

WHAT IS CLAIMED IS:

1. A fusion polypeptide comprising:
 - a) an extracellular domain and a transmembrane domain of a co-stimulatory ligand, and
 - 5 b) an intracellular domain of a first co-stimulatory molecule.
2. The fusion polypeptide of claim 1, wherein the co-stimulatory ligand is selected from the group consisting of a tumor necrosis factor (TNF) family member, an immunoglobulin (Ig) superfamily member, and combinations thereof.
3. The fusion polypeptide of claim 2, wherein the TNF family member is selected
10 from the group consisting of 4-1BBL, OX40L, CD70, GITRL, CD40L, and combinations thereof.
4. The fusion polypeptide of claim 2, wherein the Ig superfamily member is selected from the group consisting of CD80, CD86, ICOSLG, and combinations thereof.
5. The fusion polypeptide of any one of claims 1, 2, and 4, wherein the co-
15 stimulatory ligand is CD80.
6. The fusion polypeptide of claim 5, wherein the extracellular domain of CD80 comprises an amino acid sequence that is at least about 85% homologous or identical to the amino acid sequence set forth in SEQ ID NO: 1.
7. The fusion polypeptide of claim 5 or 6, wherein the extracellular domain of
20 CD80 comprises or consists of the amino acid sequence set forth in SEQ ID NO: 1 or a functional fragment thereof.
8. The fusion polypeptide of any one of claims 5-7, wherein the transmembrane domain of CD80 comprises an amino acid sequence that is at least about 85% homologous or identical to the amino acid sequence set forth in SEQ ID NO: 2.
- 25 9. The fusion polypeptide of any one of claims 5-8, wherein the transmembrane domain of CD80 comprises or consists of the amino acid sequence set forth in SEQ ID NO: 2 or a fragment thereof.

10. The fusion polypeptide of any one of claims 1-9, wherein the first co-stimulatory molecule is selected from the group consisting of CD28, 4-1BB, OX40, ICOS, DAP-10, CD27, CD40, NKG2D, CD2, and combinations thereof.
11. The fusion polypeptide of any one of claims 1-10, wherein the first co-stimulatory molecule is 4-1BB.
12. The fusion polypeptide of claim 11, wherein the intracellular domain of 4-1BB comprises an amino acid sequence that is at least about 85% homologous or identical to the amino acid sequence set forth in SEQ ID NO: 3.
13. The fusion polypeptide of claim 11 or 12, wherein the intracellular domain of 4-1BB comprises or consists of the amino acid sequence set forth in SEQ ID NO: 3 or a functional fragment thereof.
14. The fusion polypeptide of any one of claims 1, 2, and 4-13, wherein the co-stimulatory ligand is CD80 and the first co-stimulatory molecule is selected from the group consisting of CD28, 4-1BB, OX40, ICOS, DAP-10, CD27, CD40, NKG2D, CD2, and combinations thereof.
15. The fusion polypeptide of claim 14, wherein the co-stimulatory ligand is CD80 and the first co-stimulatory molecule is 4-1BB.
16. The fusion polypeptide of claim 15, wherein the fusion polypeptide comprises an amino acid sequence that is at least about 85% homologous or identical to the amino acid sequence set forth in SEQ ID NO: 4.
17. The fusion polypeptide of claim 15 or 16, wherein the fusion polypeptide comprises or consists of the amino acid sequence set forth in SEQ ID NO: 4.
18. The fusion polypeptide of any one of claims 1-17, further comprising an intracellular domain of a second co-stimulatory molecule.
19. The fusion polypeptide of claim 18, wherein the second co-stimulatory molecule is selected from the group consisting of CD28, 4-1BB, OX40, ICOS, DAP-10, CD27, CD40, NKG2D, CD2, and combinations thereof.

