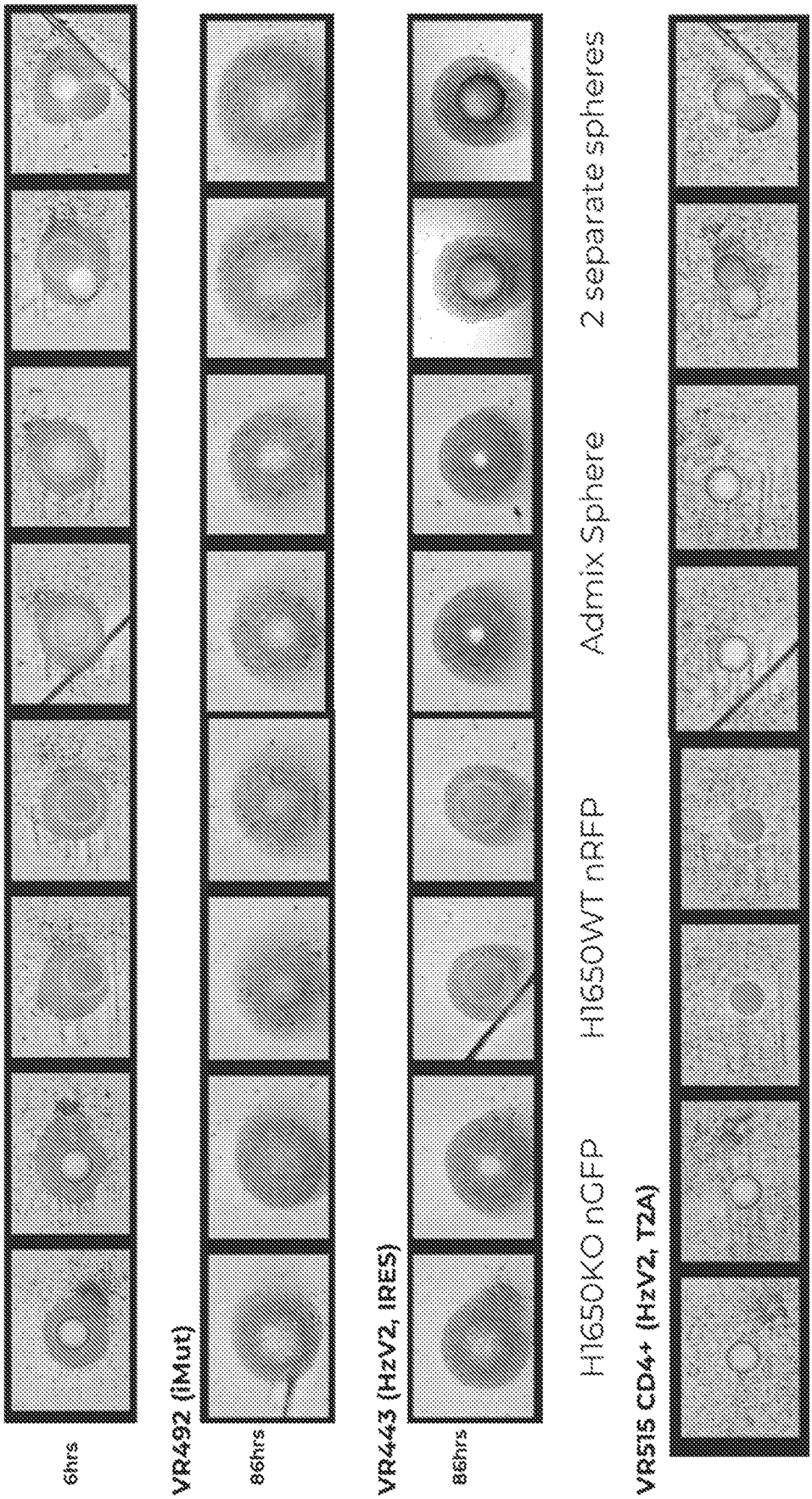

H1650KO nGFP
H1650WT nRFP
Admix Sphere
2 separate spheres
6hrs
VR492 (iMut)
86hrs
VR443 (HzV2, IRES)
86hrs
H1650KO nGFP
H1650WT nRFP
Admix Sphere
2 separate spheres
VR515 CD4+ (HzV2, T2A)

FIG. 6

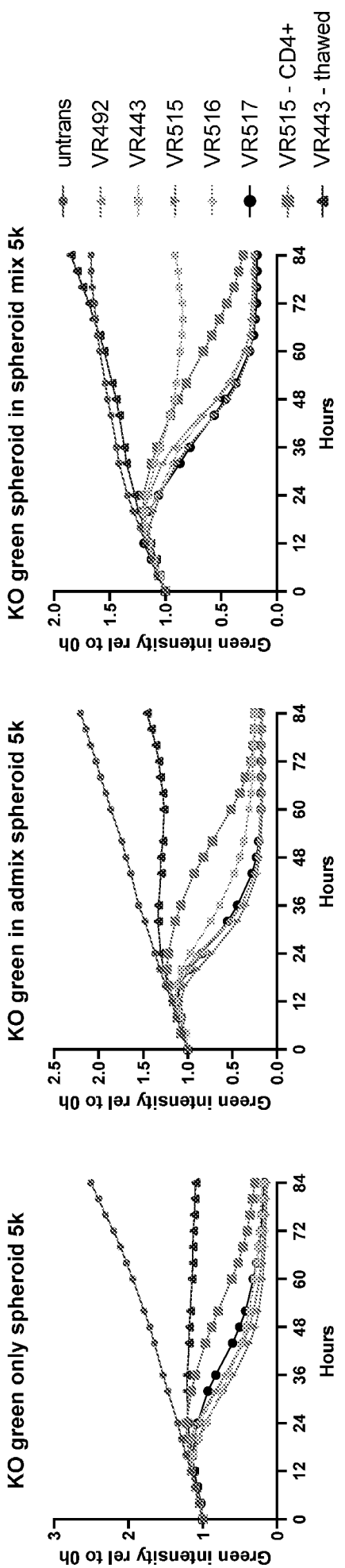

KO green only spheroid 5k
KO green in admix spheroid 5k
KO green spheroid in spheroid mix 5k
Green intensity rel to 0h
Hours
untrans
VR492
VR443
VR515
VR516
VR517
VR515 - CD4+
VR443 - thawed

FIG. 7

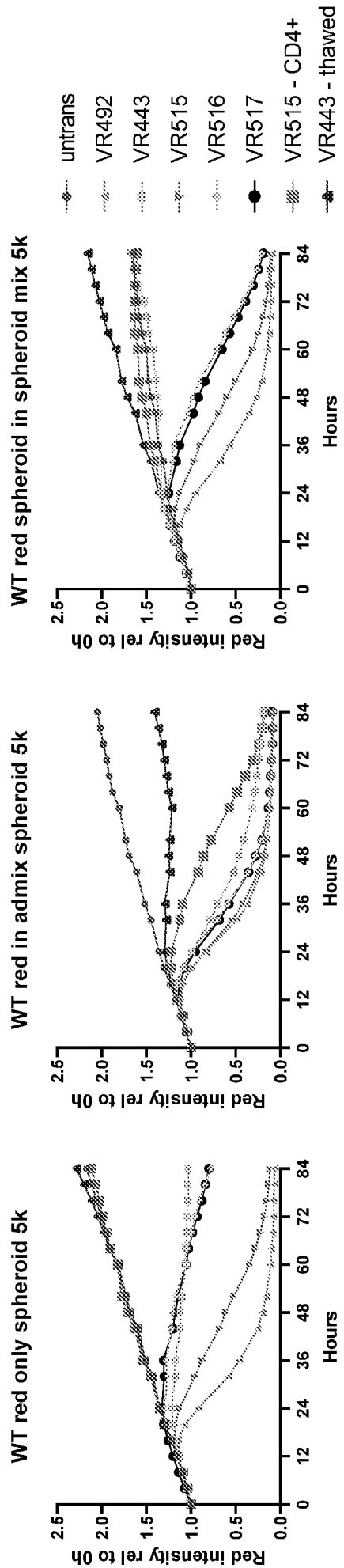

WT red only spheroid 5k
WT red in admix spheroid 5k
WT red spheroid in spheroid mix 5k
Red intensity rel to 0h
Hours
untrans
VR492
VR443
VR515
VR516
VR517
VR515 - CD4+
VR443 - thawed

FIG. 8

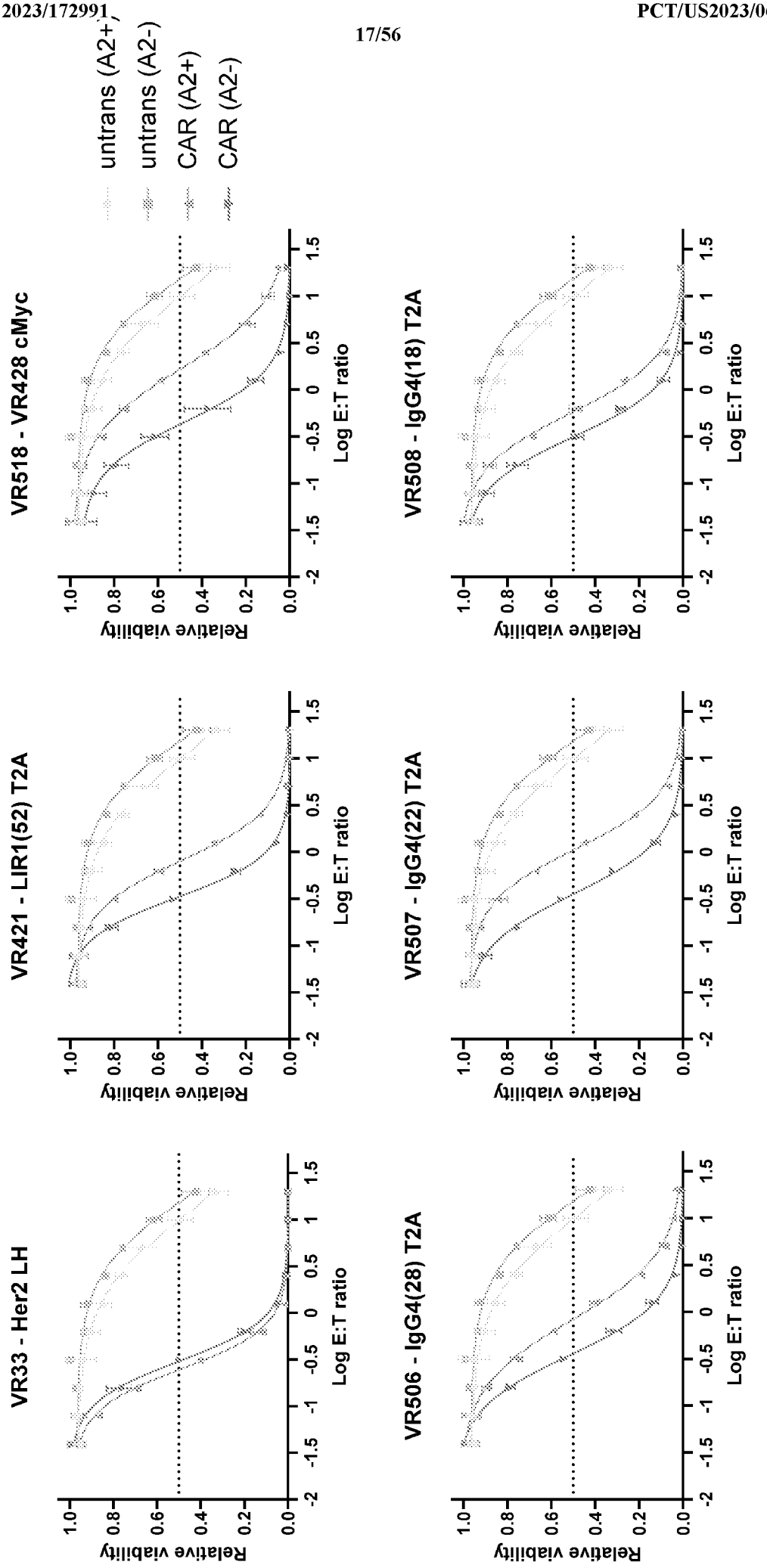

untrans (A2+)
untrans (A2-)
CAR (A2+)
CAR (A2-)
VR33 - Her2 LH
VR421 - LIR1(52) T2A
VR518 - VR428 cMyc
VR506 - IgG4(28) T2A
VR507 - IgG4(22) T2A
VR508 - IgG4(18) T2A
Relative viability
Log E:T ratio
1.0
0.8
0.6
0.4
0.2
0.0
-2
-1.5
-1
-0.5
0
0.5
1
1.5

FIG. 9A

Construct	Protection H1703 (A2+) EC50	Efficacy H1703(A2-) EC50	EC50 ratio
UTD	10.54	16.19	0.65
VR33	0.25	0.3	0.83
VR421	0.81	0.33	2.49
VR506	0.82	0.34	2.38
VR507	1.08	0.35	3.04
VR508	0.57	0.31	1.80
VR518	1.67	0.45	3.68

FIG. 9B

aCAR

	MFI			%from effector only	
	Effector only	1703-WT	1703-KO	1703-WT	1703-KO
VR0033	1966	3237	3526	165%	179%
VR0421	1424	869	5199	61%	365%
VR0506	2025	1495	8687	74%	429%
VR0507	1841	1671	9363	91%	509%
VR0508	1930	2219	9942	115%	515%
VR0518	1268	936	1775	74%	140%

iCAR

	MFI			%from effector only	
	Effector only	1703-WT	1703-KO	1703-WT	1703-KO
VR0421	7648	1130	18053	15%	236%
VR0506	5745	941	16195	16%	282%
VR0507	3149	772	11988	25%	381%
VR0508	2556	539	9822	21%	384%
VR0518	7799	1067	11107	14%	142%

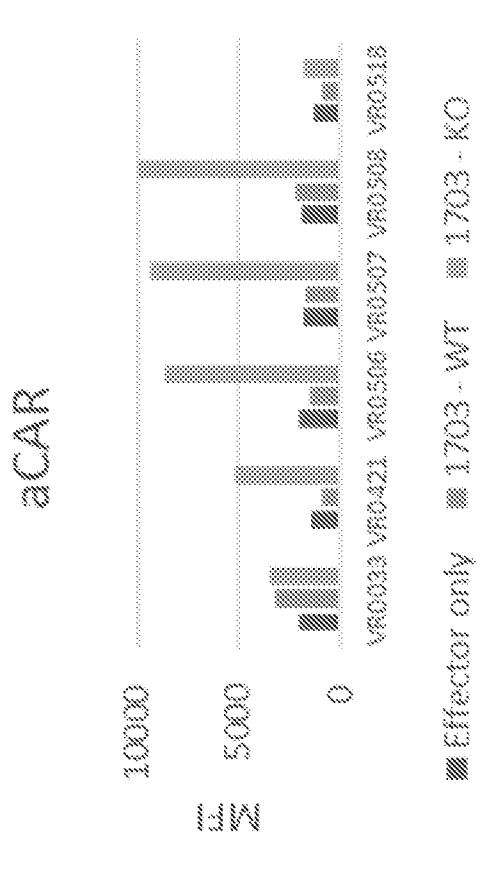


FIG. 10A

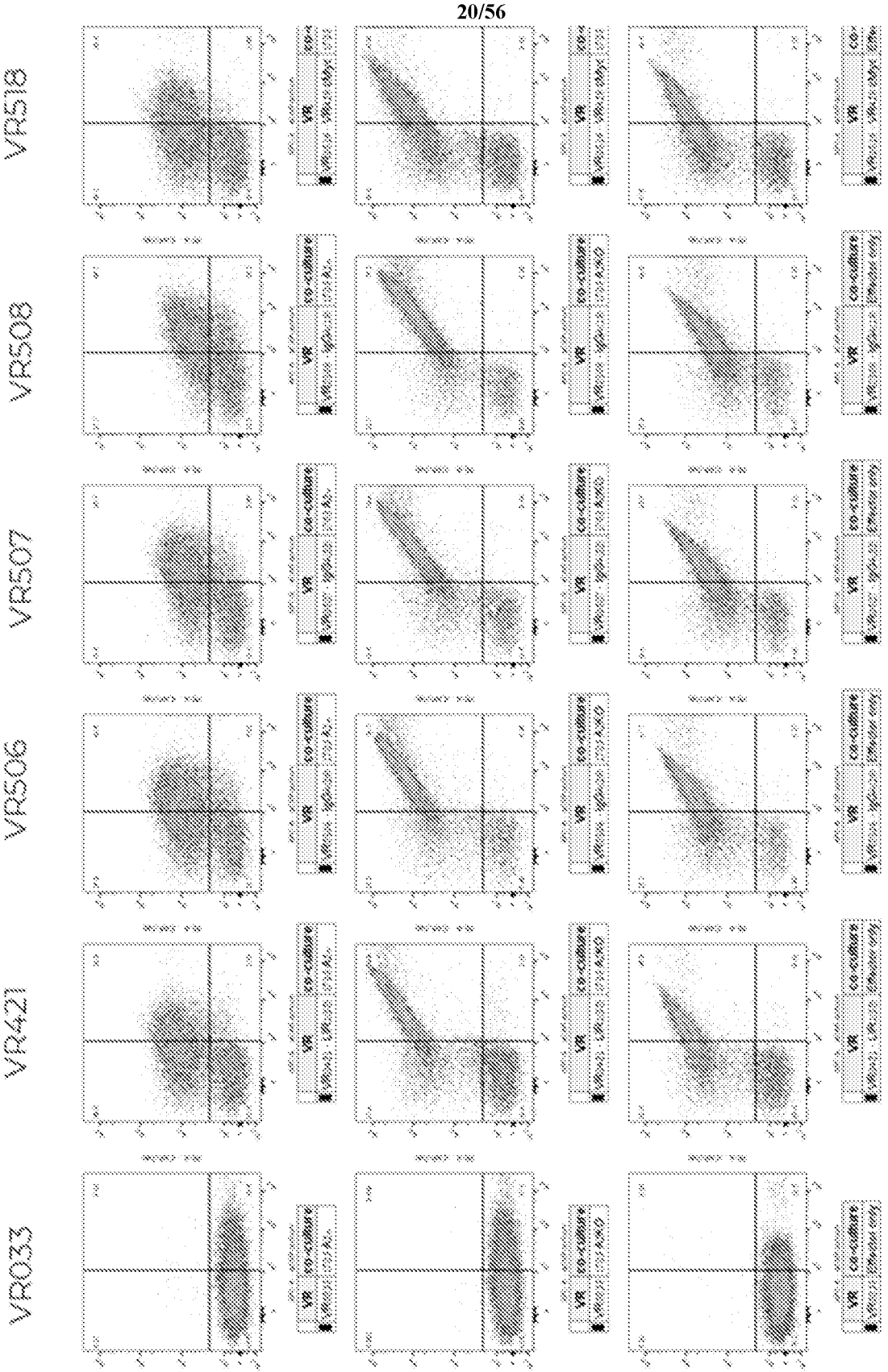

VR033
VR421
VR506
VR507
VR508
VR518
Co-culture 1703 A2+
Co-culture 1703 A2KO
Effector only

FIG. 10B

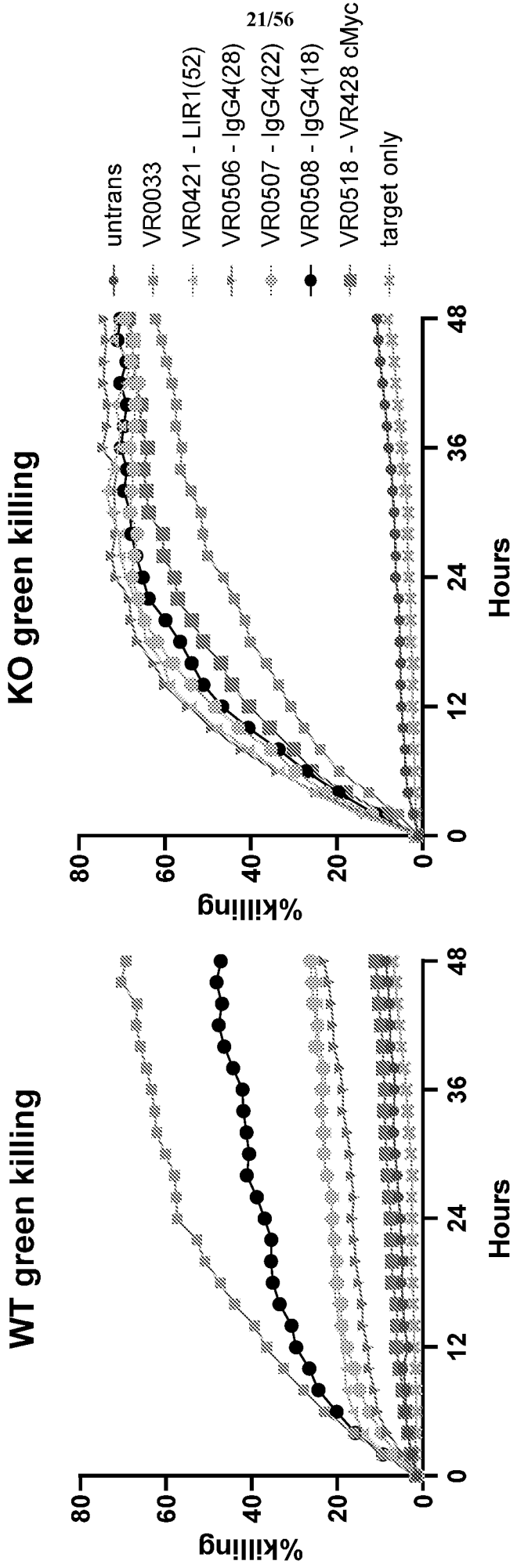

KO green killing
%killing
Hours
0
20
40
60
80
0
12
24
36
48
untrans
VR0033
VR0421 - LIR1(52)
VR0506 - IgG4(28)
VR0507 - IgG4(22)
VR0508 - IgG4(18)
VR0518 - VR428 cMyc
target only
WT green killing
%killing
Hours

