WHAT IS CLAIMED:

1. An immune cell comprising:

(a) a chimeric antigen receptor (CAR) comprising:

(i) an extracellular target-binding domain comprising an antibody moiety (a CAR antibody moiety);

(ii) a transmembrane domain (a CAR transmembrane domain); and

(iii) a primary signaling domain, and

(b) a chimeric stimulating receptor (CSR) comprising:

(i) a ligand-binding module that is capable of binding or interacting with a target ligand;

(ii) a transmembrane domain (a CSR transmembrane domain); and

(iii) a CD30 costimulatory domain,

wherein the CSR lacks a functional primary signaling domain.

2. The immune cell of claim 1, wherein the CD30 costimulatory domain comprises a sequence that can bind to an intracellular TRAF signaling protein, optionally wherein the sequence that can bind to an intracellular TRAF signaling protein corresponds to residues 561–573 or 578–586 of a full-length CD30 having the sequence of SEQ ID NO:65.

3. The immune cell of claim 1 or 2, wherein the CD30 costimulatory domain comprises a sequence that is at least 80%, 85%, 90%, 95%, or 100% identical to residues 561–573 or 578–586 of SEQ ID NO:65; or wherein the CD30 costimulatory domain comprises a sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, or 100% identical to the sequence of SEQ ID NO:75.

4. The immune cell of any one of claims 1 to 3, wherein the CSR comprises more than one CD30 costimulatory domain.

5. The immune cell of any one of claims 1 to 4, wherein the CSR further comprises at least one costimulatory domain which comprises the intracellular sequence of a costimulatory molecule that is different from CD30, optionally wherein the costimulatory molecule that is different from CD30 is selected from the group consisting of CD27, CD28, 4-1BB (CD137), OX40, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1

(LFA-1), CD2, CD7, LIGHT, NKG2C, B7-H3, and a ligand that specifically binds with CD83.

6. The immune cell of any one of claims 1 to 5, wherein the CAR further comprises a costimulatory domain (a CAR costimulatory domain), optionally wherein the CAR costimulatory domain is derived from the intracellular domain of a costimulatory receptor, and further optionally wherein the costimulatory receptor is selected from the group consisting of CD30, CD27, CD28, 4-1BB (CD137), OX40, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LIGHT, NKG2C, B7-H3, and a ligand that specifically binds with CD83.

7. The immune cell of any one of claims 1 to 6, wherein (a) the ligand-binding module of the CSR is derived from the extracellular domain of a receptor; or (b) the ligand-binding module of the CSR comprises an antibody moiety (a CSR antibody moiety), optionally wherein the CSR antibody moiety is a single chain antibody fragment.

8. The immune cell of any one of claims 1 to 7, wherein the CAR antibody moiety is a single chain antibody fragment; and/or wherein the CAR antibody moiety and/or the CSR antibody moiety is a single chain Fv (scFv), a single chain Fab, a single chain Fab', a single domain antibody fragment, a single domain multispecific antibody, an intrabody, a nanobody, or a single chain immunokine.

9. The immune cell of any one of claims 1 to 8, wherein the CAR antibody moiety and/or the CSR antibody moiety specifically binds to a disease-related antigen, optionally wherein the disease-related antigen is a cancer-related antigen or a virus-related antigen.

10. The immune cell of any one of claims 1 to 9, wherein the CAR antibody moiety and/or the CSR antibody moiety specifically binds to a cell surface antigen, optionally wherein the cell surface antigen is selected from the group consisting of protein, carbohydrate, and lipid; and/or optionally wherein the cell surface antigen is CD19, CD20, CD22, CD47, CD158e, GPC3, ROR1, ROR2, BCMA, GPRC5D, FcRL5, MUC16, MCT4, PSMA, or a variant or mutant thereof.

11. The immune cell of any one of claims 1 to 10, (a) wherein the CAR antibody moiety and the CSR antibody moiety specifically bind to the same antigen; or (b)

wherein the CAR antibody moiety and/or the CSR antibody moiety specifically binds to a MHC-restricted antigen, optionally wherein the MHC-restricted antigen is a complex comprising a peptide and an MHC protein, and wherein the peptide is derived from a protein selected from the group consisting of WT-1, AFP, GPC3, HPV16-E7, NY-ESO-1, PRAME, EBV-LMP2A, HIV-1, KRAS, FoxP3, Histone H3.3, PSA, ROR1, and a variant or mutant thereof.