20. The fusion polypeptide of claim 18 or 19, wherein the second co-stimulatory molecule is CD28.
21. The fusion polypeptide of claim 20, wherein the intracellular domain of CD28 comprises an amino acid sequence that is at least about 85% homologous or identical to the amino acid sequence set forth in SEQ ID NO: 5.
22. The fusion polypeptide of claim 20 or 21, wherein the intracellular domain of CD28 comprises or consists of the amino acid sequence set forth in SEQ ID NO: 5 or a functional fragment thereof.
23. The fusion polypeptide of any one of claims 18-22, wherein the co-stimulatory ligand is CD80, the first co-stimulatory molecule is 4-1BB, and the second co-stimulatory molecule is CD28.
24. The fusion polypeptide of claim 23, wherein the fusion polypeptide comprises an amino acid sequence that is at least about 85% homologous or identical to the amino acid sequence set forth in SEQ ID NO: 6.
25. The fusion polypeptide of claim 23 or 24, wherein the fusion polypeptide comprises or consists of the amino acid sequence set forth in SEQ ID NO: 6.
26. The fusion polypeptide of any one of claims 1-25, wherein the fusion polypeptide is capable of stimulating a cell comprising an antigen-recognizing receptor .
27. The fusion polypeptide of any one of claims 1-26, wherein the fusion polypeptide is capable of enhancing the activity of an immunoresponsive cell comprising an antigen-recognizing receptor.
28. The fusion polypeptide of claim 27, wherein the activity comprises cytotoxicity, cell proliferation, and cell persistence.
29. The fusion polypeptide of any one of claims 26-28, wherein the antigen-recognizing receptor is a chimeric antigen receptor (CAR), a T-Cell Receptor (TCR), or a TCR like fusion molecule.
30. The fusion polypeptide of any one of claims 1-29, further comprising a signaling domain of a cytokine receptor.

31. The fusion polypeptide of claim 30, wherein the cytokine receptor is selected from the group consisting of CD121a, CDw121b, IL-18Ra, IL18Rb, CD122, CD25, CD132, CD124, CD213a13, CD127, IL-9R, IL15Ra, CDw125, CDw131, CD126, CD130, IL11Ra, Cd114, CD212, CD4, CDw217, CD118, and CDw119.
- 5 32. A nucleic acid encoding a fusion polypeptide of any one of claims 1-31.
33. A vector comprising the nucleic acid of claim 32.
34. A cell comprising a fusion polypeptide of any one of claims 1-31, the nucleic acid of claim 30, or the vector of claim 33.
35. The cell of claim 34, further comprising an antigen-recognizing receptor that
10 binds to an antigen.
36. The cell of claim 35, wherein the antigen-recognizing receptor is a chimeric antigen receptor (CAR), a T cell receptor (TCR), or a TCR like fusion molecule.
37. The cell of claim 35, wherein the antigen is a tumor antigen or a pathogen antigen.
- 15 38. The cell of claim 37, wherein the antigen is a tumor antigen.
39. The cell of claim 37 or 38, wherein the tumor antigen is selected from CD19, carbonic anhydrase IX (CAIX), carcinoembryonic antigen (CEA), CD8, CD7, CD10, CD20, CD22, CD30, CD33, CLL1, CD34, CD38, CD41, CD44, CD49f, CD56, CD74, CD133, CD138, CD123, CD44V6, an antigen of a cytomegalovirus (CMV) infected cell
20 (e.g., a cell surface antigen), epithelial glycoprotein-2 (EGP-2), epithelial glycoprotein-40 (EGP-40), epithelial cell adhesion molecule (EpCAM), receptor tyrosine-protein kinases Erb-B2,3,4 (erb-B2,3,4), folate-binding protein (FBP), fetal acetylcholine receptor (AChR), folate receptor- α , Ganglioside G2 (GD2), Ganglioside G3 (GD3), human Epidermal Growth Factor Receptor 2 (HER-2), human telomerase reverse
25 transcriptase (hTERT), Interleukin-13 receptor subunit alpha-2 (IL-13R α 2), κ -light chain, kinase insert domain receptor (KDR), Lewis Y (LeY), L1 cell adhesion molecule (L1CAM), melanoma antigen family A, 1 (MAGE-A1), Mucin 16 (MUC16), Mucin 1 (MUC1), Mesothelin (MSLN), ERBB2, MAGEA3, p53, MART1, GP100, Proteinase3 (PR1), Tyrosinase, Survivin, hTERT, EphA2, NKG2D ligands, cancer-testis antigen NY-