FIG. 11

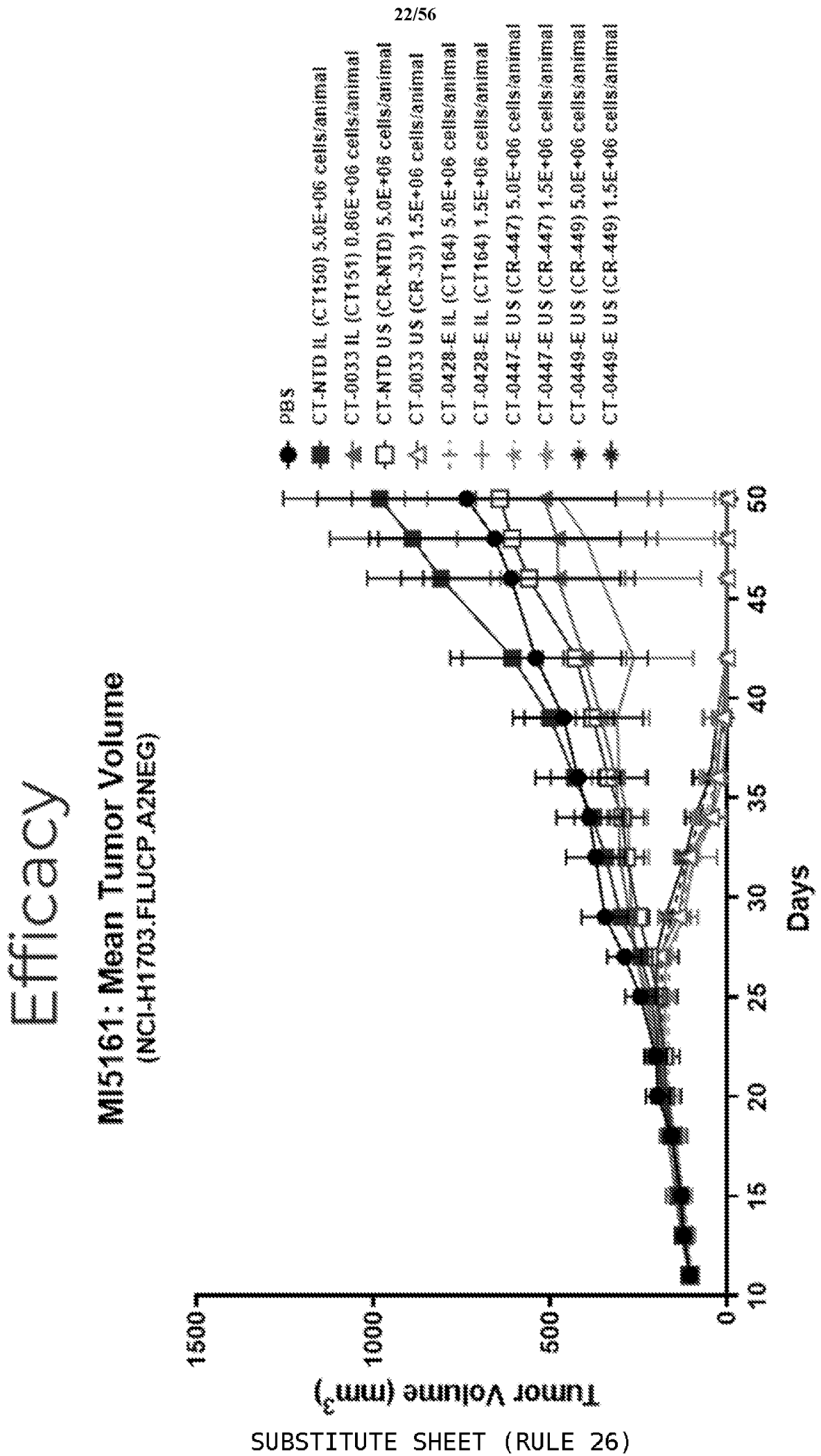

Efficacy
MI5161: Mean Tumor Volume
(NCI-H1703.FLUCP.A2NEG)
PBS
CT-NTD IL (CT150) 5.0E+06 cells/animal
CT-0033 IL (CT151) 0.86E+06 cells/animal
CT-NTD US (CR-NTD) 5.0E+06 cells/animal
CT-0033 US (CR-33) 1.5E+06 cells/animal
CT-0428-E IL (CT164) 5.0E+06 cells/animal
CT-0428-E IL (CT164) 1.5E+06 cells/animal
CT-0447-E US (CR-447) 5.0E+06 cells/animal
CT-0447-E US (CR-447) 1.5E+06 cells/animal
CT-0449-E US (CR-449) 5.0E+06 cells/animal
CT-0449-E US (CR-449) 1.5E+06 cells/animal
Tumor Volume (mm³)
1500
1000
500
0
10
15
20
25
30
35
40
45
50
Days

FIG. 12A

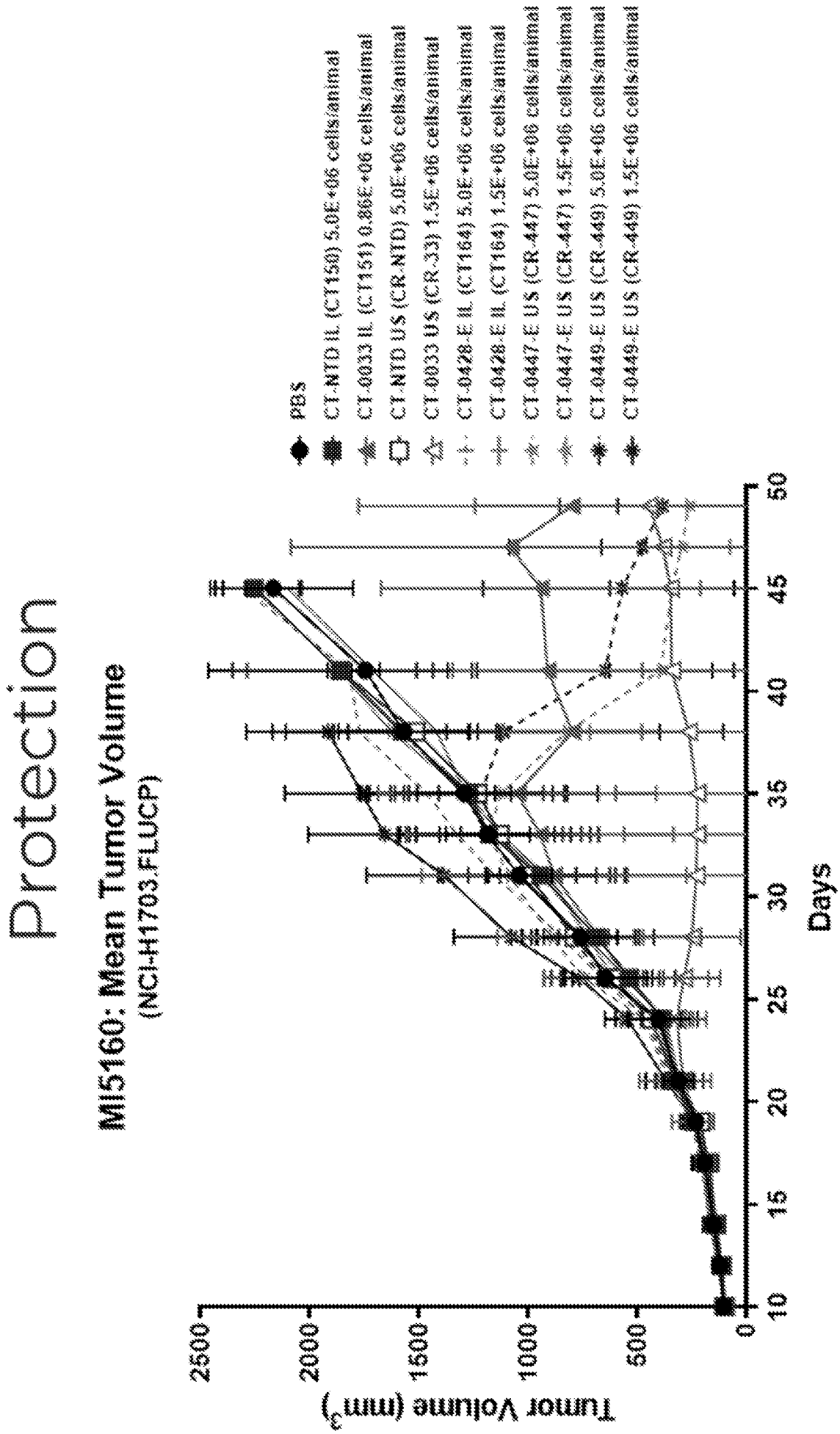

Protection
MI5160: Mean Tumor Volume
(NCI-H1703.FLUCP)
PBS
CT-NTD IL (CT150) 5.0E+06 cells/animal
CT-0033 IL (CT151) 0.86E+06 cells/animal
CT-NTD US (CR-NTD) 5.0E+06 cells/animal
CT-0033 US (CR-33) 1.5E+06 cells/animal
CT-0428-E IL (CT164) 5.0E+06 cells/animal
CT-0428-E IL (CT164) 1.5E+06 cells/animal
CT-0447-E US (CR-447) 5.0E+06 cells/animal
CT-0447-E US (CR-447) 1.5E+06 cells/animal
CT-0449-E US (CR-449) 5.0E+06 cells/animal
CT-0449-E US (CR-449) 1.5E+06 cells/animal
Tumor Volume (mm³)
2500
2000
1500
1000
500
0
10
15
20
25
30
35
40
45
50
Days

FIG. 12B

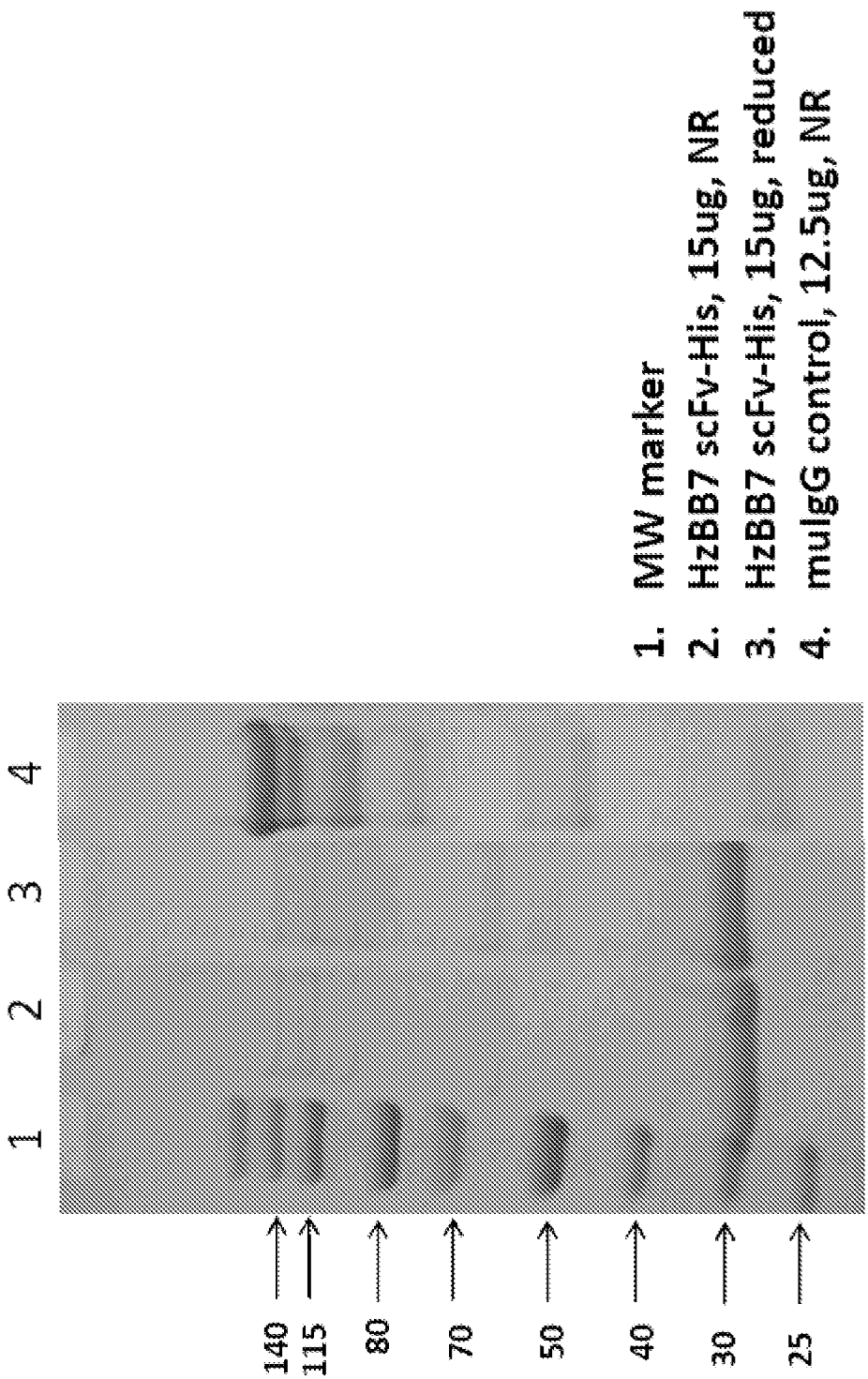

1. MW marker
2. HzBB7 scFv-His, 15ug, NR
3. HzBB7 scFv-His, 15ug, reduced
4. mulgG control, 12.5ug, NR
1
2
3
4
140
115
80
70
50
40
30
25
4-12% NuPage Gel

FIG. 13

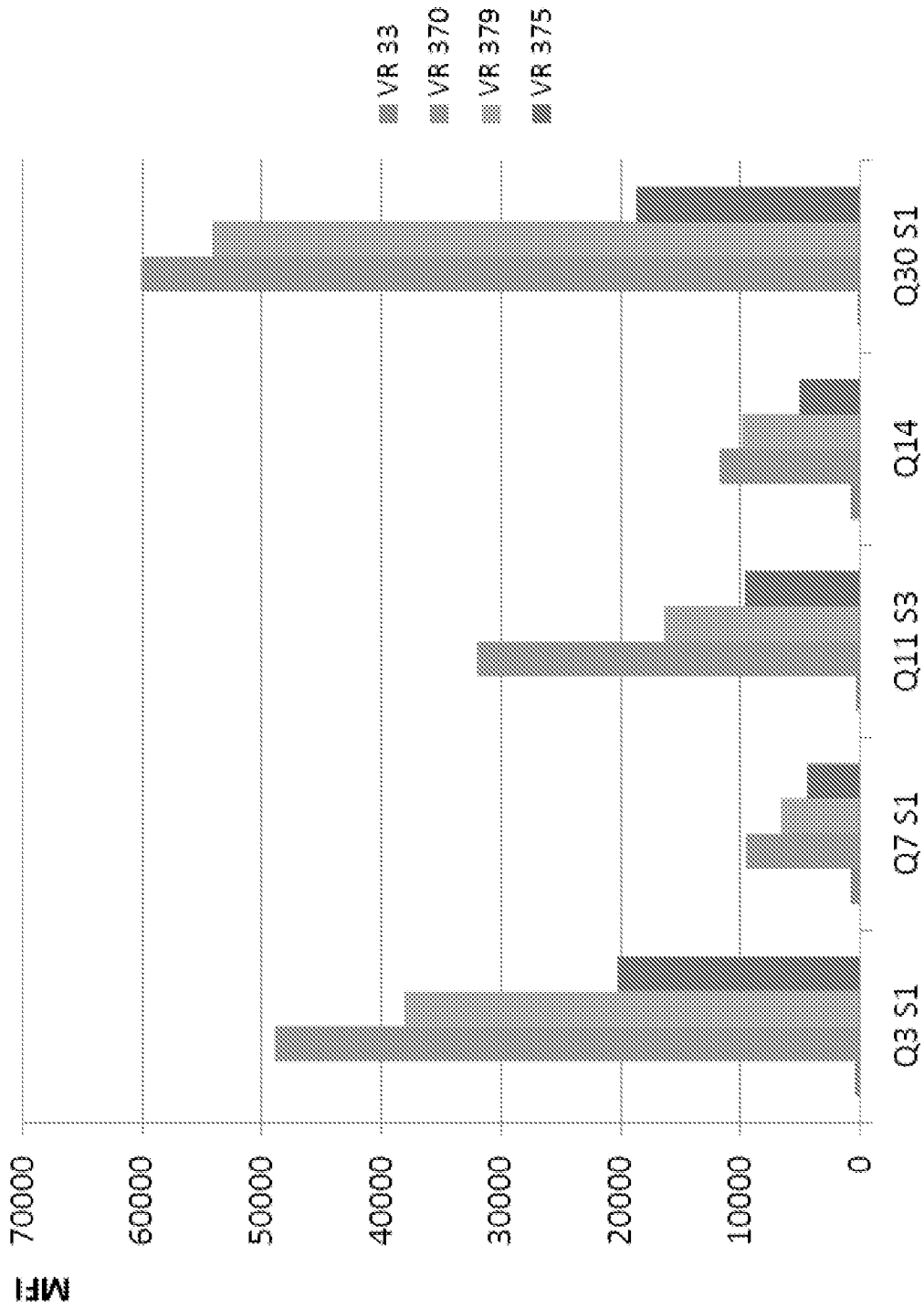

VR 33
VR 370
VR 379
VR 375
MFI
70000
60000
50000
40000
30000
20000
10000
0
Q3 S1
Q7 S1
Q11 S3
Q14
Q30 S1

FIG. 14

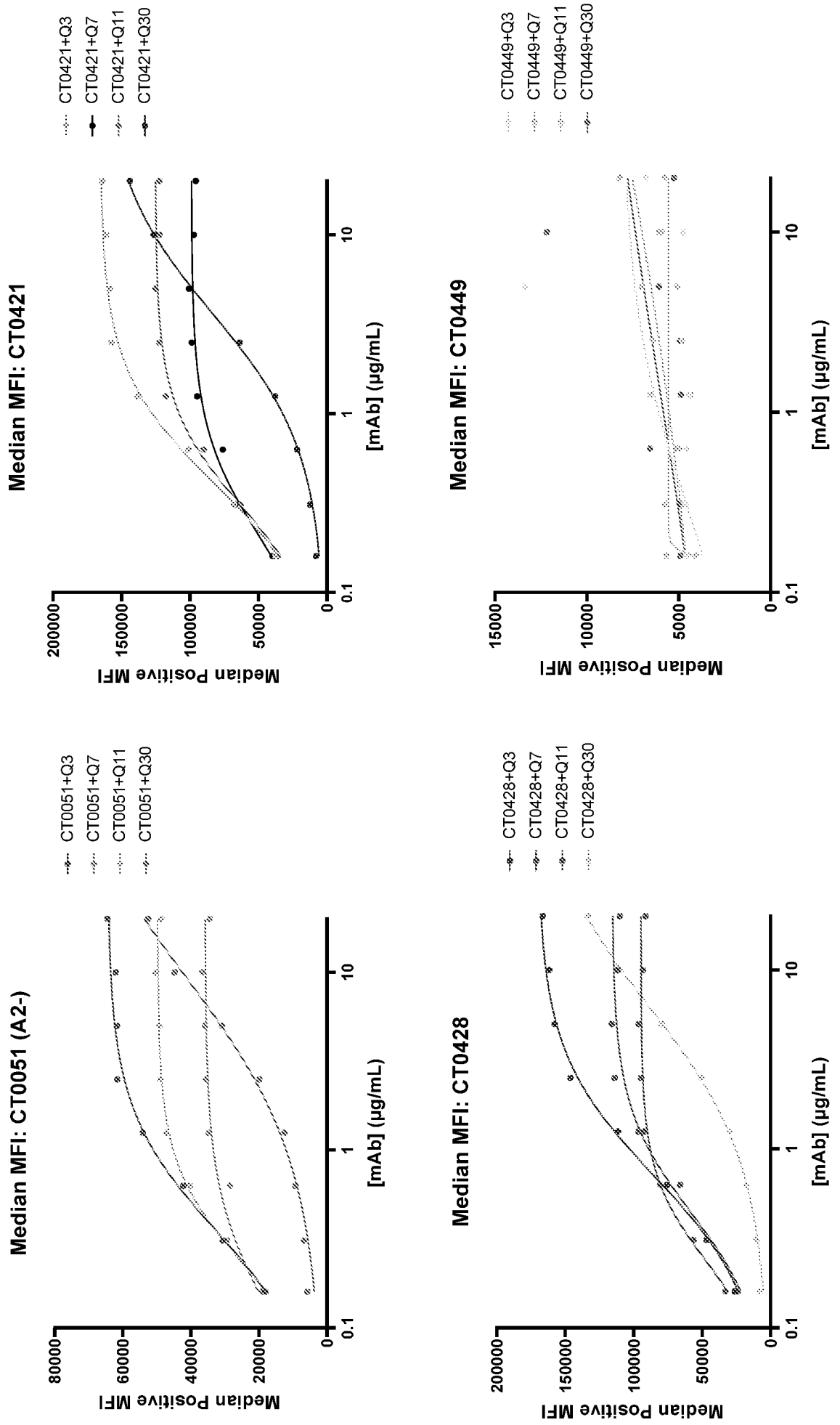

Median MFI: CT0421
CT0421+Q3
CT0421+Q7
CT0421+Q11
CT0421+Q30
Median Positive MFI
200000
150000
100000
50000
0
0.1
1
10
[mAb] (µg/mL)
Median MFI: CT0449
CT0449+Q3
CT0449+Q7
CT0449+Q11
CT0449+Q30
Median Positive MFI
15000
10000
5000
0
0.1
1
10
[mAb] (µg/mL)
Median MFI: CT0051 (A2-)
CT0051+Q3
CT0051+Q7
CT0051+Q11
CT0051+Q30
Median Positive MFI
80000
60000
40000
20000
0
0.1
1
10
[mAb] (µg/mL)
Median MFI: CT0428
CT0428+Q3
CT0428+Q7
CT0428+Q11
CT0428+Q30
Median Positive MFI
200000
150000
100000
50000
0
0.1
1
10
[mAb] (µg/mL)