12. The immune cell of any one of claims 1 to 11, wherein:

(a) the CAR antibody moiety binds to CD19, and wherein the ligand-binding module of the CSR binds to CD19; or

(b) the CAR antibody moiety binds to CD22, and wherein the ligand-binding module of the CSR binds to CD22; or

(c) the CAR antibody moiety binds to CD20, and wherein the ligand-binding module of the CSR binds to CD20; or

(d) the CAR antibody moiety binds to CD19, and wherein the ligand-binding module of the CSR binds to CD22; or

(e) the CAR antibody moiety binds to CD19, and wherein the ligand-binding module of the CSR binds to CD20; or

(f) the CAR antibody moiety binds to CD22, and wherein the ligand-binding module of the CSR binds to CD20;

(g) the CAR antibody moiety binds to CD22, and wherein the ligand-binding module of the CSR binds to CD19; or

(h) the CAR antibody moiety binds to CD20, and wherein the ligand-binding module of the CSR binds to CD19; or

(i) the CAR antibody moiety binds to CD20, and wherein the ligand-binding module of the CSR binds to CD22; or

(j) the CAR antibody moiety and/or the ligand-binding module of the CSR binds to both CD19 and CD22; or

(k) the CAR antibody moiety and/or the ligand-binding module of the CSR binds to both CD19 and CD20; or

(l) the CAR antibody moiety and/or the ligand-binding module of the CSR binds to both CD20 and CD22; or

(m) the CAR antibody moiety and/or the ligand-binding module of the CSR binds to CD19, CD20, and CD22.

13. The immune cell of any one of claims 1 to 12, wherein:

(a) the CAR antibody moiety specifically binds to a complex comprising an alpha-fetoprotein (AFP) peptide and an MHC class I protein; or

(b) the CAR antibody moiety specifically binds to glypican 3 (GPC3); or

(c) the ligand-binding module of the CSR specifically binds to GPC3; or

(d) the CAR antibody moiety binds to a complex comprising an AFP peptide and an MHC class I protein, and wherein the ligand-binding module of the CSR binds to GPC3; or

(e) both the CAR antibody moiety and the ligand-binding module of the CSR bind to GPC3; or

(f) the CAR antibody moiety and the ligand-binding module of the CSR specifically bind to different epitopes on GPC3; or

(g) the CAR antibody moiety specifically binds to a complex comprising a KRAS peptide and an MHC class I protein; or

(h) the CAR antibody moiety specifically binds to a complex comprising a PSA peptide and an MHC class I protein; or

(i) the CAR antibody moiety specifically binds to a complex comprising a PSMA peptide and an MHC class I protein; or

(j) the CAR antibody moiety and/or the ligand-binding module of the CSR bind to ROR1; or

(k) the CAR antibody moiety specifically binds to a complex comprising a NY-ESO-1 peptide and an MHC class I protein; or

(l) the CAR antibody moiety specifically binds to a complex comprising a PRAME peptide and an MHC class I protein; or

(m) the CAR antibody moiety specifically binds to a complex comprising a WT1 peptide and an MHC class I protein; or

(n) the CAR antibody moiety specifically binds to a complex comprising a histone H3.3 peptide and an MHC class I protein; or

(o) the ligand-binding module of the CSR binds to an MSLN peptide; or

(p) the ligand-binding module of the CSR binds to a ROR2 peptide; or

(q) the ligand-binding module of the CSR binds to a HER2 peptide; or

(r) the ligand-binding module of the CSR binds to an EpCAM peptide; or

(s) the ligand-binding module of the CSR binds to a MUC1 peptide; or

(t) the ligand-binding module of the CSR binds to a MUC16 peptide; or

(u) the ligand-binding module of the CSR binds to an FRα peptide; or

(v) the ligand-binding module of the CSR binds to an EGFRVIII peptide; or

(w) the ligand-binding module of the CSR binds to an HER3 peptide; or

(x) the ligand-binding module of the CSR binds to a DLL3 peptide; or

(y) the ligand-binding module of the CSR binds to a c-Met peptide; or

(z) the ligand-binding module of the CSR binds to a CD70 peptide.

14. The immune cell of any one of claims 1 to 13, wherein:

(a) the CAR transmembrane domain is the transmembrane domain of CD30; or

(b) the CAR transmembrane domain is the transmembrane domain of CD8; and/or

(c) the CSR transmembrane domain is derived from the transmembrane domain of a TCR co-receptor or a T cell co-stimulatory molecule, optionally wherein the TCR co-receptor or T cell co-stimulatory molecule is selected from the group consisting of CD8, 4-1BB, CD27, CD28, CD30, OX40, CD3ε, CD3ζ, CD45, CD4, CD5, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, and CD154; or

(d) the CAR transmembrane domain and/or the CSR transmembrane domain is the transmembrane domain of CD8, 4-1BB, CD27, CD28, CD30, OX40, CD3ε, CD3ζ, CD45, CD4, CD5, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, or CD154; and/or

(e) the CAR transmembrane domain and/or the CSR transmembrane domain comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:66-71.