- ESO-1, oncofetal antigen (h5T4), prostate stem cell antigen (PSCA), prostate-specific membrane antigen (PSMA), ROR1, tumor-associated glycoprotein 72 (TAG-72), vascular endothelial growth factor R2 (VEGF-R2), Wilms tumor protein (WT-1), BCMA, NKCS1, EGF1R, EGFR-VIII, CD99, CD70, ADGRE2, CCR1, LILRB2, PRAME CCR4, CD5, CD3, TRBC1, TRBC2, TIM-3, Integrin B7, ICAM-1, CD70, Tim3, CLEC12A, and ERBB.
40. The cell of any one of claims 37-39, wherein the tumor antigen is CD19.
41. The cell of any one of claims 35-40, wherein the antigen-recognizing receptor is exogenous or endogenous.
42. The cell of any one of claims 35-41, wherein the antigen-recognizing receptor is recombinantly expressed.
43. The cell of any one of claim 35-42, wherein the antigen-recognizing receptor is expressed from a vector.
44. The cell of any one of claims 34-43, wherein the cell is a cell of the lymphoid lineage or a cell of the myeloid lineage.
45. The cell of claim 44, wherein the cell of the lymphoid lineage is selected from T cells, B cells, Natural Killer (NK) cells, dendritic cells.
46. The cell of any one of claims 34-45, wherein the cell is a T cell.
47. The cell of claim 46, wherein the T cell is derived from an induced pluripotent stem cell.
48. The cell of claim 46 or 47, wherein the T cell is a CD8⁺ T cell.
49. The cell of claim 48, wherein the CD8⁺ T cell is CD4 independent.
50. The cell of any one of claims 46-49, wherein the T cell is selected from the group consisting of a cytotoxic T lymphocyte (CTL), a $\gamma\delta$ T cell, a tumor-infiltrating lymphocyte (TIL), a regulatory T cell, and a Natural Killer T (NKT) cell.
51. The cell of any one of claims 46-50, wherein the fusion polypeptide and the antigen-recognizing receptor are integrated at a locus within the genome of the T cell.

52. The cell of claim 51, wherein the locus is selected from the group consisting of a TRAC locus, a TRBC locus, a TRDC locus, and a TRGC locus.
53. The cell of claim 51 or 52, wherein the locus is a TRAC locus or a TRBC locus.
- 5 54. The cell of claim 53, wherein the locus is a TRAC locus.
55. The cell of any one of claims 51-54, wherein the antigen-recognizing receptor is a chimeric antigen receptor (CAR).
56. The cell of any one of claims 51-55, wherein the expressions of the antigen-recognizing receptor and the fusion polypeptides are under the control of an endogenous
10 promoter.
57. The cell of claim 56, wherein the endogenous promoter is selected from the group consisting of an endogenous TRAC promoter, an endogenous TRBC promoter, an endogenous TRDC promoter, and an endogenous TRGC promoter.
58. The cell of claim 57, wherein the endogenous promoter is a TRAC promoter.
- 15 59. The cell of any one of claims 35-58, wherein the fusion polypeptide and the antigen-recognizing receptor are integrated at a locus encoding an immune inhibitory molecule.
60. The cell of claim 59, wherein the immune inhibitory molecule is selected from the group consisting of CTLA-4, PD-1, LAG3, BTLA, B7-1, B7-H1, B7-H3, B7-H4,
20 TIM3, SHP-1, SHP-2, TIGIT, CD160, and LAIR1.
61. The cell of any one of claims 34-60, wherein said cell is autologous.
62. The cell of any one of claims 34-60, wherein said cell is allogeneic.
63. A composition comprising an effective amount of a cell of any one of claims 34-62.
- 25 64. The composition of claim 63, which is a pharmaceutical composition further comprising a pharmaceutically acceptable excipient.