FIG. 15

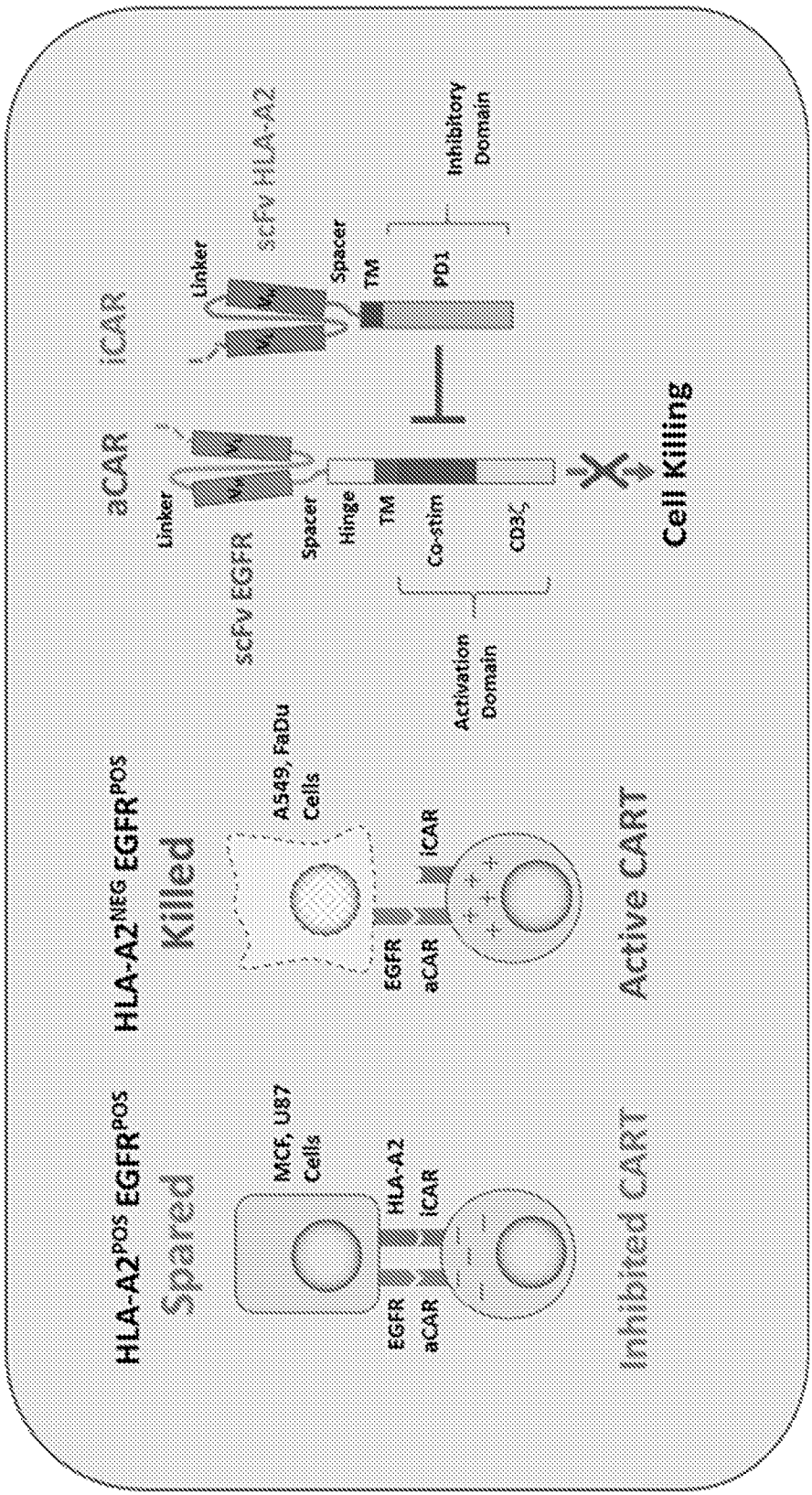

ImmPACT Dual CAR System
HLA-A2POS EGFRPOS
Spared
MCF, U87 Cells
HLA-A2
iCAR
EGFR
aCAR
HLA-A2NEG EGFRPOS
Killed
A549, FaDu Cells
EGFR
aCAR
iCAR
Inhibited CART
Active CART
aCAR
Linker
scFv EGFR
Spacer
Hinge
TM
Co-stim
CD3ζ
Activation Domain
iCAR
Linker
scFv HLA-A2
Spacer
TM
PD1
Inhibitory Domain
Cell Killing

FIG. 16A

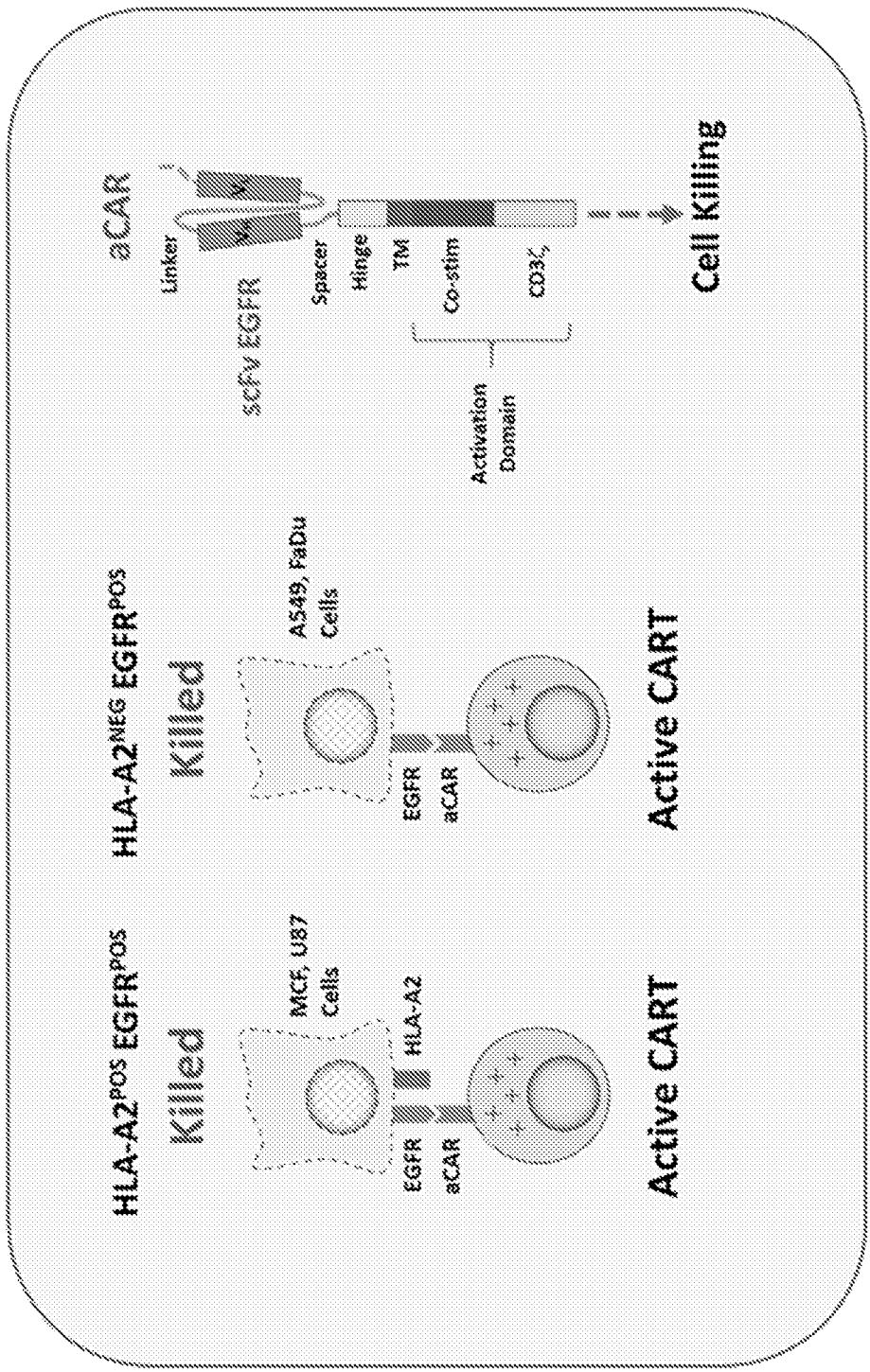

Conventional Single CAR System
HLA-A2POS EGFRPOS
Killed
MC6, U87 Cells
HLA-A2
EGFR
aCAR
Active CART
HLA-A2NEG EGFRPOS
Killed
A549, FaDu Cells
EGFR
aCAR
Active CART
aCAR
Linker
scFv EGFR
Spacer
Hinge
TM
Co-stim
CD3ζ
Activation Domain
Cell Killing

FIG. 16B

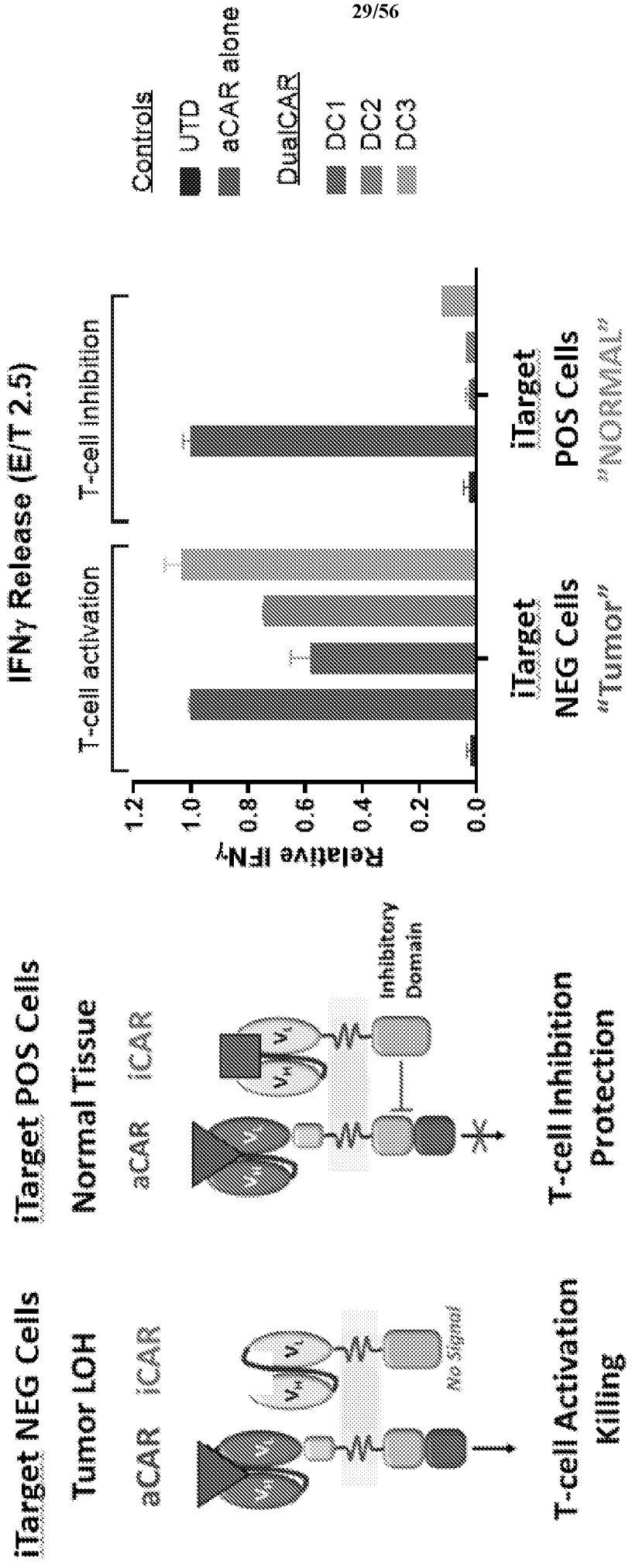
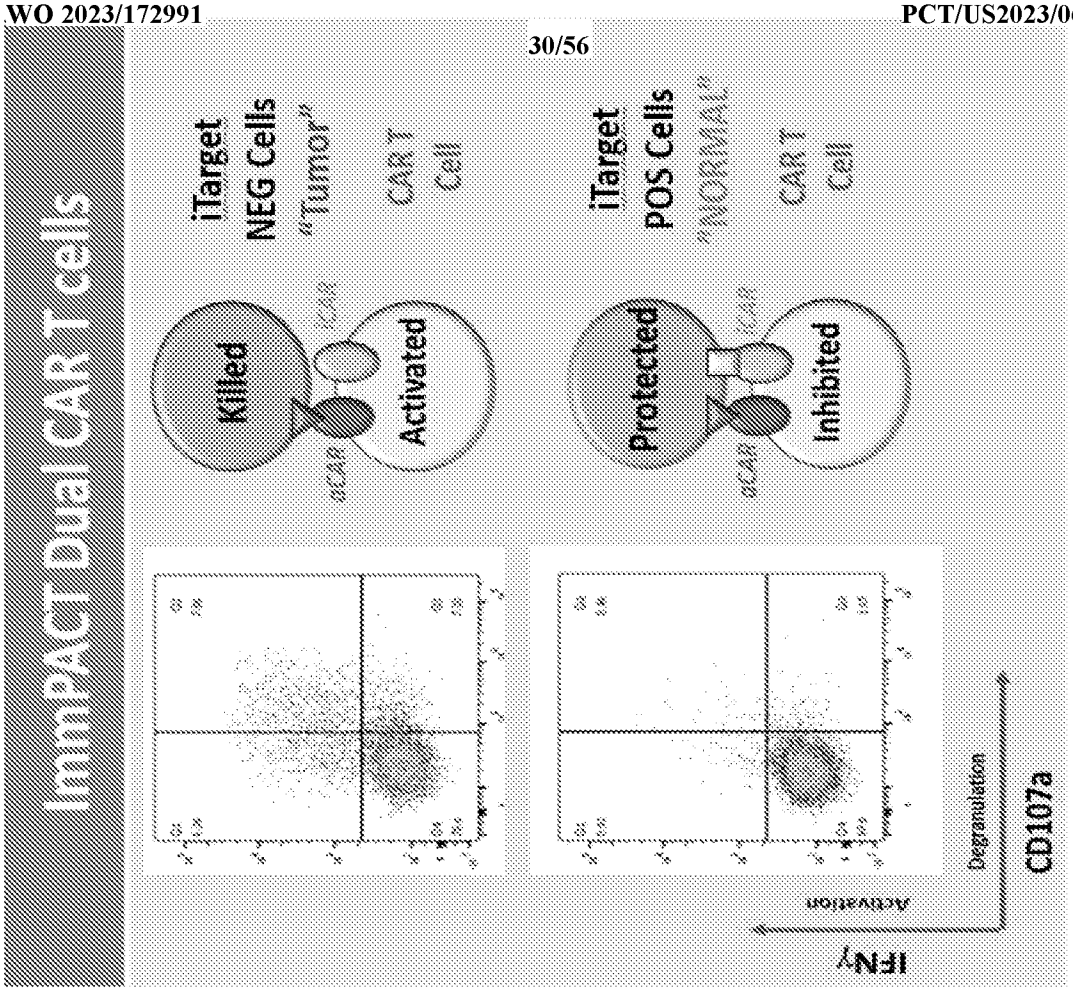

iTarget NEG Cells
Tumor LOH
aCAR iCAR
No Signal
T-cell Activation
Killing
iTarget POS Cells
Normal Tissue
aCAR iCAR
Inhibitory Domain
T-cell Inhibition
Protection
IFNγ Release (E/T 2.5)
T-cell activation
T-cell inhibition
Relative IFNγ
1.2
1.0
0.8
0.6
0.4
0.2
0.0
iTarget NEG Cells "Tumor"
iTarget POS Cells "NORMAL"
Controls
UTD
aCAR alone
DualCAR
DC1
DC2
DC3

FIG. 17


ImmPACT Dual CAR T cells
iTarget NEG Cells "Tumor"
CAR T Cell
Killed
Activated
aCAR
CAR
iTarget POS Cells "NORMAL"
CAR T Cell
Protected
Inhibited
aCAR
CAR
IFNγ
Activation
Degranulation
CD107a

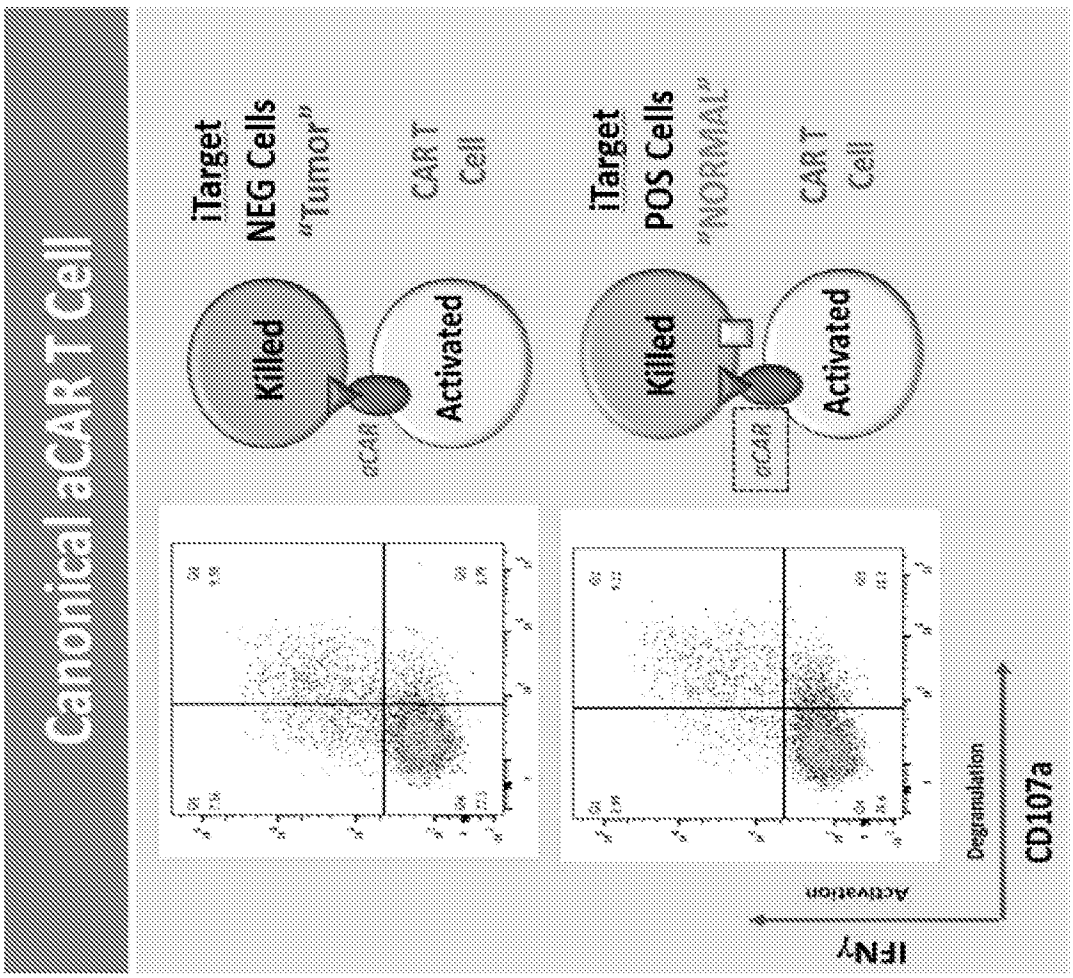

Canonical aCAR T Cell
iTarget NEG Cells "Tumor"
CAR T Cell
Killed
Activated
aCAR
iTarget POS Cells "NORMAL"
CAR T Cell
Killed
Activated
aCAR
IFNγ
Activation
Degranulation
CD107a