15. The immune cell of any one of claims 1 to 14, wherein:

(a) the primary signaling domain comprises a sequence derived from the intracellular signaling sequence of a molecule selected from the group consisting of CD3ζ, TCRζ, FcRγ, FcRβ, CD3γ, CD3δ, CD3ε, CD5, CD22, CD79a, CD79b, and CD66d; and/or

(b) the primary signaling domain comprises a sequence that is at least 80%, 85%, 90%, 95%, or 100% identical to the sequence of SEQ ID NO:77.

16. The immune cell of any one of claims 1 to 15, further comprises a peptide linker between the extracellular target-binding domain and the transmembrane domain of the CAR; and/or further comprises a peptide linker between the transmembrane domain and the costimulatory domain of the CAR; and/or further comprises a peptide linker between the costimulatory domain and the primary signaling domain of the CAR; and/or further comprises a peptide linker between the ligand-binding module and the transmembrane domain of the CSR; and/or further comprises a peptide linker between the transmembrane domain and the CD30 costimulatory domain of the CSR.

17. The immune cell of any one of claims 1 to 16, wherein the expression of the CSR is inducible, optionally wherein the expression of the CSR is inducible upon activation of the immune cell.

18. The immune cell of any one of claims 1 to 17, wherein the immune cell is selected from the group consisting of a cytotoxic T cell, a helper T cell, a natural killer T cell, and a suppressor T cell.

19. One or more nucleic acids encoding the CAR and CSR comprised by the immune cell of any one of claims 1 to 18, wherein the CAR and CSR each consist of one or more polypeptide chains encoded by the one or more nucleic acids.

20. One or more vectors comprising the one or more nucleic acids of claim 19.

21. A pharmaceutical composition comprising: (a) the immune cell of any one of claims 1 to 18, the nucleic acid(s) of claim 19, or the vector(s) of claim 20, and (b) a pharmaceutically acceptable carrier or diluent.

22. A method of killing target cells, comprising:

contacting one or more target cells with the immune cell of any one of claims 1 to 18 under conditions and for a time sufficient so that the immune cells mediate killing of the target cells,

wherein the target cells express an antigen specific to the immune cell, and

wherein the immune cell expresses a low cell exhaustion level upon contacting the target cells,

optionally wherein the immune cell is a T cell; and/or

optionally wherein the target cells are cancer cells.

23. The method of claim 22, wherein:

(a) the immune cell expresses a low cell exhaustion level of an exhaustion marker selected from the group consisting of PD-1, TIM-3, TIGIT, and LAG-3; and/or

(b) the immune cell expresses a lower level of PD-1, TIM-3, TIGIT, or LAG-3 than corresponding immune cell expressing a CSR comprising a CD28 costimulatory domain; and/or

(c) the immune cell expresses a lower level of PD-1, TIM-3, TIGIT, or LAG-3 than corresponding immune cell expressing a CSR comprising a 4-1BB costimulatory domain.

24. The method of claim 22 or 23, wherein:

(a) the cancer cells are from a cancer selected from the group consisting of adrenocortical carcinoma, bladder cancer, breast cancer, cervical cancer, cholangiocarcinoma, colorectal cancers, esophageal cancer, glioblastoma, glioma, hepatocellular carcinoma, head and neck cancer, kidney cancer, leukemia, lymphoma, lung cancer, melanoma, mesothelioma, multiple myeloma, pancreatic cancer, pheochromocytoma, plasmacytoma, neuroblastoma, ovarian cancer, prostate cancer, sarcoma, stomach cancer, uterine cancer, and thyroid cancer; and/or

(b) the cancer cells are hematological cancer cells; or

(c) the cancer cells are solid tumor cells.

25. The method of any one of claims 22 to 24, wherein the target cells are virus-infected cells, optionally wherein the virus-infected cells are from a viral infection caused by a virus selected from the group consisting of Cytomegalovirus (CMV), Epstein-Barr Virus (EBV), Hepatitis B Virus (HBV), Kaposi's Sarcoma associated herpesvirus (KSHV), Human papillomavirus (HPV), Molluscum contagiosum virus (MCV), Human T cell leukemia virus 1 (HTLV-1), HIV (Human immunodeficiency virus), and Hepatitis C Virus (HCV).

