CLAIMS

1. A composition comprising a recombinant nucleic acid encoding a chimeric fusion protein (CFP) comprising:

(a) a phagocytic or tethering receptor (PR) subunit comprising:

(i) a transmembrane domain, or

(ii) an intracellular domain comprising an intracellular signaling domain; and

(b) an extracellular domain comprising a CD137 antigen binding domain that can bind specifically to CD137 on a target cell; wherein the extracellular and the transmembrane domains are operably linked.

2. A composition comprising a recombinant nucleic acid encoding a chimeric fusion protein comprising: (a) a first CD137 antigen binding domain that specifically binds to CD137 antigen on a target cell, and (b) a second binding domain that specifically binds to a surface agent on a myeloid cell; wherein, binding of the first antigen binding domain to CD137 antigen on a target cell and binding of the second binding domain on a surface agent on a myeloid cell.

3. A composition comprising a recombinant nucleic acid encoding a chimeric fusion protein (CFP) comprising: (a) a phagocytic or tethering receptor (PR) subunit comprising: (i) a transmembrane domain, or (ii) an intracellular domain comprising an intracellular signaling domain; and (b) an extracellular domain comprising a Claudin 18.2 antigen binding domain that can bind specifically to Claudin 18.2 on a target cell; wherein the extracellular and the transmembrane domains are operably linked.

4. A composition comprising a recombinant nucleic acid encoding a chimeric fusion protein comprising: (a) a first Claudin 18.2 antigen binding domain that specifically binds to Claudin 18.2 antigen on a target cell, and (b) a second binding domain that specifically binds to a surface agent on a myeloid cell; wherein, binding of the first antigen binding domain to Claudin 18.2 antigen on a target cell and binding of the second binding domain on a sur-face agent on a myeloid cell.

5. A composition comprising a recombinant nucleic acid encoding a chimeric fusion protein (CFP) comprising: (a) a phagocytic or tethering receptor (PR) subunit comprising: (i) a transmembrane domain, or (ii) an intracellular domain comprising an intracellular signaling domain; and (b) an extracellular domain comprising a Claudin 3 antigen binding domain that can bind specifically to Claudin 3 on a target cell; wherein the extracellular and the transmembrane domains are operably linked.

6. A composition comprising a recombinant nucleic acid encoding a chimeric fusion protein comprising: (a) a first Claudin 3 antigen binding domain that specifically binds to Claudin 3 antigen on a target cell, and (b) a second binding domain that specifically binds to a surface agent on a myeloid cell; wherein, binding of the first antigen binding domain to Claudin 18.2 antigen on a target cell and binding of the second binding domain on a surface agent on a myeloid cell.

7. A composition comprising a recombinant nucleic acid encoding a chimeric fusion protein (CFP) comprising: (a) a phagocytic or tethering receptor (PR) subunit comprising: (i) a transmembrane domain, or (ii) an intracellular domain comprising an intracellular signaling domain; and (b) an extracellular domain comprising a CD70 antigen binding domain that can bind specifically to CD70 on a target cell; wherein the extracellular and the transmembrane domains are operably linked.

8. A composition comprising a recombinant nucleic acid encoding a chimeric fusion protein comprising: (a) a first CD70 antigen binding domain that specifically binds to CD70 antigen on a target cell, and (b) a second binding domain that specifically binds to a surface agent on a myeloid cell; wherein, binding of the first antigen binding domain to CD70 antigen on a target cell and binding of the second binding domain on a surface agent on a myeloid cell.

9. A composition comprising a recombinant nucleic acid encoding a chimeric fusion protein (CFP) comprising: (a) a phagocytic or tethering receptor (PR) subunit comprising: (i) a transmembrane domain, or (ii) an intracellular domain comprising an intracellular signaling domain; and (b) an extracellular domain comprising a TROP2 antigen binding domain that can bind specifically to TROP2 on a target cell; wherein the extracellular and the transmembrane domains are operably linked.

10. A composition comprising a recombinant nucleic acid encoding a chimeric fusion protein comprising: (a) a first TROP2 antigen binding domain that specifically binds to TROP2 antigen on a target cell, and (b) a second binding domain that specifically binds to a surface agent on a myeloid cell; wherein, binding of the first antigen binding domain to TROP2 antigen on a target cell and binding of the second binding domain on a surface agent on a myeloid cell.