FIG. 18

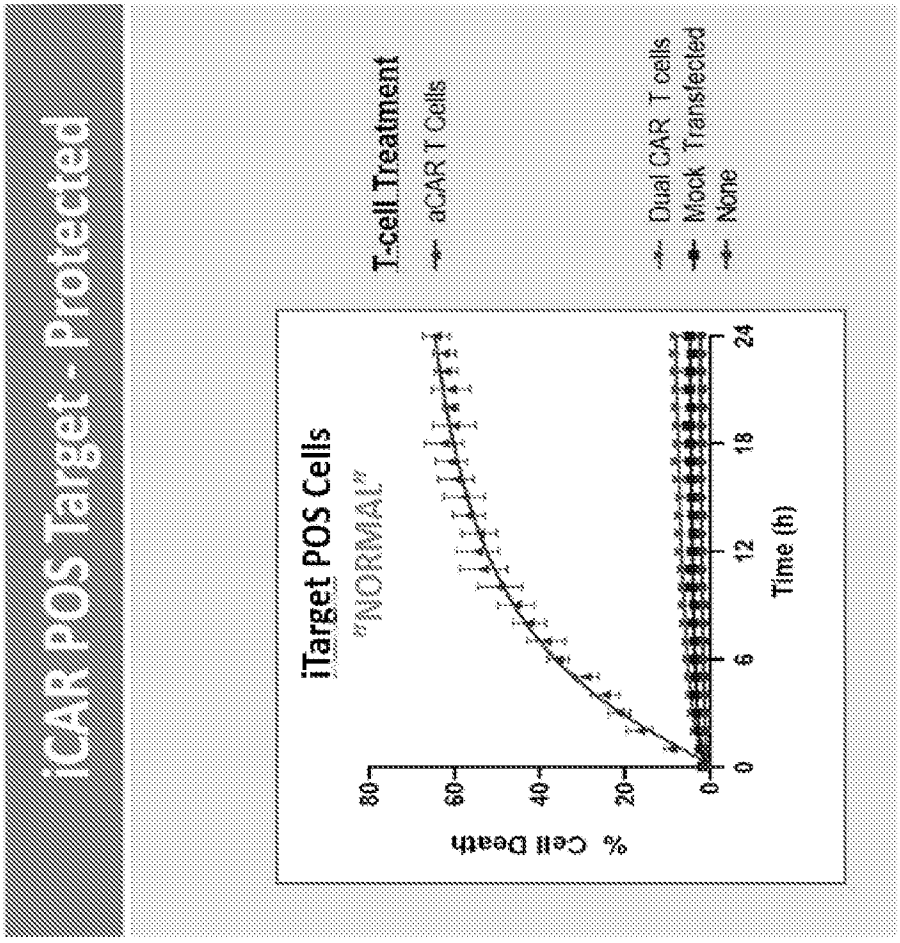

iCAR POS Target - Protected
iTarget POS Cells
"NORMAL"
% Cell Death
Time (h)
T-cell Treatment
aCAR T Cells
Dual CAR T cells
Mock Transfected
None
iCAR Target NEG - Killed
iTarget NEG Cells
"Tumor"
% Cell Death
Time (h)
T-cell Treatment
aCAR T-cells
Dual CAR T Cells
Mock Transfected
None

FIG. 19

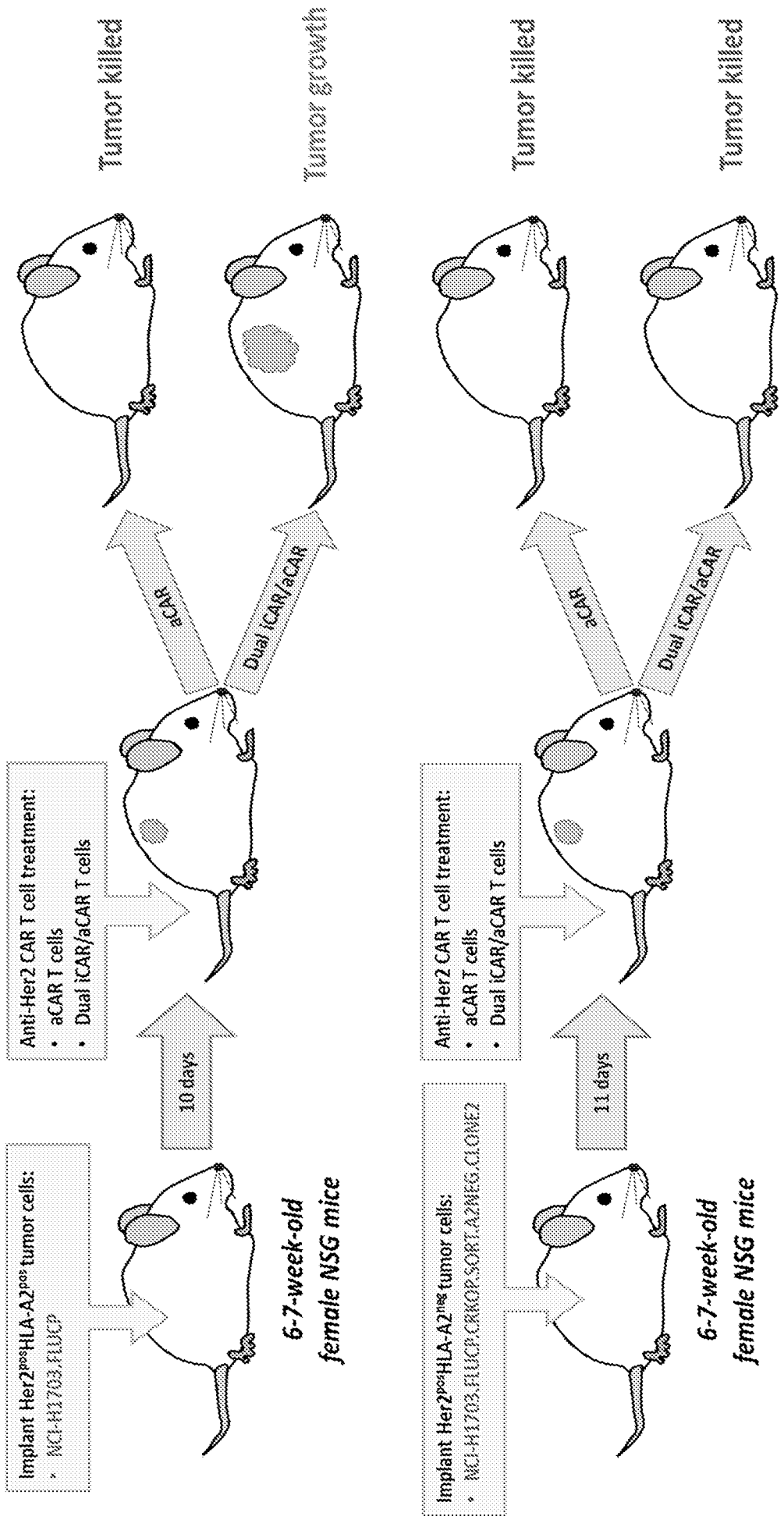
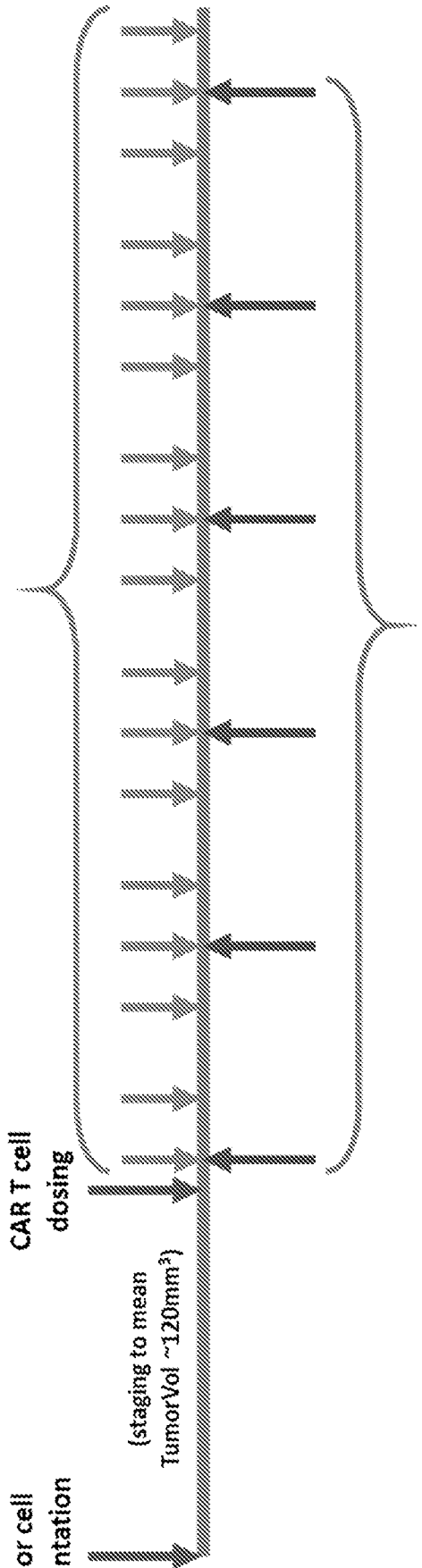

Implant Her2pos HLA-A2pos tumor cells:
• MCI-H1703.FLUCP
6-7-week-old female NSG mice
10 days
Anti-Her2 CAR T cell treatment:
• aCAR T cells
• Dual iCAR/aCAR T cells
aCAR
Dual iCAR/aCAR
Tumor killed
Tumor growth
Implant Her2pos HLA-A2neg tumor cells:
• MCI-H1703.FLUCP.CRKOP.SORT.A2NEG.CLONE2
6-7-week-old female NSG mice
11 days
Anti-Her2 CAR T cell treatment:
• aCAR T cells
• Dual iCAR/aCAR T cells
aCAR
Dual iCAR/aCAR
Tumor killed
Tumor killed

FIG. 20



Additional Endpoints: Necropsy of animals when removed from study, or at end of study

FIG. 21

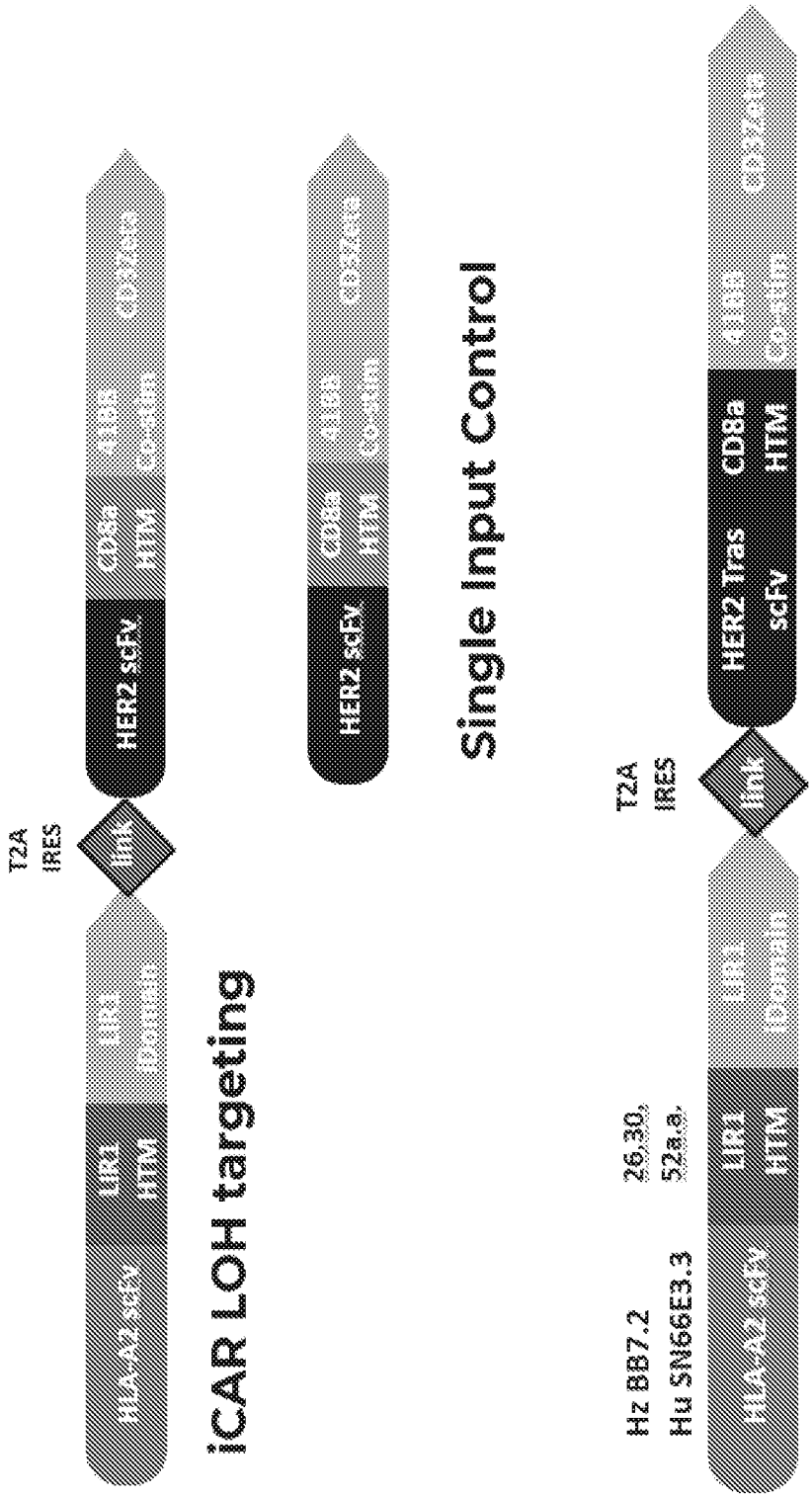

iCAR LOH targeting
HLA-A2 scFv
LIR1 HTM
LIR1 Domain
T2A IRES
link
HER2 scFv
CD8a HTM
4-1BB Co-stim
CD3ζ-ζa
Single Input Control
HER2 scFv
CD8a HTM
4-1BB Co-stim
CD3ζ-ζa
T2A IRES
Hz 8B7.2
Hu SN66E3.3
26,30, 52a.a.
HLA-A2 scFv
LIR1 HTM
LIR1 Domain
link
HER2 Tras scFv
CD8a HTM
4-1BB Co-stim
CD3ζ-ζa

FIG. 22A

Cancer	Cell Line	HLA-A Alleles		Receptors per cell		
		I	II	EGFR	Her2	HLA-A2
Skin	A-431	03:01	03:01	2,838,401	2,818	0
Lung	A549	25:01	30:01	228,990	23,268	0
Throat	FaDu	01:01	01:01	710,681	39,783	0
Breast	MCF7	02:01	02:01	3,307	56,182	126,085
Breast	MDA-MB-231	02:17	02:01	295,974	16,944	2,468,107
Lung	MRC-5	2:01	29:02	129,229	10,569	385,253
Lung	NCI-H1355	02:01	02:01	107,758	21,817	210,501
Lung	NCI-H1355-Luc	02:01	02:01	63,194	10,608	405,293
Lung	NCI-H1355-Luc A2KO	02:01	02:01	44,143	10,139	0
Lung	NCI-H1650	02:01	02:01	161,188	55,207	813,485
Lung	NCI-H1650-Luc	02:01	02:01	144,622	20,475	1,247,812
Lung	NCI-H1650-Luc A2KO	02:01	02:01	157,651	21,122	0
Lung	NCI-H1703	01:01	02:01	554,843	21,322	878,876
Lung	NCI-H1703-Luc	01:01	02:01	199,329	24,739	1,684,284
Lung	NCI-H1703-Luc A2KO	01:01	02:01	218,621	27,286	0
Lung	NCI-H1792	26:08'	02:01	373,844	18,606	483,418
Lung	NCI-H1792-Luc	26:08'	02:01	231,825	9,264	726,720
Lung	NCI-H1792-Luc A2KO	26:08'	02:01	205,460	7,925	0
Lung	NCI-H1975	01:01	01:01	288,763	49,165	0
Lung	NCI-H1975-Luc	01:01	01:01	184,178	26,792	0
Lung	NCI-H2122	03:01	01:01	96,835	32,919	0
Lung	NCI-H2228	02:01	03:01	507,599	23,268	1,029,696
Lung	NCI-H292	68:02	74:01	445,307	47,438	0
Lung	NCI-H292-Luc	68:02	74:01	293,551	14,623	0
Lung	NCI-H441	03:01	02:01'	220,768	39,368	121,410
Lung	NCI-H441-Luc A2KO	03:01	02:01'	73,936	53,857	0
Lung	NCI-H460	68:01'	24:02	102,687	19,642	0
Lung	NCI-H522	02:01	24:18'	0	68,995	90,674
Lung	NCI-H661	02:01'	24:02'	71,097	67,437	25,376
Ovarian	SK-OV-3	68:01	03:01	297,625	216,914	0
Brain	U-87 MG	02:01	02:01	175,001	0	602,864

FIG. 22B

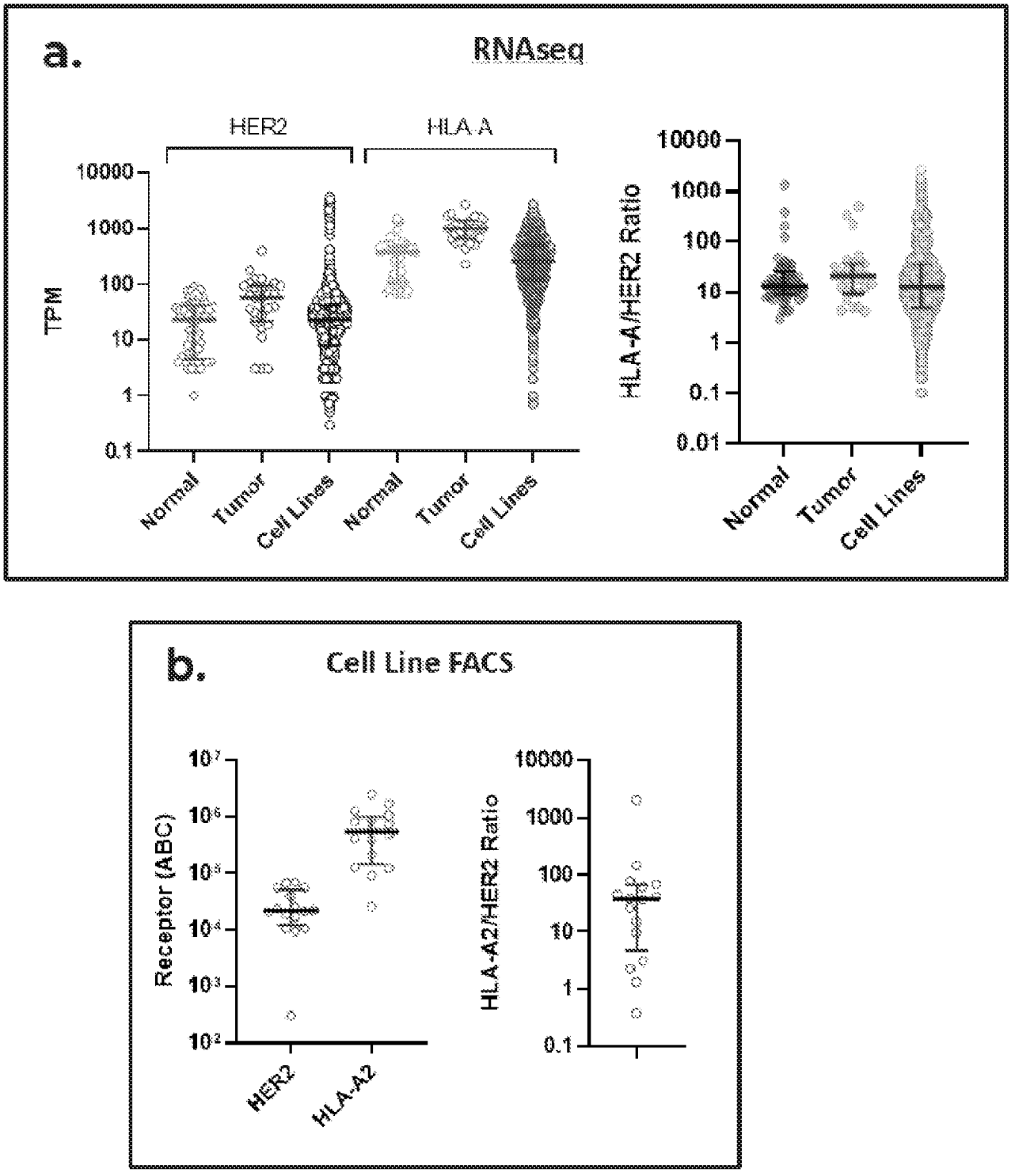

a.
RNAseq
HER2
HLA A
TPM
10000
1000
100
10
1
0.1
Normal
Tumor
Cell Lines
Normal
Tumor
Cell Lines
HLA-A/HER2 Ratio
10000
1000
100
10
1
0.1
0.01
Normal
Tumor
Cell Lines
b.
Cell Line FACS
Receptor (ABC)
HER2
HLA-A2
HLA-A2/HER2 Ratio
10000
1000
100
10
1
0.1

