CLAIMS

~~What is claimed is:~~

1. ~~An isolated~~A nucleic acid ~~comprising a nucleic acid sequence~~ encoding ~~(a)~~

a T-cell receptor (TCR) comprising an α ~~isolated~~ chain and a β chain and a CD8 polypeptide comprising an α chain ~~and a β chain, or (b) a TCR comprising an α chain and a β chain and a CD8 polypeptide comprising an α chain without a β chain~~, wherein the ~~TCR~~CD8 α chain ~~and the TCR β chain are selected from~~comprises an amino acid sequence at least 98% to SEQ ID NO: ~~15 and 16, 17 and 18, 19 and 20, 21 and 22, 23 and 24, 25 and 26, 27 and 28, 29 and 30, 31 and 32, 33 and 34, 35 and 36, 37 and 38, 39 and 40, 41 and 42, 43 and 44, 45 and 46, 47 and 48, 49 and 50, 51 and 52, 53 and 54, 55 and 56, 57 and 58, 59 and 60, 61 and 62, 63 and 64, 65 and 66, 67 and 68, 69 and 70, 71 and 303, 304 and 74, 75 and 76, 77 and 78, 79 and 80, 81 and 82, 83 and 84, 85 and 86, 87 and 88, 89 and 90, and 91 and 92, wherein the CD8 α chain is SEQ ID NO: 7, 258, 259, 262, or a variant thereof, and wherein the CD8 β chain is SEQ ID NO: 8, 9, 10, 11, 12, 13, or 14.~~5.

~~2. The isolated nucleic acid of claim 1, wherein the TCR α chain and the TCR β chain are selected from SEQ ID NO: 15 and 16, 57 and 58, 59 and 60, 61 and 62, 63 and 64, 65 and 66, 67 and 68, 69 and 70, and 71 and 303.~~

~~3.~~ 2. The ~~isolated~~ nucleic acid of claim 1 ~~or 2~~, wherein the nucleic acid sequence comprises a nucleic acid at least ~~80~~90% identical to the nucleic acid sequence of SEQ ID NO: ~~267, 269, 271, 273, 275, 277,~~ 279~~, 281, 283, 285, 287, 289, 291, 295, 297, 299, or 301~~.

~~4.~~ 3. The ~~isolated~~ nucleic acid of claim ~~3~~2, wherein the nucleic acid sequence is at least ~~90%, 91%, 92%, 93%, 94%,~~ 95~~%, 96%, 97%, 98%, 99%, or 100~~% identical to the nucleic acid sequence of SEQ ID NO: ~~267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 295, 297, 299, or 301~~279.

4. ~~5.~~ The ~~isolated~~ nucleic acid of ~~any one of claims~~claim 1 ~~4, wherein the nucleic acid comprises the nucleic acid sequence of SEQ ID NO: 267.~~

~~6. The isolated nucleic acid of any one of claims 1-4~~, wherein the nucleic acid comprises the nucleic acid sequence of SEQ ID NO: 279.

~~7. An isolated~~

5. A polypeptide encoded by the nucleic acid of ~~any one of claims 1-6~~claim 1.

6. ~~8. An isolated~~A polypeptide comprising ~~the~~an amino acid sequence at least about ~~80% identical to the amino acid sequence of SEQ ID NO: 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 296, 298, 300, or 302.~~

~~9. The isolated polypeptide of claim 8, wherein the amino acid sequence is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100~~90% identical to the amino acid sequence of SEQ ID NO: ~~268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 296, 298, 300, or 302.~~ 280.

~~10~~

7. The ~~isolated~~ polypeptide of ~~any one of claims 7-9~~claim 6, wherein the amino acid ~~comprises~~sequence is at least 95% identical to the amino acid sequence of SEQ ID NO: ~~268.~~280.

~~11~~

8. The ~~isolated~~ polypeptide of ~~any one of claims 7-9~~claim 6, wherein the amino acid comprises the amino acid sequence of SEQ ID NO: 280.

~~12~~

9. A vector comprising the nucleic acid of ~~any one of claims 1-6~~claim 1.

~~13~~

10. The vector of claim ~~12~~9, wherein the vector further comprises a nucleic acid encoding a 2A peptide or an internal ribosome entry site (IRES) positioned between the nucleic acid encoding the CD8 α chain and the nucleic acid encoding the CD8 β chain.