65. The composition of claim 63 or 64, which is for treating and/or preventing a neoplasm, an autoimmune disease, and/or an infectious disease.
66. The composition of any one of claims 63-65, further comprising a regulator that is capable of regulating or modulating expression and/or activity of the fusion polypeptide.
67. The composition of claim 66, wherein the regulator is selected from the group consisting of promoters that are capable of controlling the expression of the fusion polypeptide, molecules that are capable of regulating or modulating expression and/or activity of the co-stimulatory ligand, molecules that are capable of regulating or modulating expression and/or activity of the co-stimulatory molecule.
68. The composition of claim 67, wherein the molecules that are capable of regulating or modulating expression and/or activity of the co-stimulatory ligand are selected from the group consisting of antibodies that bind to the co-stimulatory ligand, and fusion proteins that bind to the co-stimulatory ligand and regulate or modulate the expression and/or activity of the co-stimulatory ligand.
69. The composition of any one of claims 66-68, wherein the regulator is an anti-CD80 antibody and the fusion polypeptide comprises an extracellular domain and a transmembrane domain of CD80.
70. The composition of any one of claims 66-69, wherein the regulator is a fusion protein that binds to CD80 and modulates the activity of CD80 and the fusion polypeptide comprises an extracellular domain and a transmembrane domain of CD80.
71. The composition of claim 70, wherein the fusion protein comprises an CTLA-4 fragment that binds to CD80.
72. The composition of claim 71, wherein the CTLA-4 fragment that binds to CD80 is Abatacept or belatacept.
73. The composition of claim 72, wherein the molecules that are capable of regulating or modulating expression and/or activity of the co-stimulatory molecule are selected from the group consisting of antibodies that bind to the co-stimulatory molecule,

and fusion proteins that bind to the co-stimulatory molecule and regulate or modulate the expression and/or activity of the co-stimulatory molecule.

74. A composition comprising: a) a fusion polypeptide of any one of claims 1-31; and b) an antigen-recognizing receptor that binds to an antigen.

5 75. The composition of claim 74, wherein the fusion polypeptide is operably linked to a first promoter.

76. The composition of claim 74 or 75, wherein the antigen-recognizing receptor is operably linked to a second promoter.

77. The composition of claim 75 or 76, wherein one or both of the first and second
10 promoters are endogenous or exogenous.

78. The composition of claim 77, wherein the exogenous promoter is selected from the group consisting of an elongation factor (EF)-1 promoter, a CMV promoter, a SV40 promoter, a PGK promoter, and a metallothionein promoter.

79. The composition of claim 75 or 76, wherein one or both of the first and second
15 promoters are inducible promoters.

80. The composition of claim 79, wherein the inducible promoter is selected from the group consisting of a NFAT transcriptional response element (TRE) promoter, a CD69 promoter, a CD25 promoter, and an IL-2 promoter.

81. A nucleic acid composition comprising: a) a first polynucleotide encoding a
20 fusion polypeptide of any one of claims 1-31; and b) a second polynucleotide encoding an antigen-recognizing receptor that binds to an antigen.

82. The nucleic acid composition of claim 81, further comprising a first promoter that is operably linked to the fusion polypeptide.

83. The nucleic acid composition of claim 81 or 82, further comprising a second
25 promoter that is operably linked to the antigen-recognizing receptor.

84. The nucleic acid composition of claim 82 or 83, wherein one or both of the first and second promoters are endogenous or exogenous.