FIG. 23

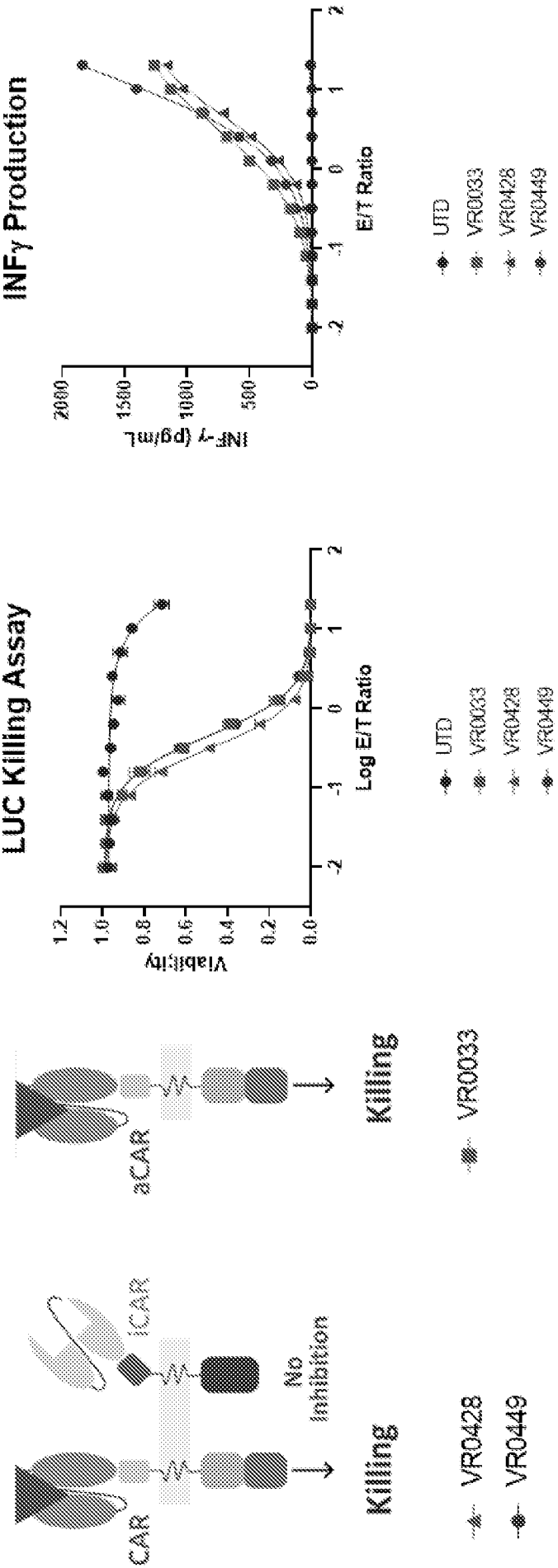

INFγ Production
INF-γ (pg/mL)
2000
1500
1000
500
0
-2
-1
0
1
2
E/T Ratio
UTD
VR0033
VR0428
VR0449
LUC Killing Assay
Viability
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-2
-1
0
1
2
Log E/T Ratio
UTD
VR0033
VR0428
VR0449
aCAR
iCAR
No Inhibition
Killing
VR0428
VR0449
aCAR
Killing
VR0033

FIG. 24A

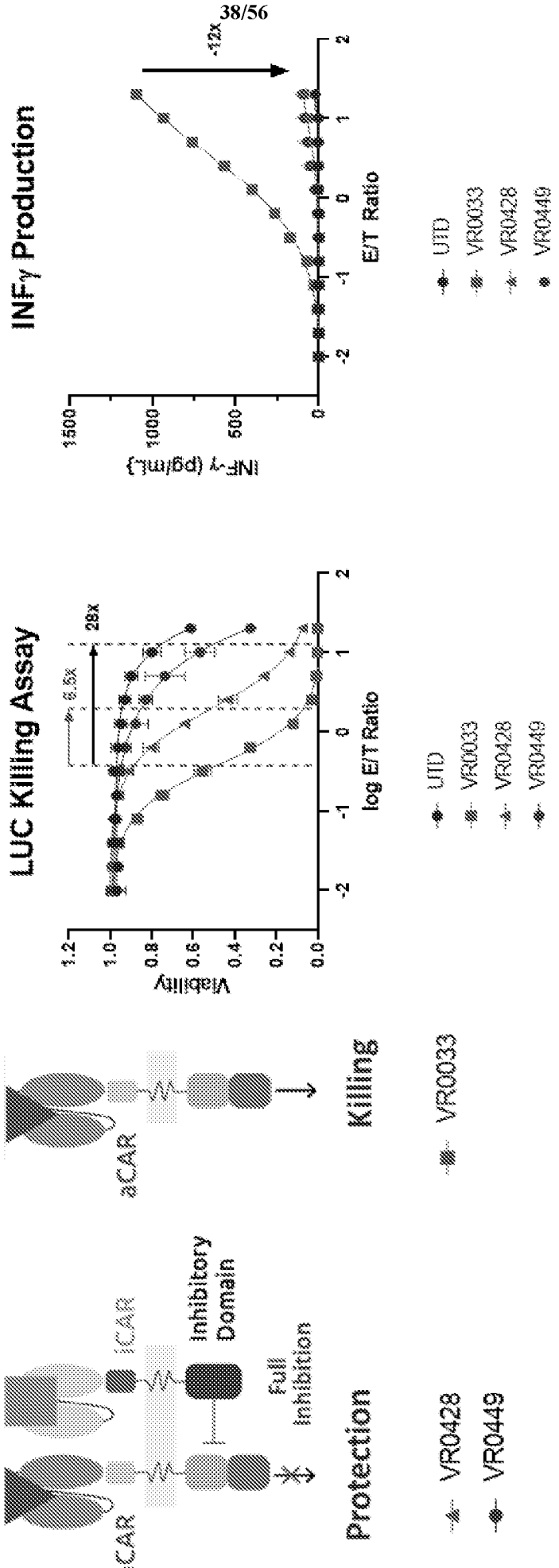

aCAR
iCAR
Inhibitory Domain
Full Inhibition
Protection
VR0428
VR0449
aCAR
Killing
VR0033
LUC Killing Assay
Viability
log E/T Ratio
6.5x
28x
UTD
VR0033
VR0428
VR0449
INFγ Production
IFN-γ (pg/mL)
E/T Ratio
~12x
UTD
VR0033
VR0428
VR0449

FIG. 24B

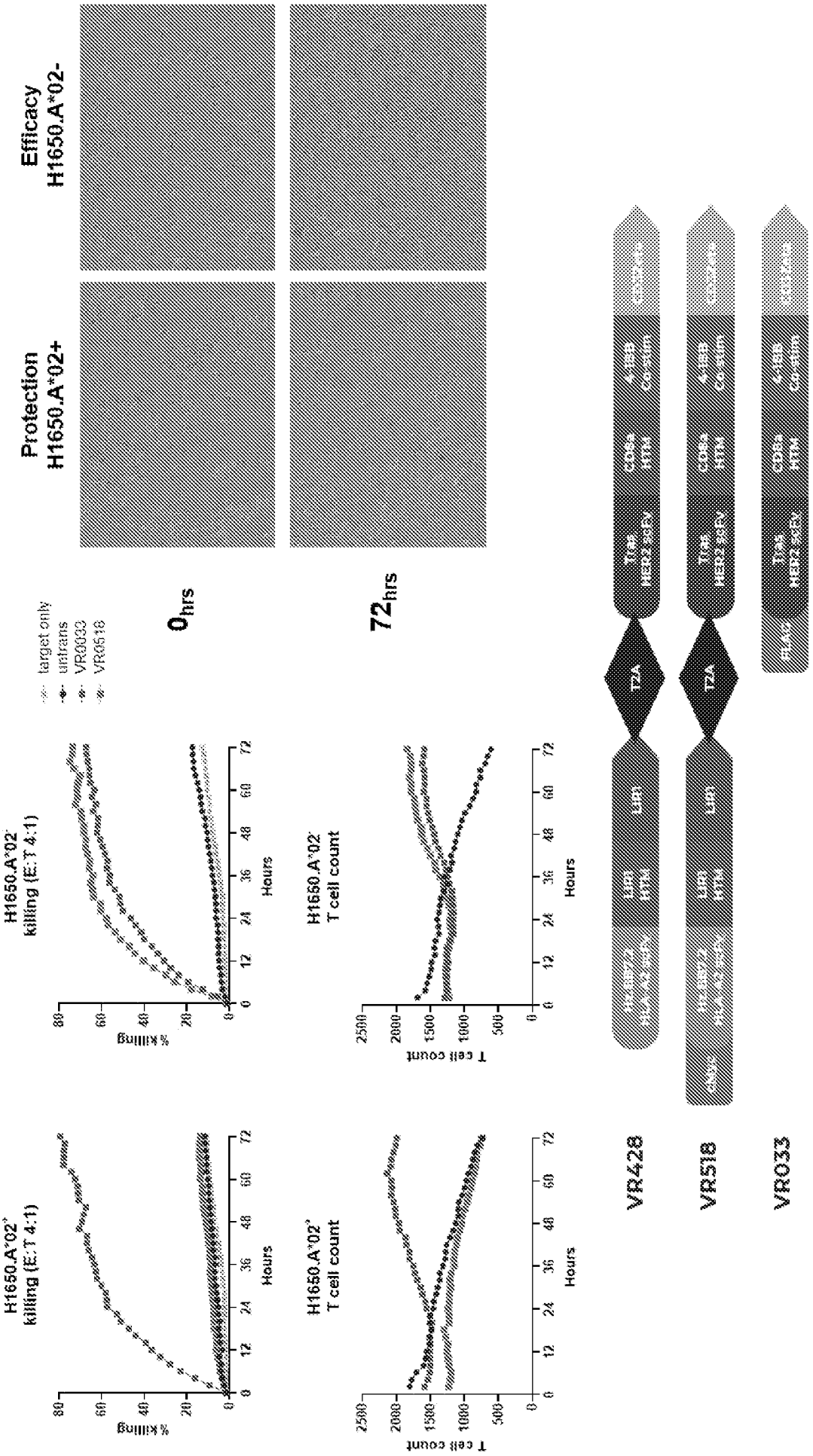

Efficacy
H1650.A*02-
Protection
H1650.A*02+
0hrs
72hrs
target only
unitrans
VR0033
VR0518
H1650.A*02
killing (E:T 4:1)
% killing
Hours
H1650.A*02
T cell count
T cell count
Hours
VR428
VR518
VR033
T2A
P2A

FIG. 25A

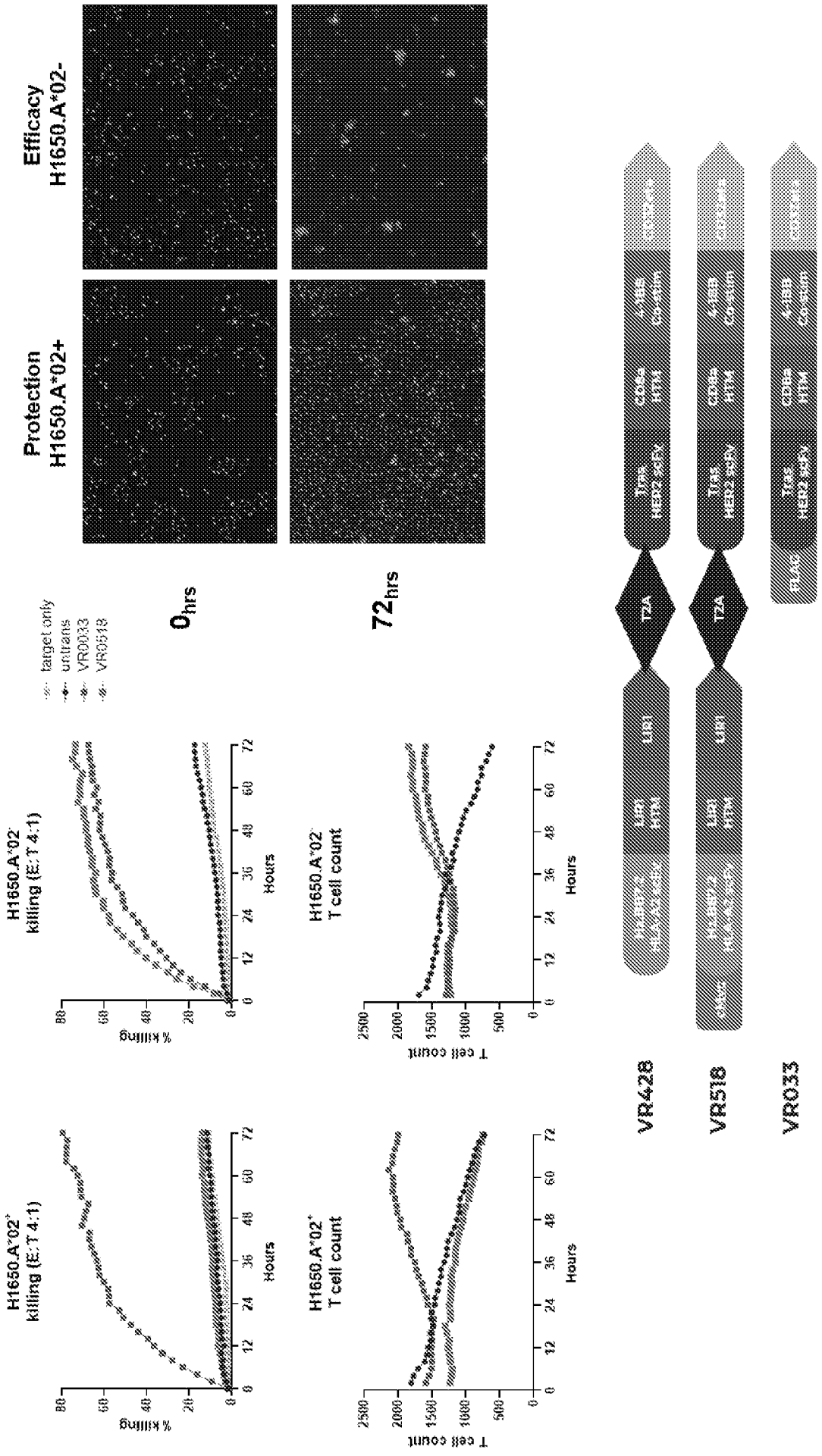
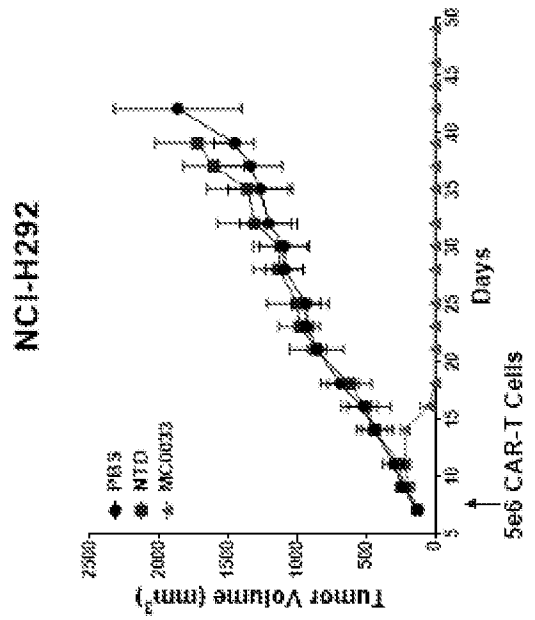
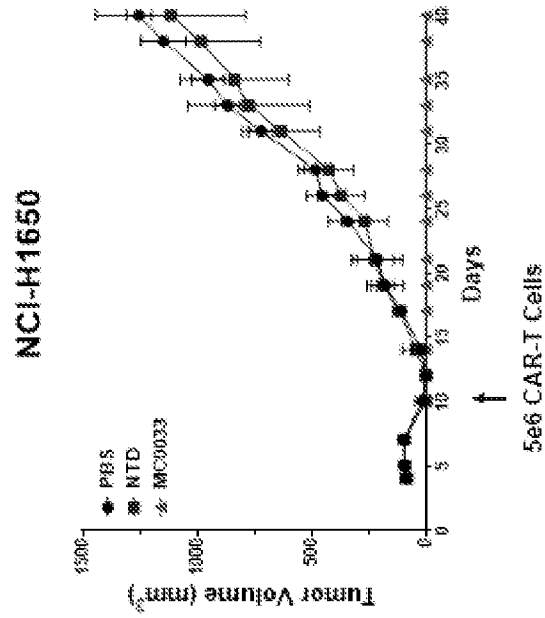

Efficacy
H1650.A*02-
Protection
H1650.A*02+
0hrs
72hrs
target only
untrans
VR0033
VR0518
H1650.A*02+
killing (E:T 4:1)
H1650.A*02-
killing (E:T 4:1)
H1650.A*02+
T cell count
H1650.A*02-
T cell count
% killing
T cell count
Hours
VR428
VR518
VR033