~~14~~

11. The vector of claim ~~12 or 13~~9, wherein the vector further comprises a nucleic acid encoding a 2A peptide or an IRES positioned between the nucleic acid encoding the TCR α chain and the nucleic acid encoding the TCR β chain.

~~15~~

12. The vector of claim ~~14~~11, wherein the 2A peptide is P2A (SEQ ID NO: 93), T2A (SEQ ID NO: 94), E2A (SEQ ID NO: 95), or F2A (SEQ ID NO: 96).

~~16~~

13. The vector of ~~any one of claims~~claim 12~~-15~~, wherein the vector further comprises a post-transcriptional regulatory element (PRE) sequence selected from a Woodchuck PRE (WPRE), Woodchuck PRE (WPRE) mutant 1, Woodchuck PRE (WPRE) mutant 2, or hepatitis B virus (HBV) PRE (HPRE).

~~17~~

14. The vector of claim ~~16~~13, wherein the post-transcriptional regulatory element (PRE) sequence ~~is~~comprises Woodchuck PRE (WPRE) mutant 1 comprising the amino acid sequence of SEQ ID NO: 256.

~~18~~

15. The vector of claim ~~16~~13, wherein the post-transcriptional regulatory element (PRE) sequence ~~is~~comprises Woodchuck PRE (WPRE) mutant 2 comprising the amino acid sequence of SEQ ID NO: 257.

~~19. The vector of any one of claims 12-18, wherein the vector further comprises a promoter selected from cytomegalovirus (CMV) promoter, phosphoglycerate kinase (PGK) promoter, myelin basic protein (MBP) promoter, glial fibrillary acidic protein (GFAP) promoter, modified MoMuLV LTR comprising myeloproliferative sarcoma virus enhancer (MNDU3), Ubiqitin C promoter, EF-1 alpha promoter, or Murine Stem Cell Virus (MSCV) promoter.~~

~~20. The vector of any one of claims 12-19, wherein the vector is a viral vector or a non-viral vector.~~

~~21. The vector of claim 20, wherein the vector is a viral vector.~~

~~22. The vector of claim 21, wherein the viral vector is selected from adenoviruses, poxviruses, alphaviruses, arenaviruses, flaviruses, rhabdoviruses, retroviruses, lentiviruses, herpesviruses, paramyxoviruses, picornaviruses, and combinations thereof.~~

~~23. The vector of claim 21 or 22, wherein the vector is pseudotyped with an envelope protein of a virus selected from the native feline endogenous virus (RD114), a version of RD114 (RD114TR), gibbon ape leukemia virus (GALV), a version of GALV (GALV-TR), amphotropic murine leukemia virus (MLV-4070A), baculovirus (GP64), vesicular stomatitis virus (VSV-G), fowl plague~~

~~virus (FPV), Ebola virus (EboV), or baboon retroviral envelope glycoprotein (BaEV), and lymphocytic choriomeningitis virus (LCMV).~~

~~24. The vector of any one of claims 12-23, wherein the vector is a lentiviral vector.~~

~~25. The vector of any one of claims 12-24, wherein the vector further comprises a nucleic acid encoding a chimeric antigen receptor (CAR).~~

~~26. An isolated T cell transduced with the nucleic acid of any one of claims 1-5.~~

~~27. An isolated T cell transduced to express the polypeptide of any one of claims 6-10.~~

~~28. An isolated T cell transduced with the vector of any one of claims 12-25.~~

~~29. The cell of any one of claims 26-28, wherein the cell is an αβ T cell, γδ T cell, and/or natural killer T cell.~~

~~30. The cell of claim 29, wherein the αβ T cell is a CD4+ T cell.~~

~~31. The cell of claim 29, wherein the αβ T cell is a CD8+ T cell.~~

~~32. The cell of claim 29, wherein the γδ T cell is a Vγ9Vδ2+ T cell.~~

~~33. A γδ T cell expressing the polypeptide of any one of claims 6-10.~~

~~34. A αβ T cell expressing the polypeptide of any one of claims 6-10.~~

~~35. A composition comprising the T cell of any one of claims 26-34.~~

~~36. The composition of claim 35, wherein the composition is a pharmaceutical composition.~~

~~37. The composition of claim 35 or 36, wherein the composition further comprises an adjuvant, excipient, carrier, diluent, buffer, stabilizer, or a combination thereof.~~

~~38. The composition of claim 35 or 36, wherein the composition further comprises an adjuvant.~~