85. The nucleic acid composition of claim 84, wherein the exogenous promoter is selected from the group consisting of an elongation factor (EF)-1 promoter, a CMV promoter, a SV40 promoter, a PGK promoter, and a metallothionein promoter.
86. The nucleic acid composition of claim 82 or 83, wherein one or both of the first
5 and second promoters are inducible promoters.
87. The nucleic acid composition of claim 86, wherein the inducible promoter is selected from the group consisting of a NFAT transcriptional response element (TRE) promoter, a CD69 promoter, a CD25 promoter, and an IL-2 promoter.
88. A cell comprising the composition of any one of claims 63-80 or the nucleic
10 acid composition of any one of claims 81-87.
89. The cell of claim 88, wherein the cell is a cell of the lymphoid lineage or a cell of the myeloid lineage.
90. The cell of claim 89, wherein the cell of the lymphoid lineage is selected from the group consisting of T cells, B cells, Natural Killer (NK) cells, dendritic cells.
- 15 91. The cell of any one of claims 88-90, wherein the cell is a T cell.
92. The cell of claim 91, wherein the T cell is derived from an induced pluripotent stem cell.
93. The cell of claim 91 or 92, wherein the T cell is a CD8⁺ T cell.
94. The cell of claim 93, wherein the CD8⁺ T cell is CD4 independent.
- 20 95. The cell of any one of claims 91-94, wherein the T cell is selected from the group consisting of a cytotoxic T lymphocyte (CTL), a $\gamma\delta$ T cell, a tumor-infiltrating lymphocyte (TIL), a regulatory T cell, and a Natural Killer T (NKT) cell.
96. The cell of any one of claims 88-95, wherein the composition or the nucleic acid composition is integrated at a locus within the genome of the T cell.
- 25 97. The cell of claim 96, wherein the locus is selected from the group consisting of a TRAC locus, a TRBC locus, a TRDC locus, and a TRGC locus.

98. The cell of claim 96 or 97, wherein the locus is a TRAC locus or a TRBC locus.
99. The cell of claim 98, wherein the locus is a TRAC locus.
100. The cell of any one of claims 96-99, wherein the antigen-recognizing receptor
5 is a chimeric antigen receptor (CAR).
101. The cell of any one of claims 96-100, wherein the expressions of the antigen-recognizing receptor and the fusion polypeptides are under the control of an endogenous promoter.
102. The cell of claim 101, wherein the endogenous promoter is selected from the
10 group consisting of an endogenous TRAC promoter, an endogenous TRBC promoter, an endogenous TRDC promoter, and an endogenous TRGC promoter.
103. The cell of claim 102, wherein the endogenous promoter is a TRAC promoter.
104. The cell of any one of claims 91-103, wherein the composition or the nucleic acid composition is integrated at a locus encoding an immune inhibitory molecule.
- 15 105. The cell of claim 104, wherein the immune inhibitory molecule is selected from the group consisting of CTLA-4, PD-1, LAG3, BTLA, B7-1, B7-H1, B7-H3, B7-H4, TIM3, SHP-1, SHP-2, TIGIT, CD160, and LAIR1.
106. A method for producing a cell, the method comprising introducing into a cell a nucleic acid of claim 32 or a vector of claim 33.
- 20 107. A kit comprising a nucleic acid of claim 32, a vector of claim 33, a cell of any one of claims 34-62 and 88-105, or a composition of any one of claims 63-80, or the nucleic acid composition of any one of claims 81-87.
108. The kit of claim 99, wherein the kit further comprises written instructions for treating and/or preventing a neoplasm, a pathogen infection, and/or an infectious disease.
- 25 109. ~~Use of A method of reducing tumor burden in a subject, the method comprising administering to the subject~~ an effective amount of the cells of any one of claims 34-62 and 88-105, or the composition of any one of claims 63-80, or the nucleic acid composition of any one of claims 81-87 in the manufacture of a medicament for reducing

tumor burden in a subject, wherein the cells of any one of claims 34-62 and 88-105, or the composition of any one of claims 63-80, or the nucleic acid composition of any one of claims 81-87 is to be administered to the subject.