FIG. 25B



CAR Target	Sites Cell
HER2	24,449
HLA-A2	1,281,580



CAR Target	Sites Cell
HER2	32,268
HLA-A2	1,030,648

CAR Target	Sites Cell
HER2	31,030
HLA-A2	0

FIG. 26

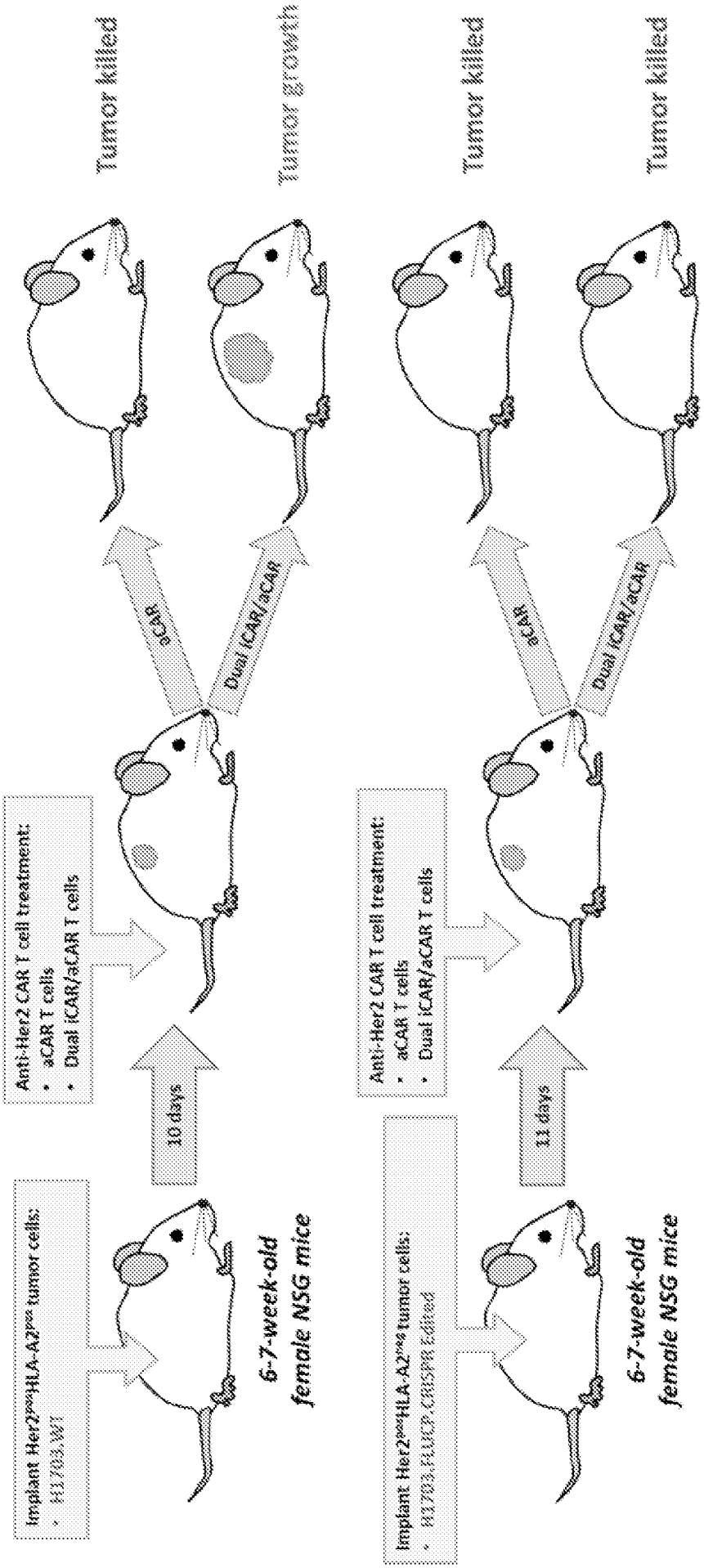

Implant Her2^{pos}HLA-A2^{pos} tumor cells:
• H1703.WT
10 days
6-7-week-old female NSG mice
Anti-Her2 CAR T cell treatment:
• aCAR T cells
• Dual iCAR/aCAR T cells
aCAR
Dual iCAR/aCAR
Tumor killed
Tumor growth
Implant Her2^{pos}HLA-A2^{neg} tumor cells:
• H1703.FLUC.CRISPR Edited
11 days
6-7-week-old female NSG mice
Anti-Her2 CAR T cell treatment:
• aCAR T cells
• Dual iCAR/aCAR T cells
aCAR
Dual iCAR/aCAR
Tumor killed
Tumor killed

FIG. 27

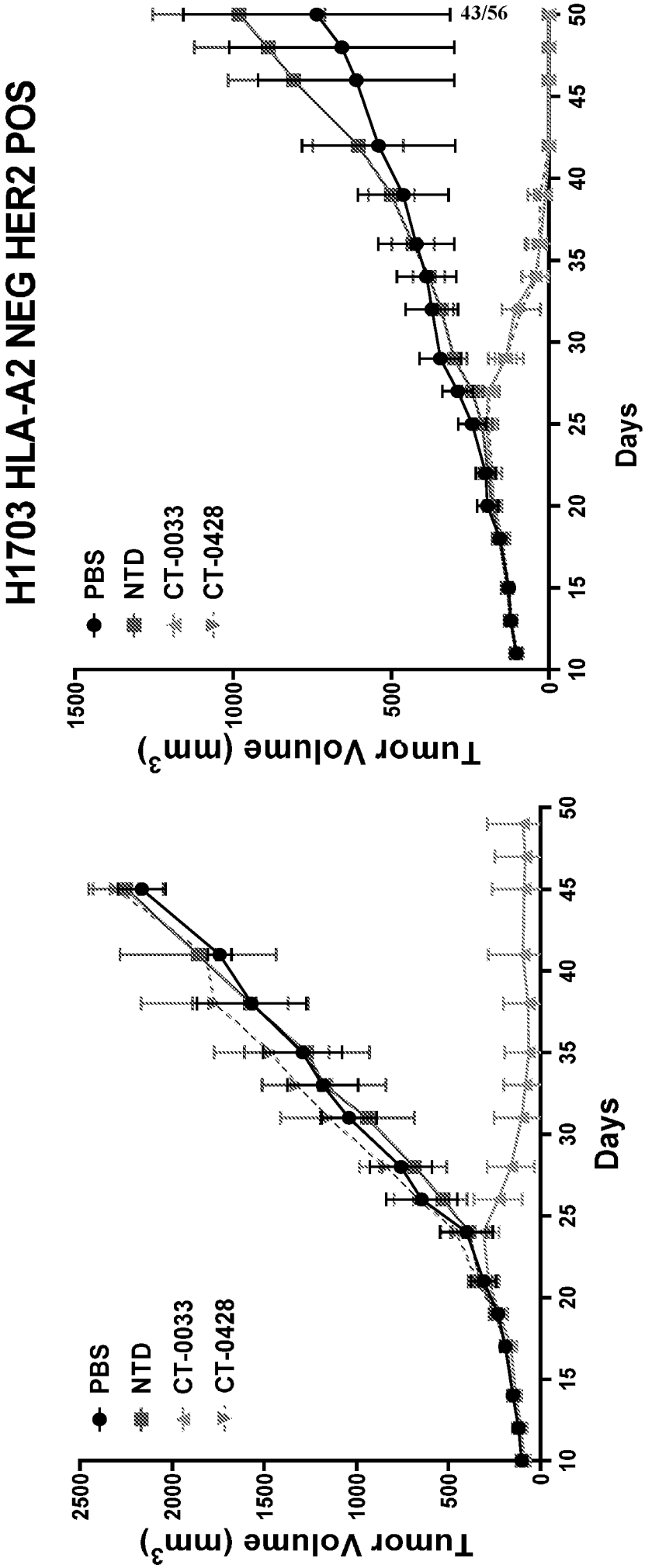

H1703 HLA-A2 NEG HER2 POS
PBS
NTD
CT-0033
CT-0428
Tumor Volume (mm3)
Days
0
500
1000
1500
2000
2500
10
15
20
25
30
35
40
45
50

FIG. 28

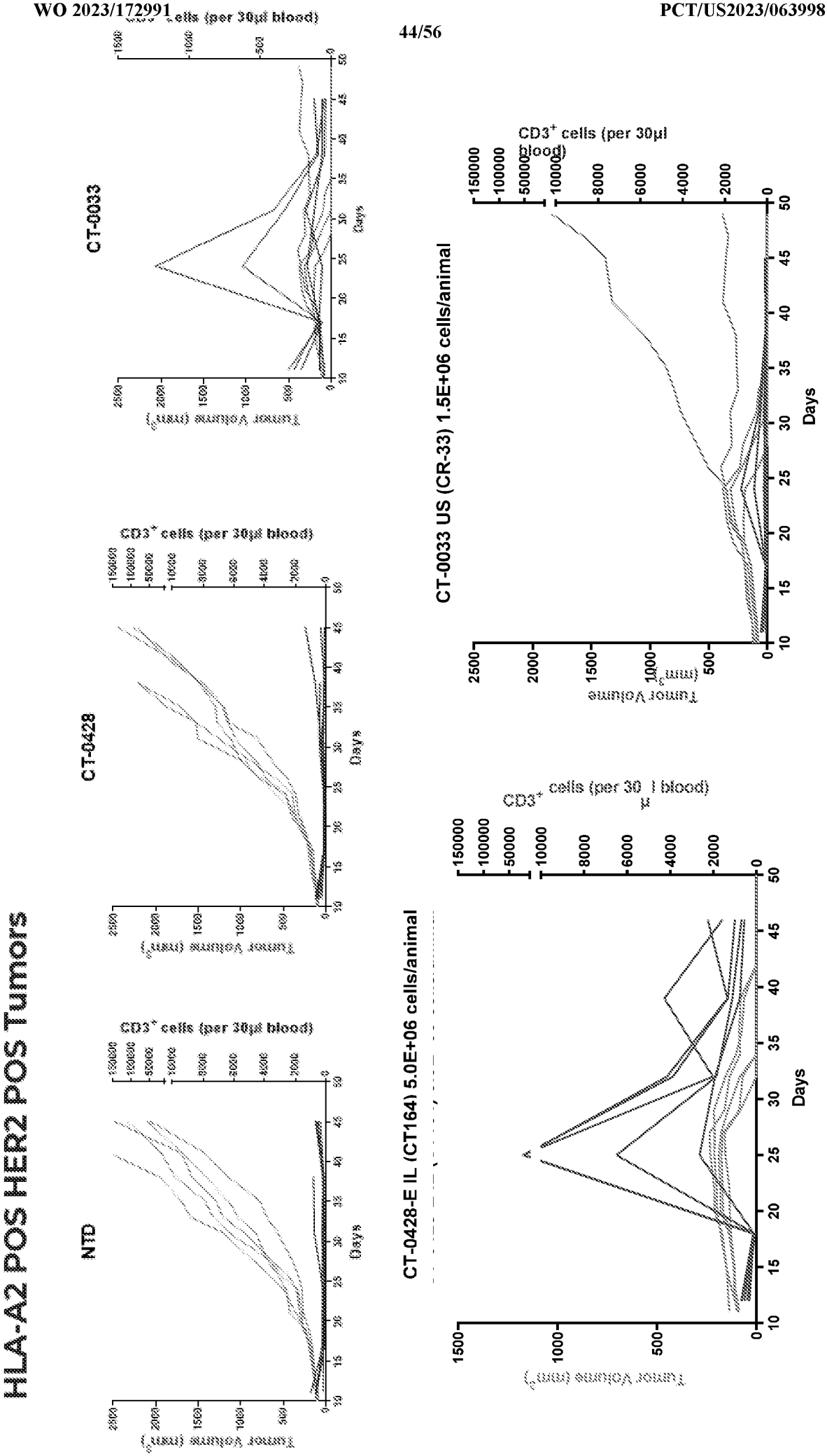

HLA-A2 POS HER2 POS Tumors
NTD
CT-0428
CT-0033
CT-0428-E IL (CT164) 5.0E+06 cells/animal
CT-0033 US (CR-33) 1.5E+06 cells/animal
CD3+ cells (per 30µl blood)
Tumor Volume (mm3)
Days

FIG. 29

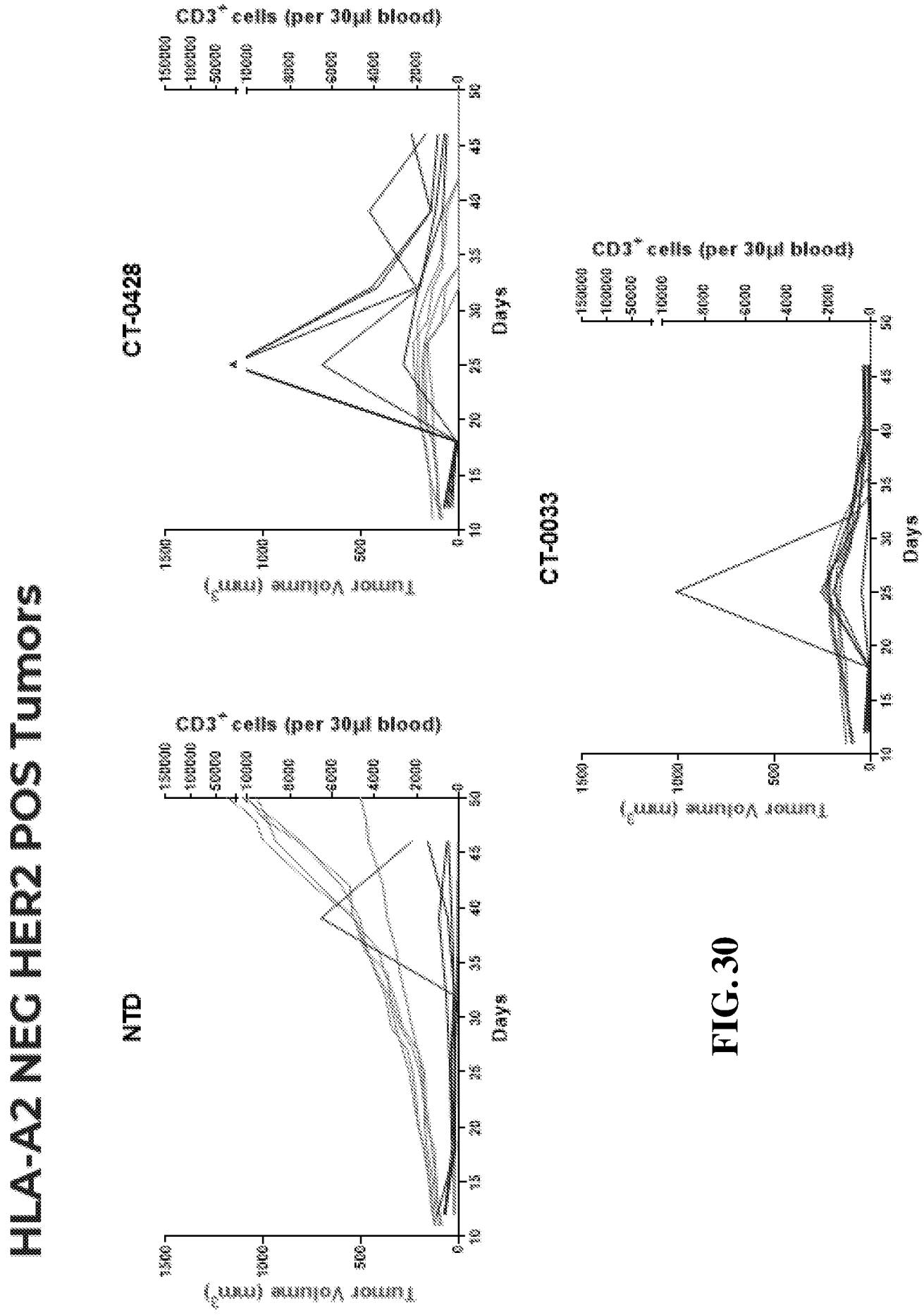

HLA-A2 NEG HER2 POS Tumors
NTD
CT-0428
CT-0033
CD3+ cells (per 30µl blood)
Tumor Volume (mm3)
Days

FIG. 30

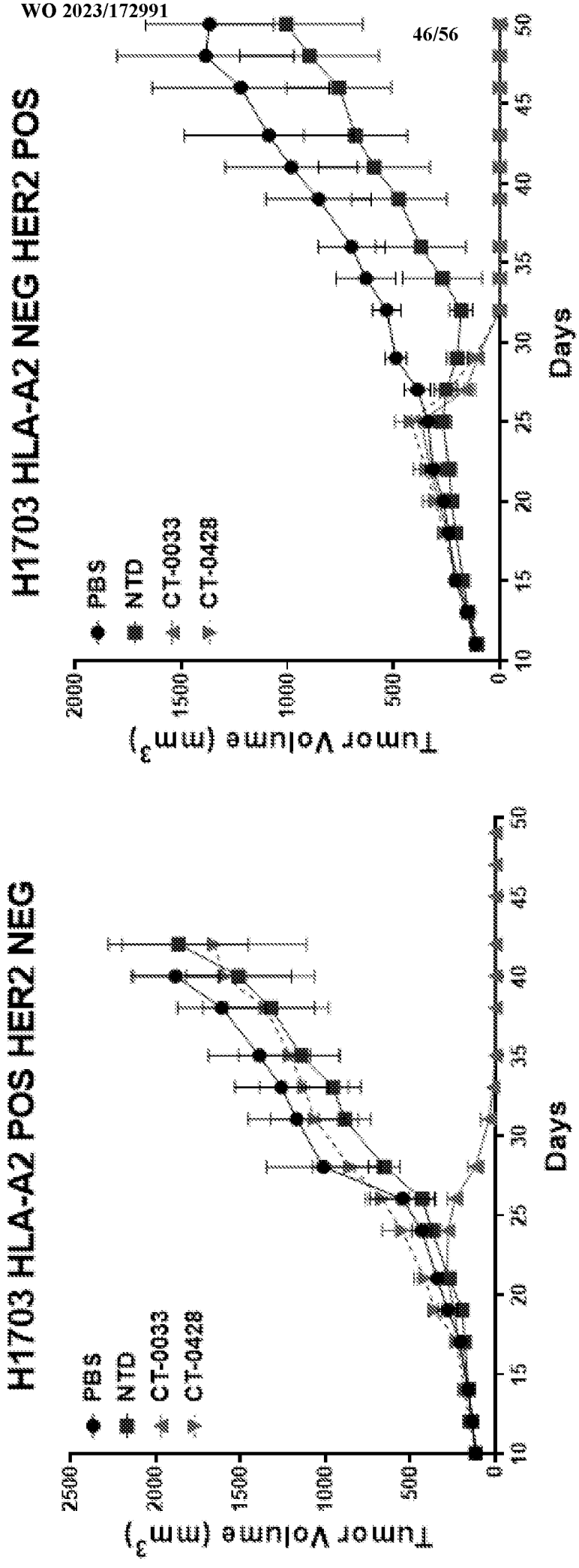
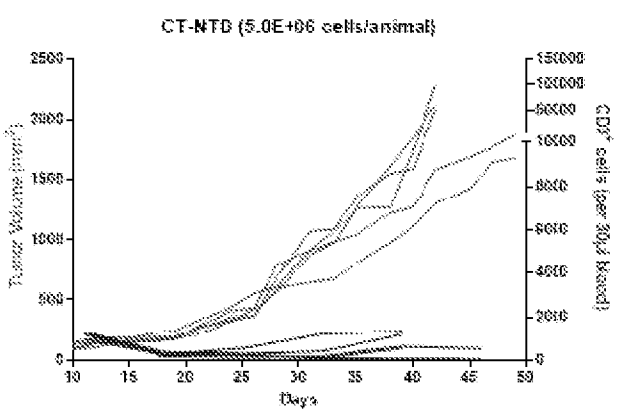
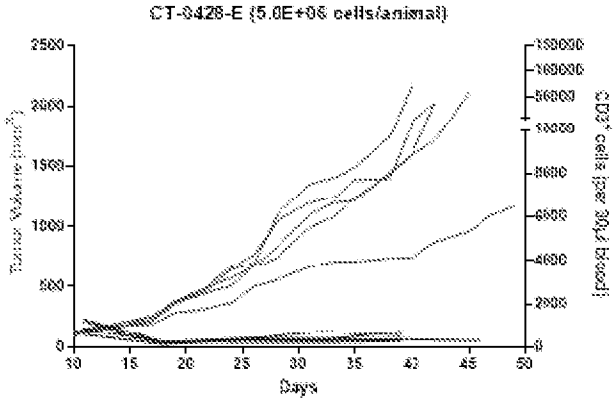
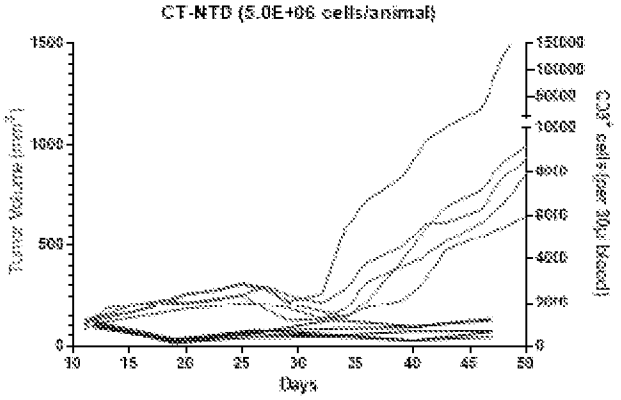
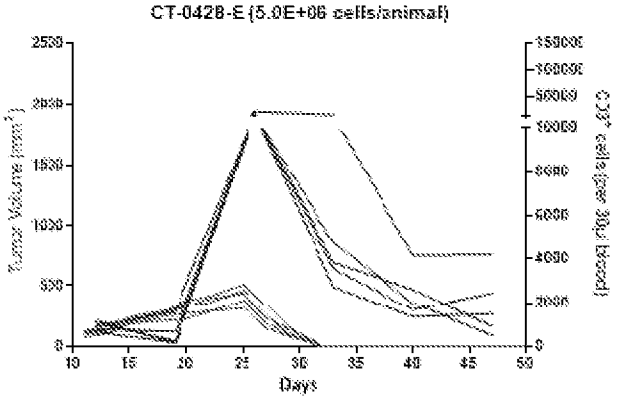

H1703 HLA-A2 POS HER2 NEG
PBS
NTD
CT-0033
CT-0428
Tumor Volume (mm3)
Days
H1703 HLA-A2 NEG HER2 POS
PBS
NTD
CT-0033
CT-0428
Tumor Volume (mm3)
Days

FIG. 31


CT-NTD (5.0E+06 cells/animal)
Tumor Volume (mm³)
CD3⁺ cells (per 30µl blood)
Days


CT-0428-E (5.0E+06 cells/animal)
Tumor Volume (mm³)
CD3⁺ cells (per 30µl blood)
Days