~~39. The composition of claim 37 or 38, wherein the adjuvant is an anti-CD40 antibody, imiquimod, resiquimod, GM-CSF, cyclophosphamide, sunitinib, bevacizumab, atezolizumab, interferon-alpha, interferon-beta, CpG oligonucleotides and derivatives, poly(I:C) and derivatives, RNA, sildenafil, particulate formulations with poly(lactide co-glycolide) (PLG), virosomes, interleukin-1 (IL-1), interleukin-2 (IL-2), interleukin-4 (IL-4), interleukin-7 (IL-7), interleukin-12 (IL-12), interleukin-13 (IL-13), interleukin-15 (IL-15), interleukin-21 (IL-21), interleukin-23 (IL-23), and combinations thereof.~~

~~40~~

16. A method of preparing T cells for immunotherapy comprising

isolating T cells from a blood sample of a human subject,

activating the isolated T cells,

transducing the activated T cells with the nucleic acid of ~~any one of claims 1-6 or the vector of any one of claims 12-25~~claim 1, and

expanding the transduced T cells.

~~41~~

17. The method of claim ~~40~~16, wherein the blood sample comprises peripheral blood mononuclear cells (PMBC).

~~42~~

18. The ~~method~~nucleic acid of claim ~~40 or 41~~1, wherein the ~~activating comprises contacting the T cells with an anti-CD3 and an anti-CD28 antibody.~~

~~43. The method of any one of claims 40-42, wherein the T cell is CD4+ T cell.~~

~~44. The method of any one of claims 40-42, wherein the T cell is CD8+ T cell.~~

~~45. The method of claim 40 or 41, wherein the T cell is γδ T cell or αβ T cell.~~

~~46. The method of any one of claims 40-45, wherein the activation and/or expanding steps are in the presence of a combination of IL-2 and IL-15 and optionally with zoledronate.~~

~~47. A method of treating a patient who has cancer,~~ α chain further comprises a signal peptide comprising ~~administering to the patient the composition of any one of claims 35-39, wherein the cancer is selected from the group consisting of non-small cell lung cancer, small cell lung cancer, melanoma, liver cancer, breast cancer, uterine cancer, Merkel cell carcinoma, pancreatic cancer, gallbladder cancer, bile duct cancer, colorectal cancer, urinary bladder cancer, kidney cancer, leukemia, ovarian cancer, esophageal cancer, brain cancer, gastric cancer, and prostate cancer.~~

~~48. A method of eliciting an immune response in a patient who has cancer, comprising administering to the patient the composition of any one of claims 35-39, wherein the cancer is selected from the group consisting of non-small cell lung cancer, small cell lung cancer, melanoma, liver cancer, breast cancer, uterine cancer, Merkel cell carcinoma, pancreatic cancer, gallbladder cancer, bile duct cancer, colorectal cancer, urinary bladder cancer, kidney cancer, leukemia, ovarian cancer, esophageal cancer, brain cancer, gastric cancer, and prostate cancer.~~

~~49. The method of claim 47 or 48, wherein the T cells kill cancer cells that present a peptide in a complex with an MHC molecule on the surface, wherein the peptide consists of the amino acid sequence of SLLQHLIGL (~~SEQ ID NO: ~~147).~~294.

~~50~~

19. The ~~isolated~~ nucleic acid of ~~any one of claims~~claim 1~~-4~~, wherein

the ~~nucleic acid comprises the nucleic acid sequence of~~TCR α chain is SEQ ID NO: ~~285 or 301.~~15 and the TCR β chain is SEQ ID NO: 16, or

~~51. The isolated polypeptide of any one of claims 7-9, wherein the amino acid comprises the amino acid sequence of SEQ ID NO: 286 or 302.~~

~~52. The vector of claim 14, wherein the IRES is selected from the group consisting of IRES from picornavirus, IRES from flavivirus, IRES from pestivirus, IRES from retrovirus, IRES from lentivirus, IRES from insect RNA virus, and IRES from cellular mRNA.~~