110. The ~~use~~method of claim 109, wherein ~~the method reduces~~ the number of tumor cells is reduced, ~~reduces~~ tumor size is reduced, and/or ~~eradicates~~ the tumor is eradicated in the subject.

111. Use of A method of treating a subject having a relapse of a neoplasm, administering to the subject an effective amount of the cells of any one of claims 34-62 and 88-105, or the composition of any one of claims 63-80, or the nucleic acid composition of any one of claims 81-87 in the manufacture of a medicament for treating a subject having a relapse of a neoplasm, wherein the cells of any one of claims 34-62 and 88-105, or the composition of any one of claims 63-80, or the nucleic acid composition of any one of claims 81-87 is to be administered to the subject.

112. Use of A method of treating and/or preventing a neoplasm in a subject, administering to the subject an effective amount of the cells of any one of claims 34-62 and 88-105, or the composition of any one of claims 63-80, or the nucleic acid composition of any one of claims 81-87 in the manufacture of a medicament for treating and/or preventing a neoplasm in a subject, wherein the cells of any one of claims 34-62 and 88-105, or the composition of any one of claims 63-80, or the nucleic acid composition of any one of claims 81-87 is to be administered to the subject.

113. The ~~use~~method of claim 112, wherein the subject received an immunotherapy prior to said administration of the cells or the composition.

114. The ~~use~~method of any one of claims 109-114, wherein the neoplasm or tumor is cancer.

115. The ~~method-use~~ of any one of claims 109-114, wherein the neoplasm or tumor is selected from the group consisting of blood cancers and solid tumors.

116. The ~~use~~method of claim 115, wherein the blood cancer is selected from the group consisting of B cell leukemia, multiple myeloma, acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia, and non-Hodgkin's lymphoma.

117. ~~Use of A method of treating and/or preventing an autoimmune disease or an infectious disease in a subject, administering to the subject~~ an effective amount of the cells of any one of claims 34-62 and 88-105, or the composition of any one of claims 63-80, or the nucleic acid composition of any one of claims 81-87 in the manufacture of a medicament for treating and/or preventing an autoimmune disease or an infectious disease in a subject, wherein the cells of any one of claims 34-62 and 88-105, or the composition of any one of claims 63-80, or the nucleic acid composition of any one of claims 81-87 is to be administered to the subject.

118. The ~~method-use~~ of claim 117, wherein the autoimmune disease or an infectious disease is selected from the group consisting of rheumatoid arthritis (RA), Type I diabetes, systemic lupus erythematosus (SLE), inflammatory bowel disease, ulcerative colitis, psoriasis, psoriatic arthritis, scleroderma, autoimmune thyroid disease, Grave's disease, Crohn's disease, multiple sclerosis, systemic sclerosis, asthma, organ transplant rejection, a disease or condition associated with transplant, Takayasu arteritis, giant-cell arteritis, Kawasaki disease, polyarteritis nodosa, Behcet's syndrome, Wegener's granulomatosis, ANCA-vasculitides, Churg-Strauss syndrome, microscopic polyangiitis, vasculitis of connective tissue diseases, Hennoch-Schonlein purpura, cryoglobulinemic vasculitis, cutaneous leukocytoclastic angiitis, Sarcoidosis, Cogan's syndrome, Wiskott-Aldrich Syndrome, primary angiitis of the CNS, thromboangiitis obliterans, paraneoplastic arteritis, myelodysplastic syndrome, erythema elevatum diutinum, amyloidosis, autoimmune myositis, Guillain-Barre Syndrome, histiocytosis, atopic dermatitis, pulmonary fibrosis, glomerulonephritis, Whipple's disease, Still's disease, Sjogren's syndrome, osteomyelofibrosis, chronic inflammatory demyelinating polyneuropathy, Kimura's disease, systemic sclerosis, chronic periaortitis, chronic prostatitis, idiopathic pulmonary fibrosis, chronic granulomatous disease, idiopathic, bleomycin-induced lung inflammation, cytarabine-induced lung inflammation, autoimmune thrombocytopenia, autoimmune neutropenia, autoimmune hemolytic anemia, autoimmune lymphocytopenia, chronic autoimmune thyroiditis, autoimmune hepatitis, Hashimoto's thyroiditis, atopic thyroiditis, Graves disease, autoimmune polyglandular syndrome, autoimmune Addison syndrome, and/or myasthenia gravis.