CT-NTD (5.0E+06 cells/animal)
Tumor Volume (mm³)
CD3⁺ cells (per 30µl blood)
Days


CT-0428-E (5.0E+06 cells/animal)
Tumor Volume (mm³)
CD3⁺ cells (per 30µl blood)
Days

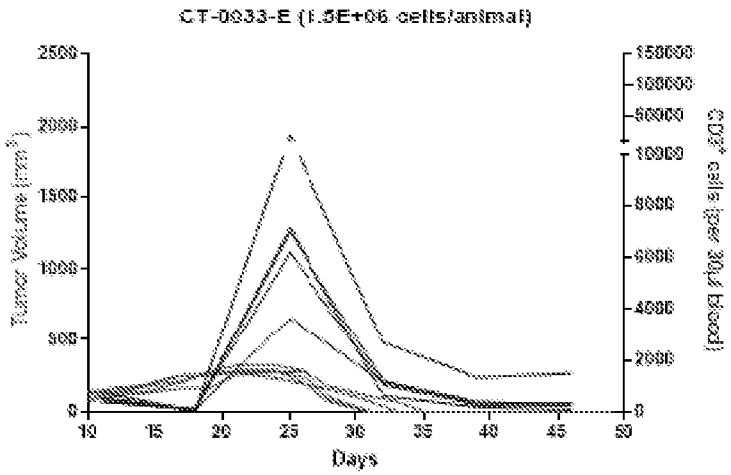
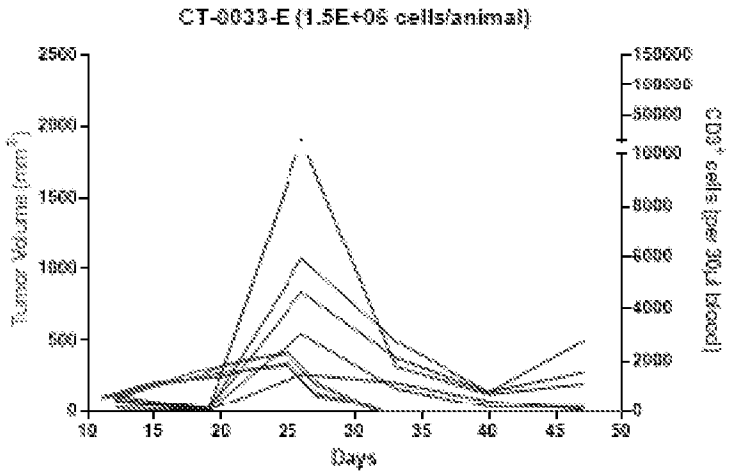
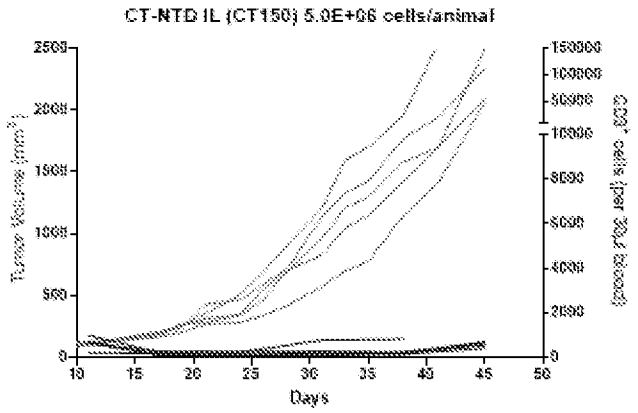
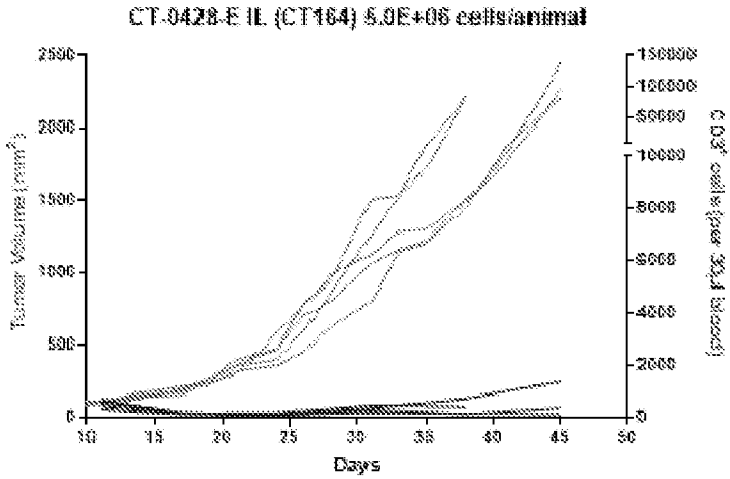
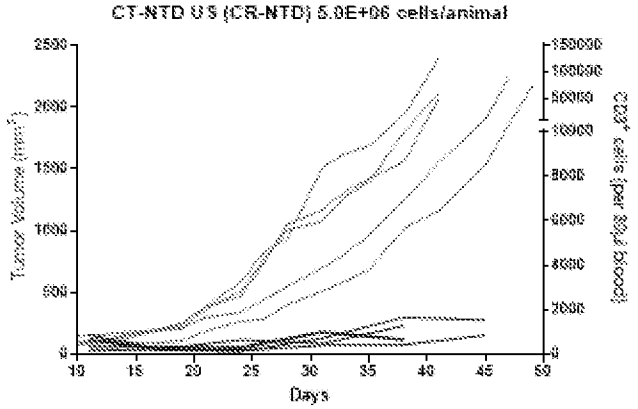

CT-0033-E (1.5E+06 cells/animal)
Tumor Volume (mm³)
CD3⁺ cells (per 30µl blood)
Days

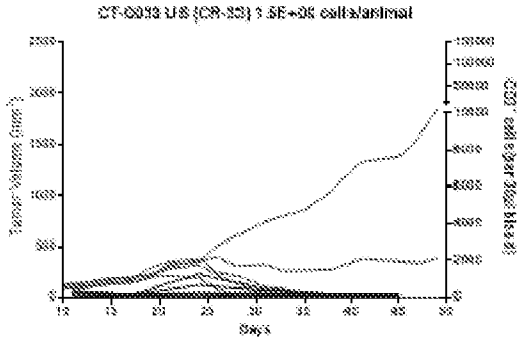
FIG. 32


CT-0033-E (1.5E+06 cells/animal)
Tumor Volume (mm³)
CD3⁺ cells (per 30µl blood)
Days


CT-NTD IL (CT150) 5.0E+06 cells/animal
Tumor Volume (mm³)
CD3⁺ cells (per 30µl blood)
Days


CT-0428-E IL (CT164) 5.0E+06 cells/animal
Tumor Volume (mm³)
Days


CT-NTD US (CR-NTD) 5.0E+06 cells/animal
Tumor Volume (mm³)
CD3⁺ cells (per 30µl blood)
Days


Days

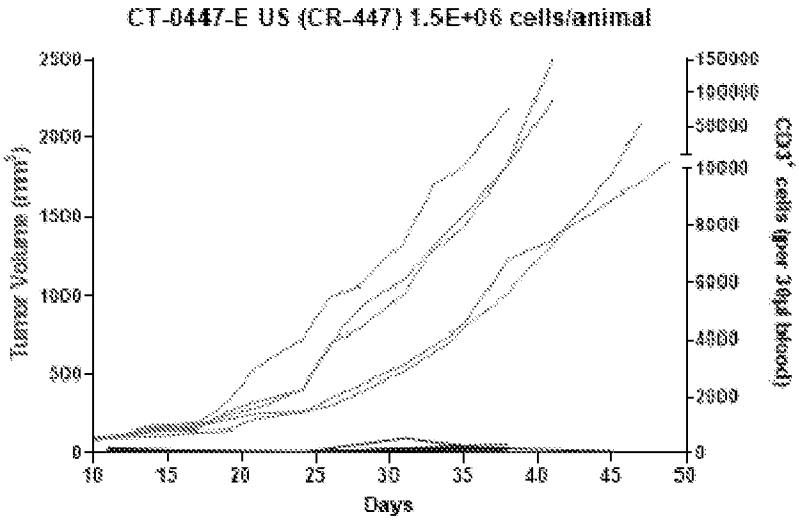
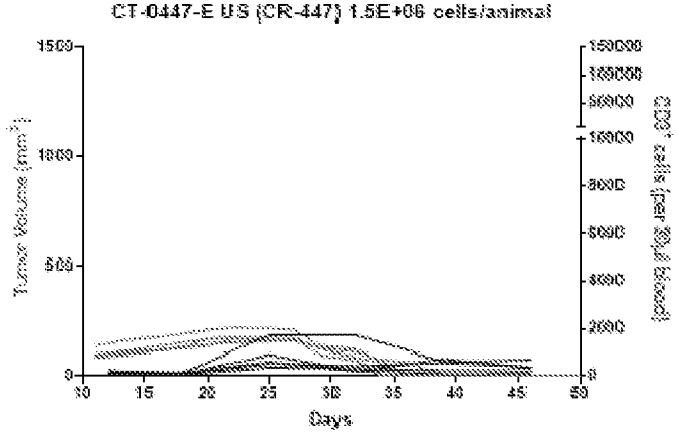

CT-0447-E US (CR-447) 1.5E+06 cells/animal
Tumor Volume (mm³)
CD3⁺ cells (per 30µl blood)
Days

FIG. 33


CT-0447-E US (CR-447) 1.5E+06 cells/animal
Tumor Volume (mm³)
CD3⁺ cells (per 30µl blood)
Days

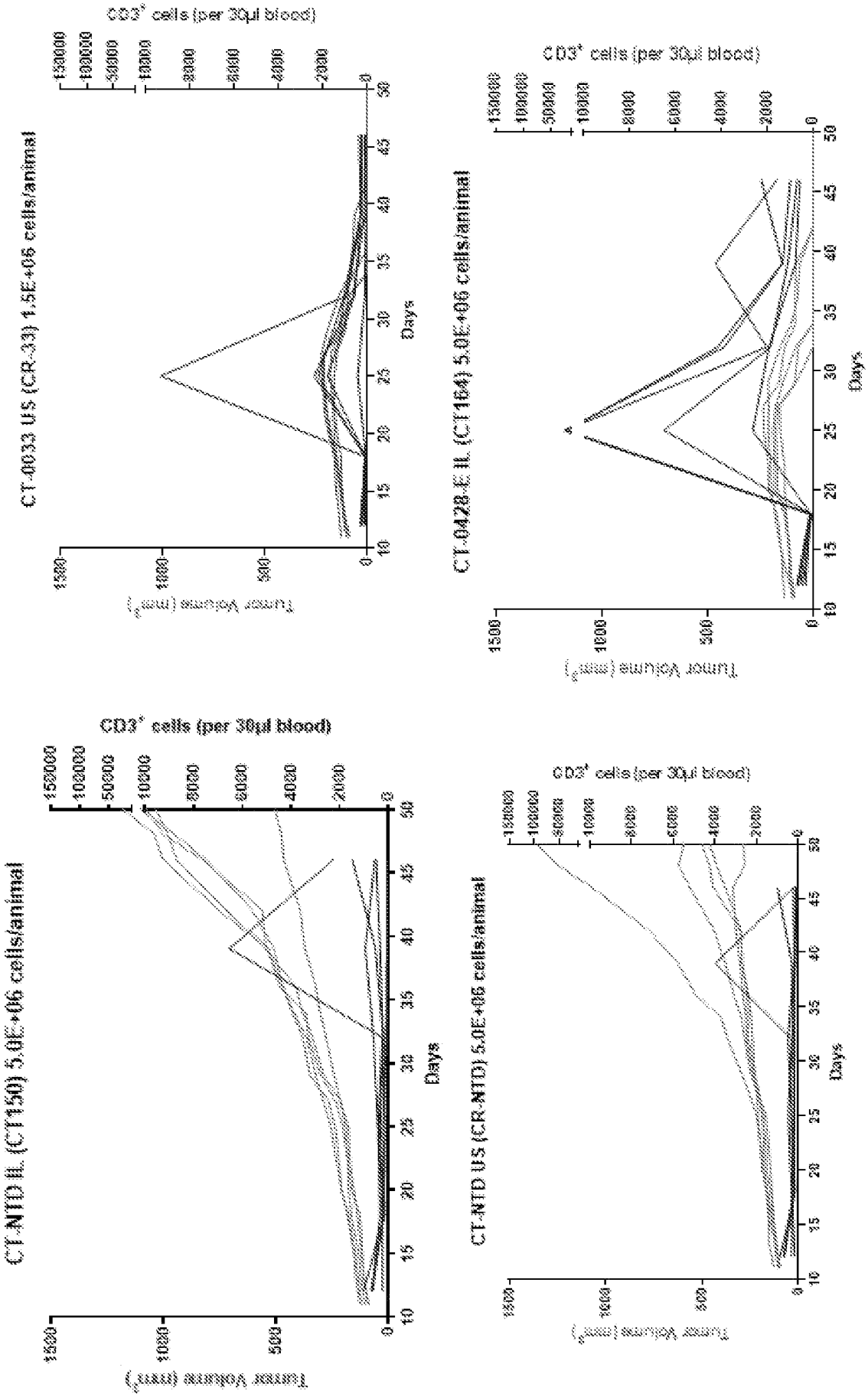

CT-0033 US (CR-33) 1.5E+06 cells/animal
CT-0428-E IL (CT164) 5.0E+06 cells/animal
CT-NTD IL (CT150) 5.0E+06 cells/animal
CT-NTD US (CR-NTD) 5.0E+06 cells/animal
CD3+ cells (per 30µl blood)
Tumor Volume (mm3)
Days

FIG. 34

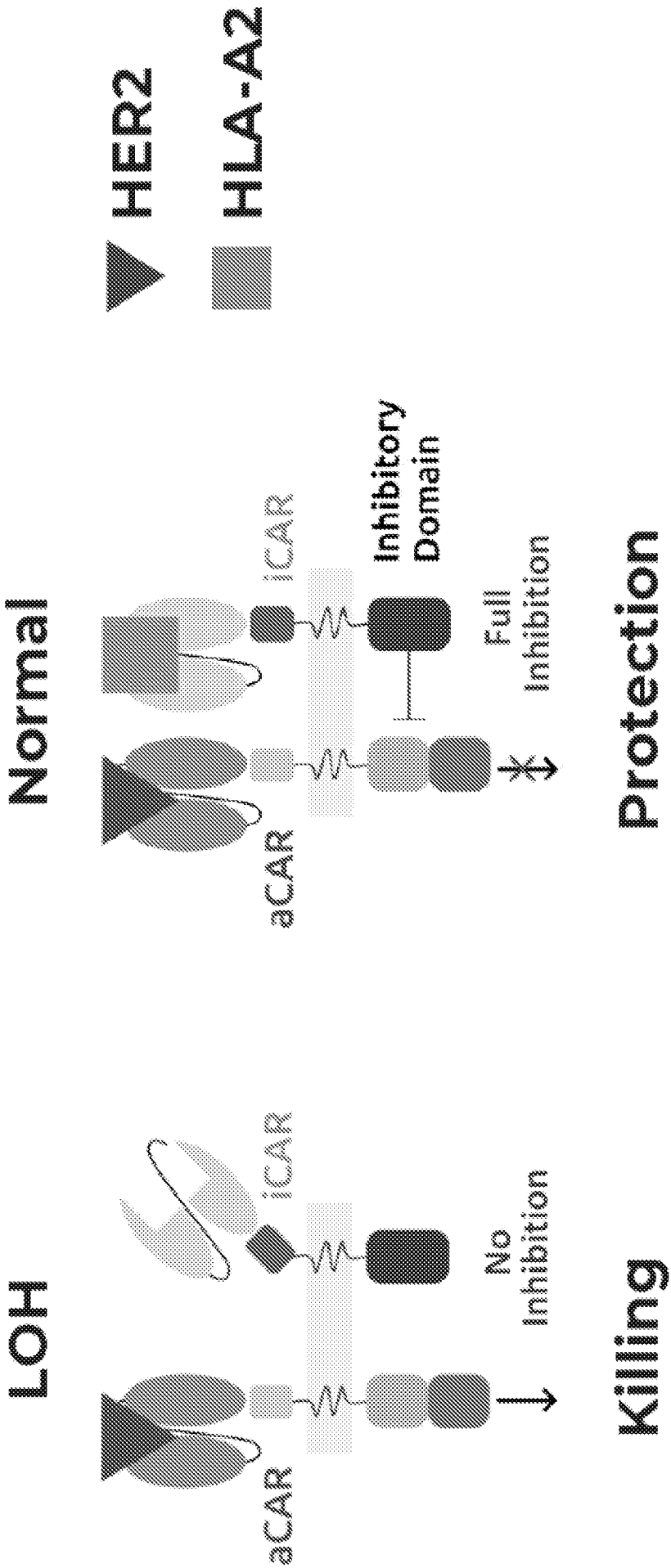
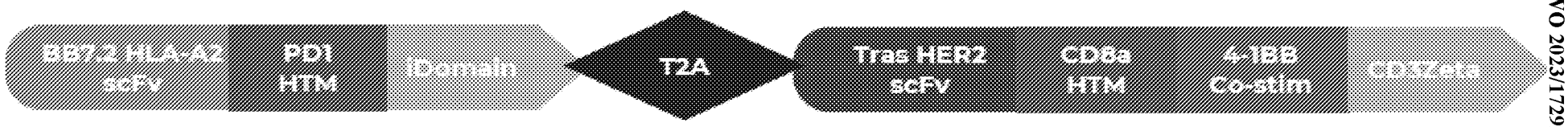

HER2
HLA-A2
Normal
aCAR
iCAR
Inhibitory Domain
Full Inhibition
Protection
LOH
aCAR
iCAR
No Inhibition
Killing

FIG. 35

A



B

Checkpoint	Inhibitory Ig & Immune Signaling			NK Receptors	
PD1	SIGLEC2/CD22	LAIR1	CD300A	KIR2DL1	LIR1
BTLA	SIGLEC3/CD33	CD160	CD300F	KIR2DL2	LIR2
LAG3	SIGLEC5	CEACAM1	PECAM1	KIR2DL3	LIR3
TIM3	SIGLEC6	SIRPα	CD300R1	KIR2DL4	LIR5
VISTA	SIGLEC7	FcγRIIB	FCRL1	KIR2DL5A	LIR8
TIGIT	SIGLEC8	CD5	FCRL2	KIR3DL1	2B4/CD244
	SIGLEC9	Ly9	FCRL3	KIR3DL2	
	SIGLEC10		FCRL5	KIR3DL3	
	SIGLEC11		FCRL14		
	SIGLEC12		SLAMF1		
			SLAMF5		