11. A composition comprising a recombinant nucleic acid encoding a chimeric fusion protein (CFP) comprising: (a) a phagocytic or tethering receptor (PR) subunit comprising: (i) a transmembrane domain, or (ii) an intracellular domain comprising an intracellular signaling domain; and (b) an extracellular domain comprising a TMPRSS antigen binding domain that can bind specifically to TMPRSS on a target cell; wherein the extracellular and the transmembrane domains are operably linked.

12. A composition comprising a recombinant nucleic acid encoding a chimeric fusion protein comprising: (a) a first TMPRSS antigen binding domain that specifically binds to TMPRSS antigen on a target cell, and (b) a second binding domain that specifically binds to a surface agent on a myeloid cell; wherein, binding of the first antigen binding domain to TMPRSS antigen on a target cell and binding of the second binding domain on a surface agent on a myeloid cell.

13. A composition comprising a recombinant nucleic acid encoding a phagocytic or tethering receptor (PR) fusion protein (PFP) comprising: (a) a PR subunit comprising: (i) a transmembrane domain, and (ii) an intracellular domain comprising an intracellular signaling domain; and (b) an extracellular domain comprising an antigen binding domain of any one of the claims 1, 3, 5, 7, 9 or 11 having a strong binding affinity to an antigen of a target cell; wherein the transmembrane domain and the extracellular domain are operatively linked; and wherein upon binding of the PFP to the antigen of the target cell, the killing or phagocytosis activity of a cell expressing the PFP is increased by at least greater than 20% compared to a cell not expressing the PFP.

14. The composition of any one of the claims 1, 3, 5, 7, 9, 11 or 13, wherein the intracellular signaling domain is derived from a phagocytic or tethering receptor or wherein the intracellular signaling domain comprises a phagocytosis activation domain.

15. The composition of any one of the claims 1, 3, 5, 7, 9, 11, 13 or 14, wherein the intracellular signaling domain comprises a proinflammatory signaling domain.

16. The composition of any one of the claims 1, 3, 5, 7, 9, 11 or 13-15, wherein the proinflammatory signaling domain comprises a kinase activation domain or a kinase binding domain.

17. The composition of any one of the claims 11, 3, 5, 7, 9, 11 or 13-16, wherein the intracellular signaling domain comprises a PI3 kinase recruitment domain.

18. The composition of any one of the claims 1, 3, 5, 7, 9, 11 or 13-17, wherein the proinflammatory signaling domain comprises an IL-1 signaling cascade activation domain.

19. The composition of any one of the claims 1, 3, 5, 7, 9, 11 or 13-18, wherein the proinflammatory signaling domain comprises an intracellular signaling domain derived from TLR3, TLR4, TLR7, TLR 9, TRIF, RIG-1, MYD88, MAL, IRAK1, MDA-5, an IFN receptor, an NLRP family member, NLRP1-14, NOD1, NOD2, Pyrin, AIM2, NLRC4, FCGR3A, FCERIG, CD40, a caspase domain or a procaspase binding domain or any combination thereof.

20. The composition of any one of the claims 1, 3, 5, 7, 9, 11 and 13-19, further comprising a transmembrane domain derived from a CD2, CD8, CD28 or CD68 protein TM domain.

21. The composition of any one of the claims 1, 3, 5, 7, 9, 11 and 13-20, further comprising a hinge domain.

22. The composition of any one of the claims 1, 3, 5, 7, 9, 11 or 13-22, wherein upon binding of the PFP to the antigen of the target cell, the killing activity of a cell expressing the PFP is increased by at least greater than 20% compared to a cell not expressing the PFP.

23. The composition of any one of the claims 1, 3, 5, 7, 9, 11 or 13-22, wherein upon binding of the PFP to the antigen of the target cell, the killing activity of a cell expressing the PFP is increased by at least 1.1-fold compared to a cell not expressing the PFP.