119. The ~~use method~~ of any one of claims 109-118, ~~wherein further comprising administering to the subject~~ is to be further administered a regulator that is capable of regulating or modulating expression, activity of the fusion polypeptide.

120. The ~~usemethod~~ of claim 119, wherein the regulator is selected from the group consisting of promoters that are capable of controlling the expression of the fusion polypeptide, molecules that are capable of regulating or modulating expression and/or activity of the co-stimulatory ligand, molecules that are capable of regulating or
5 modulating expression and/or activity of the co-stimulatory molecule.

121. The ~~usemethod~~ of claim 120, wherein the molecules that are capable of regulating or modulating expression and/or activity of the co-stimulatory ligand are selected from the group consisting of antibodies that bind to the co-stimulatory ligand, and fusion proteins that bind to the co-stimulatory ligand and regulate or modulate the
10 expression and/or activity of the co-stimulatory ligand.

122. The ~~usemethod~~ of any one of claims 119-121, wherein the regulator is an anti-CD80 antibody and the fusion polypeptide comprises an extracellular domain and a transmembrane domain of CD80.

123. The ~~usemethod~~ of any one of claims 119-121, wherein the regulator is a fusion
15 protein that binds to CD80 and modulates the activity of CD80 and the fusion polypeptide comprises an extracellular domain and a transmembrane domain of CD80.

124. The ~~usemethod~~ of claim 123, wherein the fusion protein is a CTLA-4 fragment that binds to CD80.

125. The ~~usemethod~~ of claim 124, wherein the CTLA-4 fragment that binds to CD80
20 is Abatacept or belatacept.

126. The ~~usemethod~~ of claim 120, wherein the molecules that are capable of regulating or modulating expression, activity of the co-stimulatory molecule are selected from the group consisting of antibodies that bind to the co-stimulatory molecule, fusion proteins that bind to the co-stimulatory molecule and regulate or modulate the
25 expression, activity of the co-stimulatory molecule.

127. The ~~usemethod~~ of any one of claims 119-126, wherein the regulator is capable of depleting the cell.

128. The ~~use~~method of any one of claims 119-127, wherein the regulator is capable of lessening or eliminating one or more side effects associated with administration of the cell.

129. The ~~use~~method of claim 128, wherein the one or more side effects are selected from the group consisting of off-tumor target effects, cytokine release syndrome, neurotoxicity, and combinations thereof.

130. The ~~use~~method of any one of claims 109-129, ~~further comprising administering to the subject~~ is to be further administered a checkpoint immune blockade agent.

131. The ~~use~~method of claim 130, wherein the checkpoint immune blockade agent is selected from the group consisting of anti-PD-L1 antibodies, anti-CTLA-4 antibodies, anti-PD-1 antibodies, anti-LAG3 antibodies, anti-B7-H3 antibodies, anti-TIM3 antibodies, and combinations thereof.

132. The ~~use~~method of claim 130 or 131, wherein the checkpoint immune blockade agent is an anti-PD-1 antibody.

133. The cells of any one of claims 34-62 and 88-105, or the composition of any one of claims 63-80, or the nucleic acid composition of any one of claims 81-87 for use in ~~therapy reducing tumor burden, treating and/or preventing a neoplasm, and/or treating a subject having a relapse of a neoplasm, and/or treating and/or preventing an autoimmune disease or an infectious disease.~~