C

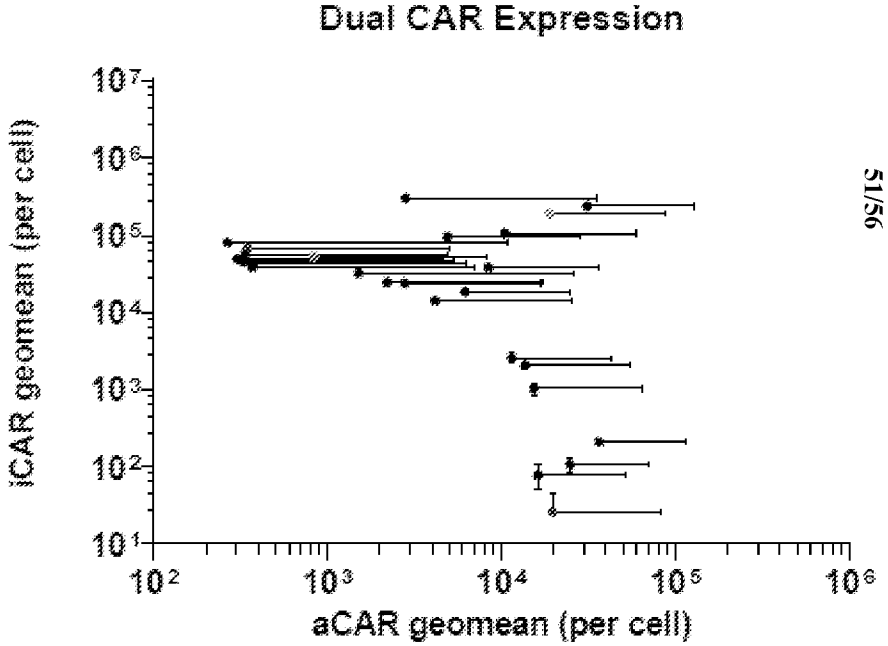


FIG. 36

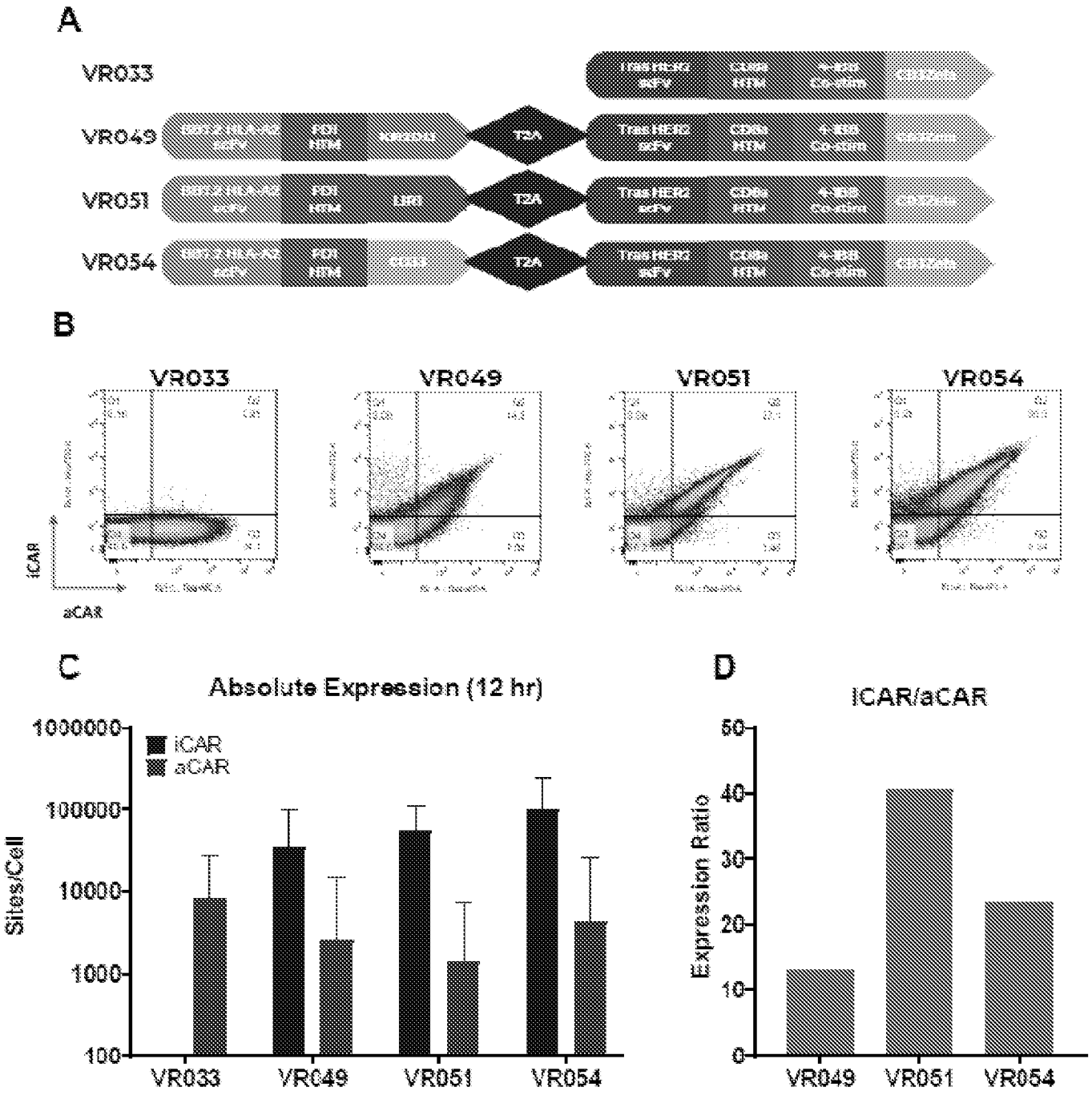
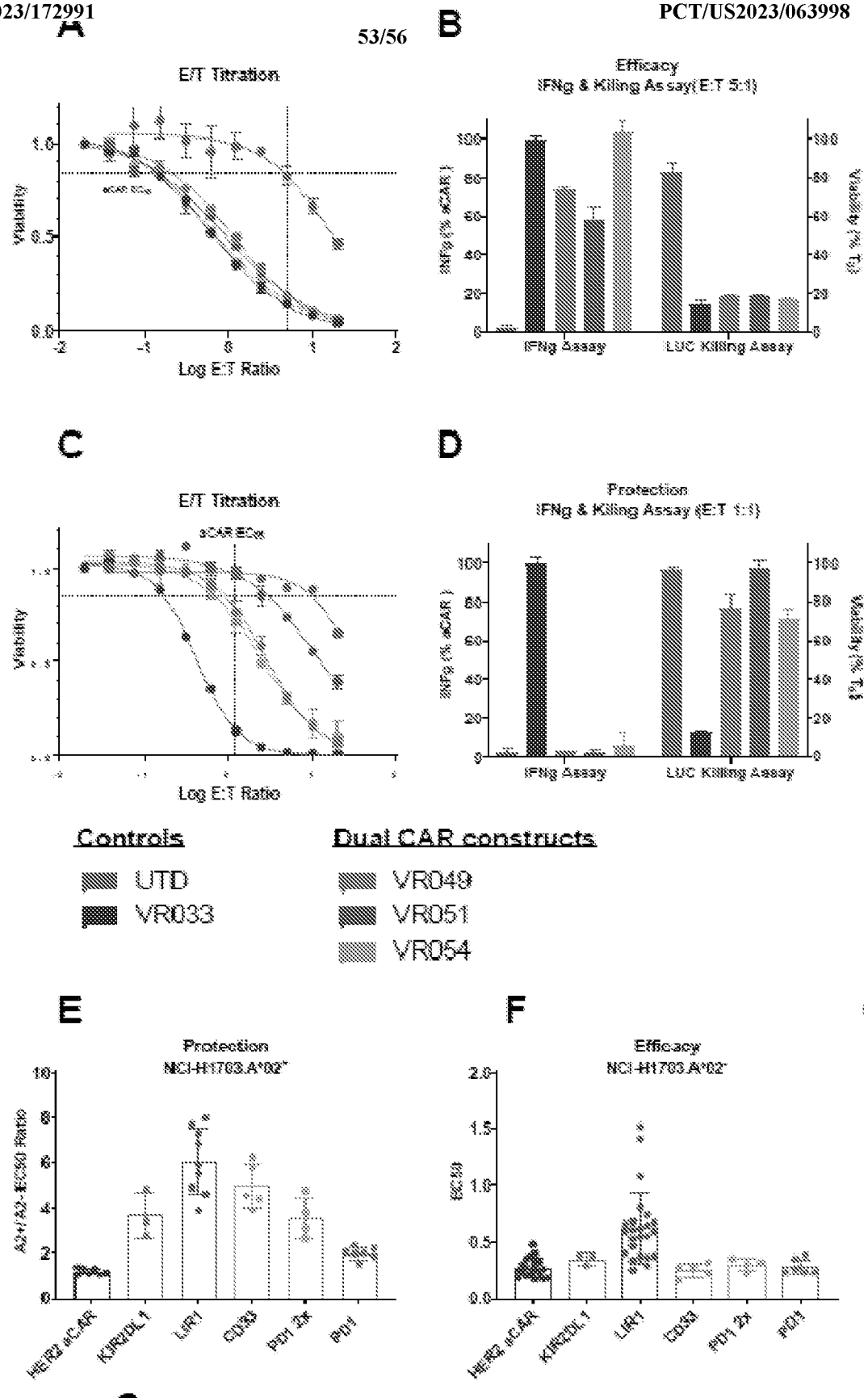

A
VR033
VR049
VR051
VR054
T2A
B
VR033
VR049
VR051
VR054
iCAR
aCAR
C
Absolute Expression (12 hr)
iCAR
aCAR
Sites/Cell
1000000
100000
10000
1000
100
VR033
VR049
VR051
VR054
D
ICAR/aCAR
Expression Ratio
50
40
30
20
10
0
VR049
VR051
VR054

FIG. 37



G

Cell line	HLA-A*02 sfreq/cell	HER2 sfreq/cell
NCI-H1650.A*02+	761345	51545
NCI-H1650.A*02-	NA	
NCI-H1703.A*02+	831304	17346
NCI-H1703.A*02-	NA	
FaDu	NA	39783

FIG. 38

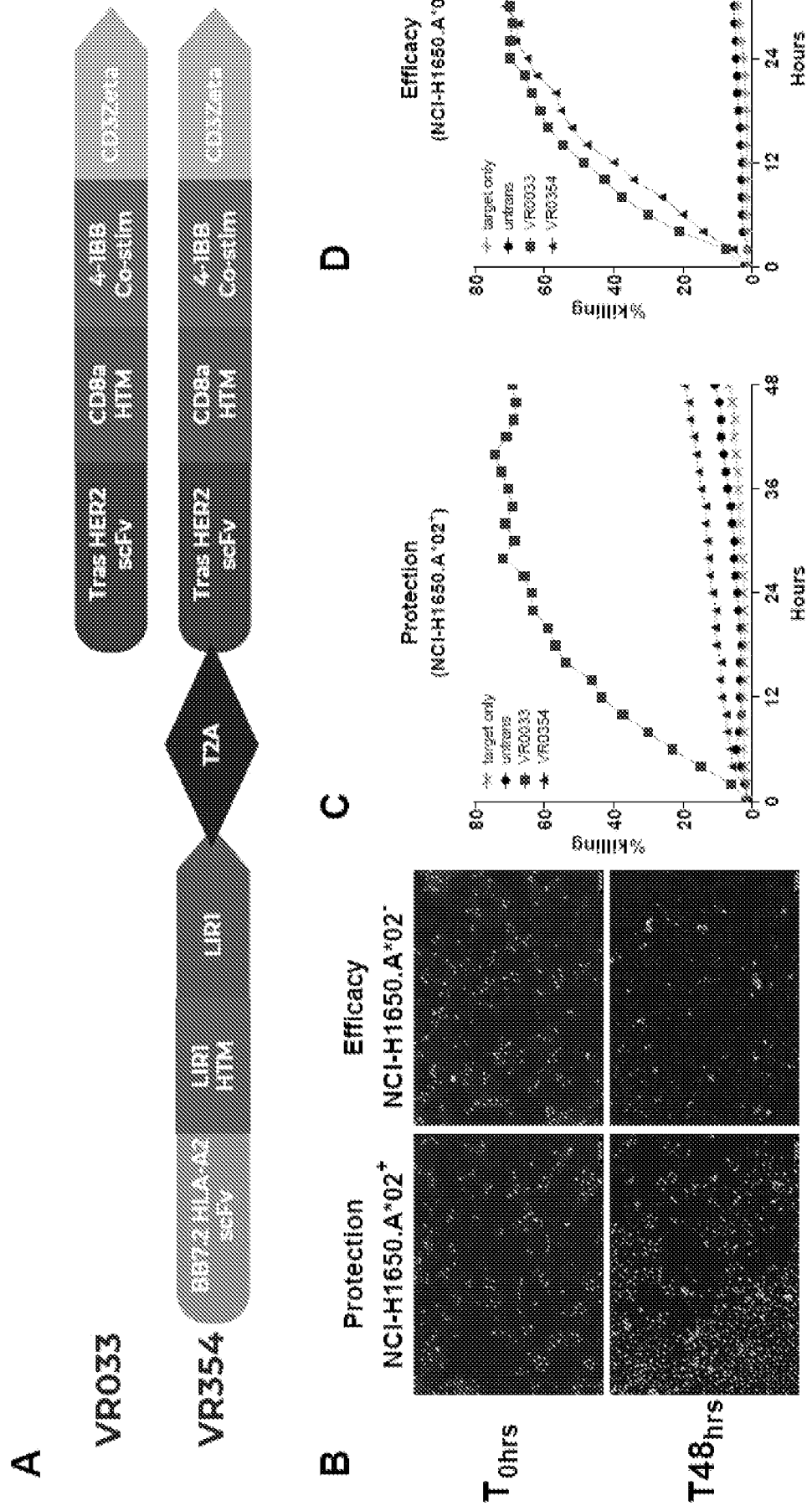

A
VR033
Tras H3Z2 scFv
CD8a HTM
4-1BB Co-stim
CD3zeta
VR354
BB7.2 HLA-A*02 scFv
LIR1 HTM
LIR1
T2A
Tras H3Z2 scFv
CD8a HTM
4-1BB Co-stim
CD3zeta
B
Protection NCI-H1650.A*02+
Efficacy NCI-H1650.A*02-
T0hrs
T48hrs
C
Protection (NCI-H1650.A*02+)
%killing
Hours
target only
untrans
VR033
VR354
D
Efficacy (NCI-H1650.A*02-)
%killing
Hours
target only
untrans
VR033
VR354

FIG. 39

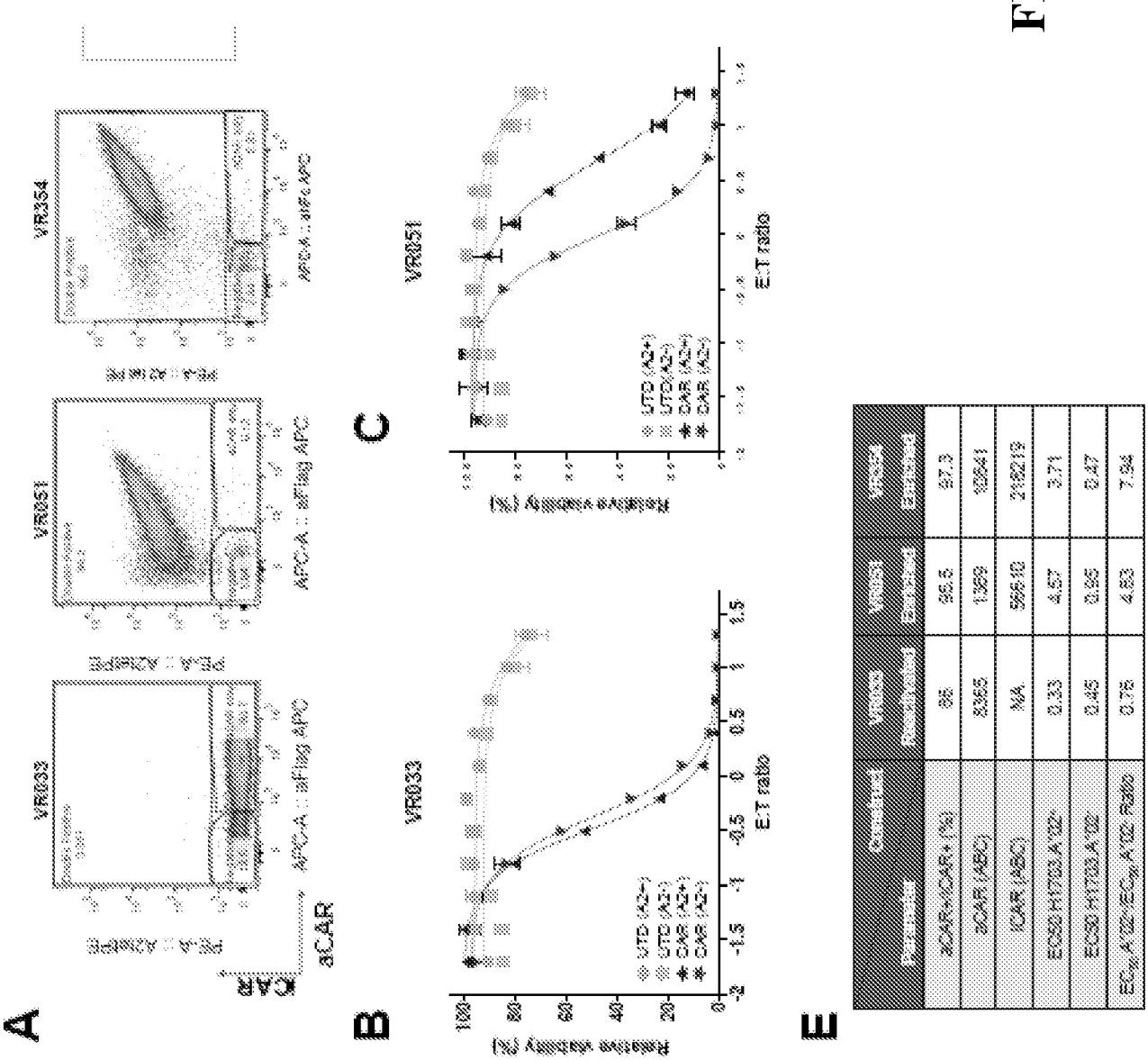


FIG. 40

E

Parameter	Donor Matched	VR033	VR051	VR354
aCAR+/CAR+ (%)	86	86.6	87.3	
aCAR (ABC)	8365	1389	12641	
CAR (ABC)	NA	96610	218219	
EC50 H1703A102	0.33	4.57	3.71	
EC50 H1703A102	0.45	0.95	0.47	
EC_{50} A102/EC_{50} A102 R360	0.76	4.83	7.94	

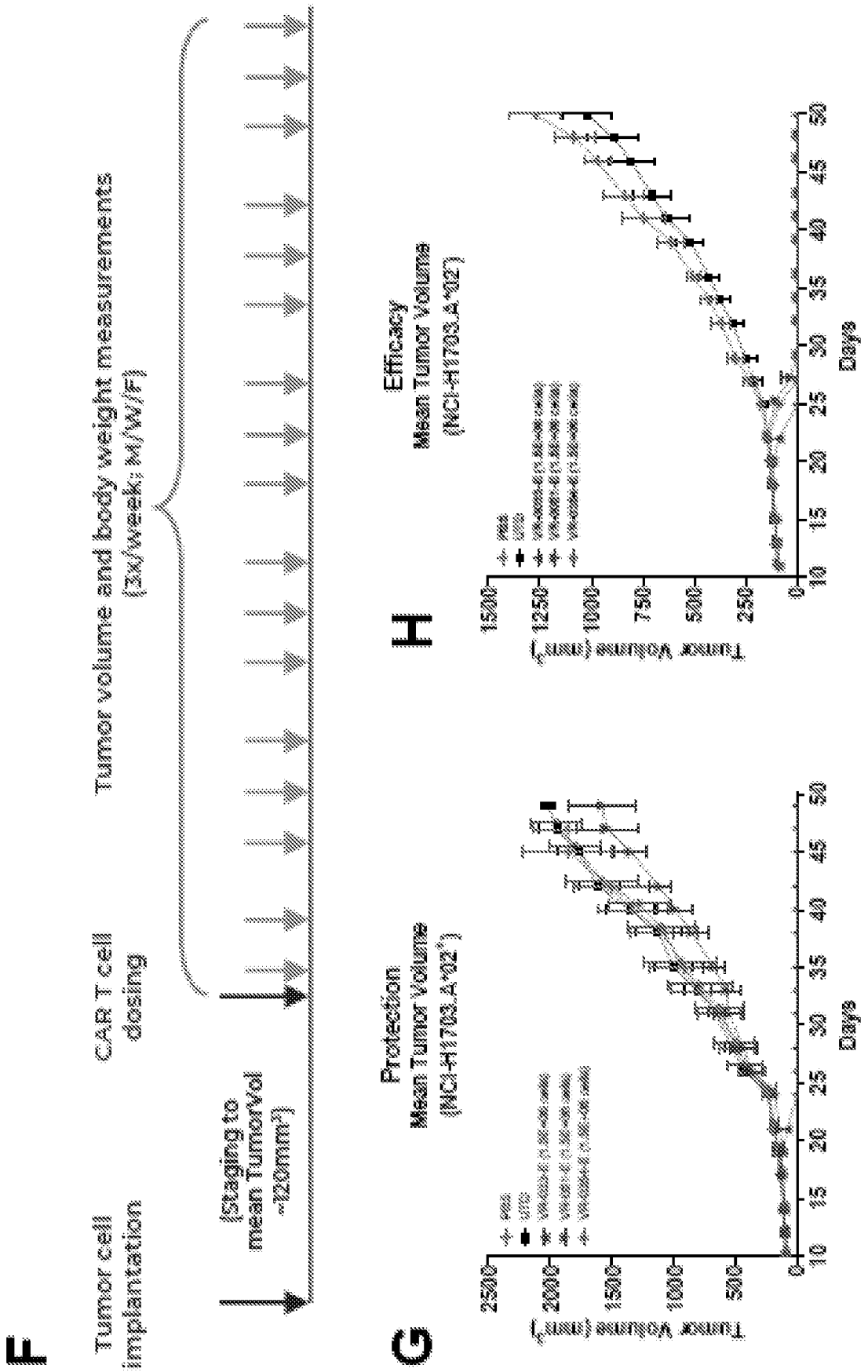

F
Tumor cell implantation
CAR T cell dosing
Tumor volume and body weight measurements (3x/week; M/W/F)
(Staging to mean TumorVol ~120mm³)
G
Protection
Mean Tumor Volume (NCI-H1703.A*02¹)
Tumor Volume (mm³)
Days
H
Efficacy
Mean Tumor Volume (NCI-H1703.A*02¹)
Tumor Volume (mm³)
Days

FIG. 40 [Cont'd.]