24. The composition of any one of the claims 2, 4, 6, 8, 10 or 12 comprising a first therapeutic agent, wherein the therapeutic agent comprises:

a first binding domain, wherein the first binding domain is a first antibody or functional fragment thereof that specifically interacts with an antigen on a target cell, and

a second binding domain, wherein the second binding domain is a second antibody or functional fragment thereof that specifically interacts with a myeloid cell; wherein,

(i) the first therapeutic agent is coupled to a first component, wherein the first component is an additional therapeutic agent or a third binding domain, or

(ii) the composition comprises an additional therapeutic agent.

25. The composition of any one of the claims 2, 4, 6, 8, 10, 12 or 24, wherein the therapeutic agent comprises: (a) a first binding domain that specifically interacts with an antigen of a target cell, (b) a second binding domain that specifically interacts with a myeloid cell, and (c) a third binding domain that specifically interacts with the myeloid cell.

26. The composition of any one of claims 1-25, wherein any one of binding domains of the therapeutic agent comprises the binding domain of a an antibody, a functional fragment of an antibody, a variable domain thereof, a VH domain, a VL domain, a VNAR domain, a VHH domain, a single chain variable fragment (scFv), an Fab, a single domain antibody (sdAb), a nanobody, a bispecific antibody, a diabody, or a functional fragment or a combination thereof.

27. The composition of any one of claims 1-26, wherein the antigen on the target cell to which the first binding domain binds, is a cancer antigen or a pathogenic antigen on the target cell or an autoimmune antigen.

28. The composition of any one of claims 2, 4, 6, 8, 10, 12 or 24, wherein the first therapeutic agent comprises a polypeptide that is less than 1000 amino acids or 1000 nm in length.

29. The composition of any one of claims 2, 4, 6, 8, 10, 12, 24, or 28, wherein the first therapeutic agent comprises a polypeptide that is less than 500 amino acids or 500 nm in length.

30. The composition of any one of claims 2, 4, 6, 8, 10, 12, 24, 28, or 29, wherein the first therapeutic agent comprises a polypeptide that is 200-1000 amino acids or 200-1000 nm in length.

31. The composition of any one of claims 2, 4, 6, 8, 10, 12, 24, or 28-30, wherein engagement of the binding domains of the first therapeutic agent contacts the cancer cell to the myeloid cell.

32. The composition of any one of the claims 2, 4, 6, 8, 10, 12, 24, or 28-31, wherein the second binding domain specifically interacts with a myeloid cell and promotes phagocytosis activity of the myeloid cell.

33. The composition of any one of the claims 2, 4, 6, 8, 10, 12, 24, or 28-32, wherein the second binding domain specifically interacts with a myeloid cell and promotes inflammatory signaling of the myeloid cell.

34. The composition of any one of the claims 2, 4, 6, 8, 10, 12, 24, or 28-33, wherein the second binding domain specifically interacts with a myeloid cell or an adhesion molecule and promotes adhesion of the myeloid cell to the target cell.

35. The composition of any one of the claims 2, 4, 6, 8, 10, 12, 24, or 28-34, wherein the second binding domain specifically interacts with a myeloid cell and inhibits anti-phagocytic activity of the myeloid cell mediated by the target cell.

36. The composition of any one of the claims 2, 4, 6, 8, 10, 12, 24, or 28-35, wherein the second binding domain specifically interacts with a myeloid cell and inhibits anti-inflammatory activity of the myeloid cell mediated by the target cell.

37. The composition of any one of the claims 2, 4, 6, 8, 10, 12, 24, or 28-36, wherein the second and/or the third binding domain promotes phagocytic activity of the myeloid cell.

38. The composition of any one of the claims 2, 4, 6, 8, 10, 12, 24, or 28-37, wherein the second and/or the third binding domain promotes inflammatory signaling of the myeloid cell.

39. The composition of any one of the claims 2, 4, 6, 8, 10, 12, 24, or 28- 38, wherein the second and/or the third binding domain specifically interacts with a myeloid cell or an adhesion molecule and promotes adhesion of the myeloid cell to the target cell.

40. The composition of any one of the claims 2, 4, 6, 8, 10, 12, 24, or 28-39, wherein the second and/or the third binding domain inhibits anti-phagocytic activity of the myeloid cell mediated by the target cell.