26. The immune cell of any one of claims 1 to 18, the nucleic acid(s) of claim 19, or the vector(s) of claim 20, or the pharmaceutical composition of claim 21 for use in therapy.

27. Use of the immune cell of any one of claims 1 to 18, the nucleic acid(s) of claim 19, or the vector(s) of claim 20, or the pharmaceutical composition of claim 21 in the manufacture of a medicament for treating a disease in a subject, wherein the disease is a

viral infection or cancer, optionally wherein the cancer is a hematological cancer or a solid tumor cancer; and/or optionally wherein the cancer is selected from the group consisting of adrenocortical carcinoma, bladder cancer, breast cancer, cervical cancer, cholangiocarcinoma, colorectal cancers, esophageal cancer, glioblastoma, glioma, hepatocellular carcinoma, head and neck cancer, kidney cancer, leukemia, lymphoma, lung cancer, melanoma, mesothelioma, multiple myeloma, pancreatic cancer, pheochromocytoma, plasmacytoma, neuroblastoma, ovarian cancer, prostate cancer, sarcoma, stomach cancer, uterine cancer, and thyroid cancer.

28. The use of claim 27, wherein:

(a) the subject has a higher density of the immune cell of any one of claims 1 to 18 in the solid tumor cancer than in the rest of the subject's body; and/or

(b) the subject has a higher density of the immune cell of any one of claims 1 to 18 in the peripheral blood of the subject as compared to treating the same type of disease with same number of immune cells expressing the same CAR and a corresponding CSR comprising a CD28 or 4-1BB costimulatory domain.

29. Use of the nucleic acid(s) of claim 19, or the vector(s) of claim 20, or the pharmaceutical composition of claim 21 comprising the nucleic acid(s) or the vector(s) in the manufacture of a medicament for preventing and/or reversing T cell exhaustion in a subject, optionally wherein the expression of an exhaustion marker in a T cell is decreased, further optionally wherein the exhaustion marker is selected from the group consisting of PD-1, TIM-3, TIGIT, and LAG-3.

30. Use of corresponding immune cells and a corresponding CSR comprising a CD30 costimulatory domain in the manufacture of a medicament for treating a solid tumor cancer in a subject with increased tumor infiltration as compared to treating the same type of solid tumor cancer with immune cells expressing a CAR and a CSR comprising a CD28 or 4-1BB costimulatory domain, wherein the corresponding immune cells express the same CAR, and wherein the corresponding immune cells comprise the immune cell of any one of claims 1 to 18.

31. Use of corresponding immune cells and a corresponding CSR comprising a CD30 costimulatory domain in the manufacture of a medicament for treating a

solid tumor cancer in a subject with increased tumor regression as compared to treating the same type of solid tumor cancer with immune cells expressing a CAR and a CSR comprising a CD28 or 4-1BB costimulatory domain, wherein the corresponding immune cells express the same CAR, and wherein the corresponding immune cells comprise the immune cell of any one of claims 1 to 18.

32. Use of the nucleic acid(s) of claim 19, or the vector(s) of claim 20, or the pharmaceutical composition of claim 21 comprising the nucleic acid(s) or the vector(s) in the manufacture of a medicament for generating central memory T cells in a subject, optionally wherein the number of central memory T cells and/or the percentage of central memory T cells among all T cells in the subject is increased.

33. A method for generating central memory T cells *in vitro* comprising: contacting one or more target cells with the immune cell of any one of claims 1 to 18 under conditions and for a time sufficient so that the immune cell develops into central memory T cells, wherein the target cells express an antigen specific to the immune cell.

34. The method of claim 33, wherein:

(a) the method increases the number of central memory T cells and/or the percentage of central memory T cells among all T cells decended from the immune cell; and/or

(b) the method generates higher number of central memory T cells and/or higher percentage of central memory T cells than corresponding immune cell expressing a CSR comprising a CD28 costimulatory domain, optionally wherein the method generates at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, 200%, 300%, 400%, or 500% higher number of central memory T cells and/or percentage of central memory T cells than corresponding immune cell expressing a CSR comprising a CD28 costimulatory domain.

35. The method of any one of claims 33 or 34, wherein the central memory T cells express high levels of CCR7 and low levels of CD45RA; and/or wherein the central memory T cells are $CD8^+$ T cells.

36. Corresponding immune cells and a corresponding CSR comprising a CD30 costimulatory domain for use in therapy, wherein the corresponding immune cells

express the same CAR as a solid tumor cancer with immune cells expressing a CAR and a CSR comprising a CD28 or 4-1BB costimulatory domain.