~~53. The method of claim 40, further comprising isolating CD4+CD8+ T cells from the transduced T cells and expanding the isolated CD4+CD8+ transduced T cells.~~

the TCR α chain is SEQ ID NO: 23 and the TCR β chain is SEQ ID NO: 24, or

the TCR α chain is SEQ ID NO: 25 and the TCR β chain is SEQ ID NO: 26, or

the TCR α chain is SEQ ID NO: 27 and the TCR β chain is SEQ ID NO: 28, or

the TCR α chain is SEQ ID NO: 29 and the TCR β chain is SEQ ID NO: 30, or

the TCR α chain is SEQ ID NO: 31 and the TCR β chain is SEQ ID NO: 32, or

the TCR α chain is SEQ ID NO: 33 and the TCR β chain is SEQ ID NO: 34, or

the TCR α chain is SEQ ID NO: 35 and the TCR β chain is SEQ ID NO: 36, or

the TCR α chain is SEQ ID NO: 37 and the TCR β chain is SEQ ID NO: 38, or

the TCR α chain is SEQ ID NO: 39 and the TCR β chain is SEQ ID NO: 40, or

the TCR α chain is SEQ ID NO: 41 and the TCR β chain is SEQ ID NO: 42, or

the TCR α chain is SEQ ID NO: 43 and the TCR β chain is SEQ ID NO: 44, or

the TCR α chain is SEQ ID NO: 45 and the TCR β chain is SEQ ID NO: 46, or

the TCR α chain is SEQ ID NO: 47 and the TCR β chain is SEQ ID NO: 48, or

the TCR α chain is SEQ ID NO: 49 and the TCR β chain is SEQ ID NO: 50, or

the TCR α chain is SEQ ID NO: 51 and the TCR β chain is SEQ ID NO: 52, or
the TCR α chain is SEQ ID NO: 53 and the TCR β chain is SEQ ID NO: 54, or
the TCR α chain is SEQ ID NO: 55 and the TCR β chain is SEQ ID NO: 56, or
the TCR α chain is SEQ ID NO: 57 and the TCR β chain is SEQ ID NO: 58, or
the TCR α chain is SEQ ID NO: 59 and the TCR β chain is SEQ ID NO: 60, or
the TCR α chain is SEQ ID NO: 61 and the TCR β chain is SEQ ID NO: 62, or
the TCR α chain is SEQ ID NO: 63 and the TCR β chain is SEQ ID NO: 64, or
the TCR α chain is SEQ ID NO: 65 and the TCR β chain is SEQ ID NO: 66, or
the TCR α chain is SEQ ID NO: 67 and the TCR β chain is SEQ ID NO: 68, or
the TCR α chain is SEQ ID NO: 69 and the TCR β chain is SEQ ID NO: 70, or
the TCR α chain is SEQ ID NO: 71 and the TCR β chain is SEQ ID NO: 303, or
the TCR α chain is SEQ ID NO: 304 and the TCR β chain is SEQ ID NO: 74, or
the TCR α chain is SEQ ID NO: 75 and the TCR β chain is SEQ ID NO: 76, or
the TCR α chain is SEQ ID NO: 77 and the TCR β chain is SEQ ID NO: 78, or
the TCR α chain is SEQ ID NO: 79 and the TCR β chain is SEQ ID NO: 80, or
the TCR α chain is SEQ ID NO: 81 and the TCR β chain is SEQ ID NO: 82, or
the TCR α chain is SEQ ID NO: 83 and the TCR β chain is SEQ ID NO: 84, or
the TCR α chain is SEQ ID NO: 85 and the TCR β chain is SEQ ID NO: 86, or
the TCR α chain is SEQ ID NO: 87 and the TCR β chain is SEQ ID NO: 88, or
the TCR α chain is SEQ ID NO: 89 and the TCR β chain is SEQ ID NO: 90, or
the TCR α chain is SEQ ID NO: 91 and the TCR β chain is SEQ ID NO: 92.

20. The nucleic acid of claim 19, wherein
the TCR α chain is SEQ ID NO: 15 and the TCR β chain is SEQ ID NO: 16, or
the TCR α chain is SEQ ID NO: 57 and the TCR β chain is SEQ ID NO: 58, or
the TCR α chain is SEQ ID NO: 59 and the TCR β chain is SEQ ID NO: 60, or
the TCR α chain is SEQ ID NO: 61 and the TCR β chain is SEQ ID NO: 62, or
the TCR α chain is SEQ ID NO: 63 and the TCR β chain is SEQ ID NO: 64, or
the TCR α chain is SEQ ID NO: 65 and the TCR β chain is SEQ ID NO: 66, or

the TCR α chain is SEQ ID NO: 67 and the TCR β chain is SEQ ID NO: 68, or the TCR α chain is SEQ ID NO: 69 and the TCR β chain is SEQ ID NO: 70, or the TCR α chain is SEQ ID NO: 71 and the TCR β chain is SEQ ID NO: 303.