41. The composition of any one of the claims 2, 4, 6, 8, 10, 12, 24, or 28-40, wherein the second and/or the third binding domain inhibits anti-inflammatory activity of the myeloid cell mediated by the target cell.

42. The composition of any one of the claims 2, 4, 6, 8, 10, 12, 24, or 28-41, wherein the third binding domain or the additional therapeutic agent comprises a CD47 antagonist, a CD47 blocker, an antibody, a chimeric CD47 receptor, a sialidase, a cytokine, a proinflammatory gene, a pro-caspase, or an anti-cancer agent.
43. The composition of any one of the preceding claims, wherein the first binding domain, the second binding domain and the third binding domain bind to distinct non-identical target antigens.
44. The composition of any one of the claims 2, 4, 6, 8, 10, 12, 24, or 28-43, wherein the first binding domain, the second binding domain or the third binding domain is a ligand binding domain.
45. The composition of any one of the preceding claims, wherein the first, the second or the third binding domains are operably linked by one or more linkers.
46. The composition of claim 45, wherein the linker is a polypeptide.
47. The composition of claim 46, wherein the linker is a functional peptide.
48. The composition of any one of the claims 45-47, wherein the linker is a ligand for a receptor.
49. The composition of claim 45, wherein the linker is a ligand for a monocyte or macrophage receptor.
50. The composition of any one of the claims 45-49, wherein the linker activates the receptor.
51. The composition of any one of the claims 45-50, wherein the linker inhibits the receptor.
52. The composition of claim 51, wherein the linker is a ligand for a M2 macrophage receptor.
53. The composition of claim 48 or 49, wherein the linker is a ligand for a TLR receptor, such as TLR4.
54. The composition of claim any of the claims 48, 49 or 50, wherein the linker activates a TLR receptor.
55. The composition of any one of the claims 45-54, wherein the first, the second and /or the third binding domains are associated with a mask that binds to the binding domain.
56. The composition of claim 55, wherein the mask is an inhibitor that inhibits the interaction of binding domain to its target when the mask remains associated with the respective binding domain.
57. The composition of claim 56, wherein the mask is associated with the binding domain via a peptide linker.
58. The composition of claim 57, wherein the peptide linker comprises a cleavable moiety.
59. The composition of claim 58, wherein the cleavable moiety is cleaved by a protein or an enzyme selectively abundant in the site of the cancer or tumor.

60. The composition of any one of the claims 1-59, wherein the recombinant nucleic acid is an RNA.

61. The composition of any one of the claims 1-60, wherein the recombinant nucleic acid is an mRNA.

62. The composition of any one of the claims 1-61, wherein the recombinant nucleic acid is associated with one or more lipids.

63. The composition of any one of the claims 1-62, wherein the recombinant nucleic acid is encapsulated in a liposome.

64. The composition of claim 63, wherein the liposome is a nanoparticle.

65. The composition of any one of the claims 1-64, wherein the recombinant nucleic acid is comprised in a vector.

66. A pharmaceutical composition comprising any one of the recombinant nucleic acids of the composition of any one of claims 1-65, and an excipient.

67. A pharmaceutical composition comprising a polypeptide encoded by a recombinant nucleic acid of any one of the claims 1-65.

68. A cell comprising the recombinant nucleic acid of any one of the claims 1-65.

69. The cell of claim 68, wherein the cell is a myeloid cell.

70. The cell of claim 69, wherein the cell is $CD14^+$, $CD16^-$.

71. A pharmaceutical composition comprising a population of cells that comprise a recombinant nucleic acid of any one of the claims 1-65, wherein at least 50% of the cells are $CD14^+CD16^-$.

72. The pharmaceutical composition of claim 71, wherein less than 10% of the cells are dendritic cells.

73. The pharmaceutical composition of claim 71 or 72, further comprising a suitable excipient.

74. A method of making any one of the compositions of claims 1-73.

75. A method of treating a cancer in a subject, comprising administering to the subject a pharmaceutical composition of any one of the claims 71-73.

76. A method of treating a cancer in a subject, comprising administering to the subject the pharmaceutical composition of any one of claims 66, 67 and 71-73.

77. The method of claim 75 or 76, wherein the cancer is selected from a group consisting of gastric cancer, ovarian cancer, renal cancer, breast cancer, prostate cancer, liver cancer, brain cancer, lymphoma, leukemia, skin cancer, pancreatic cancer, colorectal cancer, glioblastoma and lung cancer.

78. A composition comprising a recombinant polynucleic acid comprising a sequence encoding a chimeric fusion protein (CFP), the CFP comprising:

(a) an extracellular domain comprising an antigen binding domain, and

(b) a transmembrane domain operatively linked to the extracellular domain;

wherein the transmembrane domain is a transmembrane domain from a protein that dimerizes with endogenous FcR-gamma receptors in myeloid cells; wherein the recombinant polynucleic acid is encapsulated by a nanoparticle delivery vehicle; and wherein after administration of the composition to a human subject the CFP is expressed on the surface of myeloid cells of the human subject.

79. The composition of claim 78, wherein the antigen binding domain comprises a Fab fragment, an scFv domain or an sdAb domain.

80. The composition of claim 78, wherein the transmembrane domain is an transmembrane domain from CD8, CD16a, CD64, CD68 or CD89.

81. The composition of claim 78, wherein the extracellular domain further comprises a hinge domain derived from CD8, wherein the hinge domain is operatively linked to the transmembrane domain and the antigen-binding domain.

82. The composition of claim 78, wherein the transmembrane domain is a transmembrane domain from a protein that dimerizes with endogenous FcR-gamma receptors in myeloid cells, monocytes or macrophages; wherein after administration of the pharmaceutical composition to a human subject the CFP is specifically expressed in myeloid cells, monocytes or macrophages of the human subject.

83. The composition of claim 78, wherein the transmembrane domain is a transmembrane domain from CD16a, CD64, CD68 or CD89.

84. The composition of claim 78, wherein the CFP further comprises an intracellular domain.

85. The composition of claim 84, wherein the intracellular domain comprises one or more intracellular signaling domains, and wherein the one or more intracellular signaling domains comprises an intracellular signaling domain from FcγR, FcαR, FcεR, CD40 or CD3zeta.

86. The composition of claim 84, wherein the one or more intracellular signaling domains further comprises a phosphoinositide 3-kinase (PI3K) recruitment domain.

87. The composition of claim 86, wherein the PI3K recruitment domain comprises a sequence with at least 90% sequence identity to SEQ ID NO: 26.

88. The composition of claim 84, wherein the intracellular domain comprises an intracellular domain from CD16a, CD64, CD68 or CD89.

89. The composition of claim 78, wherein the recombinant polynucleic acid is an mRNA.

90. The composition of claim 78, wherein the nanoparticle delivery vehicle comprises a lipid nanoparticle.

~~91. The composition of claim 90, wherein the lipid nanoparticle comprises a polar lipid~~

~~92. The composition of claim 90, wherein the lipid nanoparticle comprises a non-polar lipid.~~

~~93. The composition of claim 90, wherein the lipid nanoparticle is from 100 to 300 nm in diameter.~~

~~94. The composition of any one of claims 78-93, wherein the antigen binding domain binds to an antigen selected from the group consisting of TROP2, GPC3, CD5, HER2, CD137, CD70, Claudin 3, Claudin 18.2, TMPRSS, CD19, CD22, CD7 and GP75.~~

~~95. A pharmaceutical composition comprising the composition of any one of claims 78-94, and a pharmaceutically acceptable excipient.~~

~~96. The pharmaceutical composition of claim 95 wherein pharmaceutical composition comprises an effective amount of the composition of any one of claims 78-94, wherein to inhibit growth of a cancer when administered to a human subject with the cancer.~~

~~97. A method of treating cancer in a subject in need thereof comprising administering the pharmaceutical composition of claim 95 or 96 to the subject.~~

~~98. A method of introducing the composition of any one of claims 78-94 into a myeloid cell comprising: electroporating a myeloid cell in the presence of a recombinant polynucleic acid comprising a sequence encoding a chimeric fusion protein (CFP), the CFP comprising: (a) an extracellular domain comprising an anti-TROP2 binding domain, and (b) a transmembrane domain operatively linked to the extracellular domain; wherein the recombinant polynucleic acid is (i) present in a myeloid cell, or (ii) is encapsulated by a nanoparticle delivery vehicle; wherein the recombinant polynucleic acid is configured for expression of the recombinant polynucleic acid in a myeloid cell of a human subject.~~

1~~99~~. A composition comprising a recombinant polynucleic acid comprising a sequence encoding a chimeric fusion protein (CFP)~~, the CFP~~ comprising:

(a) an extracellular domain comprising an anti-tumor-associated calcium signal transducer-2 (anti-TROP2) ~~-~~binding domain~~ comprising at least one of the sequences set forth SEQ ID NO: 34 and SEQ ID NO: 35, or a sequence that is at least 80% identical to SEQ ID NO: 34 or SEQ ID NO: 35;~~, and

(b) a transmembrane domain ~~operably~~operatively linked ~~with~~to the extracellular domain~~, comprising a sequence from ~~; wherein the transmembrane domain is a transmembrane domain from a protein that dimerizes with endogenous FcR-gamma receptors expressed in myeloid cells, monocytes, or macrophages; wherein the CFP is expressed on the surface of myeloid cells, monocytes, or macrophages that express endogenous FcR-gamma receptors.~~of an FcgR1 molecule (CD64), an FcgRIIIA molecule (CD16), or an FcaR1 molecule (CD89); and

~~(c) optionally, a hinge domain operably linked to the extracellular domain and the transmembrane domain, wherein the hinge domain comprises an amino acid sequence from a CD16 protein, a CD64 protein or a CD89 protein, or a CD8a hinge domain.~~

2. The composition of claim 1, wherein the anti-TROP2 binding domain comprises a Fab fragment or an scFv domain comprising a heavy chain variable domain and a light chain variable domain; and wherein the anti-TROP2 binding domain comprises:

(a) a heavy chain complementarity determining region 1 (HC CDR1), a HC CDR2 and a HC CDR3 of SEQ ID NO: 34 and a light chain complementarity determining region 1 (LC CDR1), a LC CDR2 and a LC CDR3 of SEQ ID NO: 34; or

(b) a HC CDR1, a HC CDR2 and a HC CDR3 of SEQ ID NO: 35 and a LC CDR1, a LC CDR2 and a LC CDR3 of SEQ ID NO: 35.

3. The composition of claim 1 or 2, wherein the transmembrane domain is a transmembrane domain from CD16a, CD64, CD68 or CD89, or a fragment thereof.

4. The composition of any one of claims 1-3, wherein the extracellular domain further comprises an extracellular domain from CD16a, CD64, CD68 or CD89, or a fragment thereof.

5. The composition of any one of claims 1-4, wherein the CFP further comprises an intracellular domain comprising one or more intracellular signaling domains, wherein the one or more intracellular signaling domains comprise an intracellular signaling domain from CD16a, CD64, CD68, CD89, FCERIG, CD40 or CD3 zeta.

~~100. The composition of claim 99, further comprising an intracellular domain comprising an amino acid sequence selected from the sequences set forth in SEQ ID NOs: 26, 27 or 28; or a sequence that is at least 80% identical to the amino acid sequence selected from the sequences set forth in SEQ ID NOs: 26, 27 or 28 and optionally, an intracellular domain from a CD16 protein, a CD64 protein or a CD89 protein or a fragment thereof.~~

~~101. The composition of claim 99 or 100, wherein the recombinant polynucleic acid is an mRNA.~~

~~102. A cell comprising the composition of claim 99 -101, wherein the cell is a CD14+ cell.~~

~~103. Use of the composition any one of the claims 1-65, 78-94 or 99-101 or a pharmaceutical composition of any one of the claims 66-67, 71-73, or 95-96, or the cell of claim 68-70 or 102 in treating a disease or a disorder.~~

~~104. Use of the pharmaceutical composition of claim 66-67, 71-73, or 95-96 or the cell of claim 68-70 or102 in treating a cancer in a subject.~~

~~105. Use of the pharmaceutical composition according to claim 103 or 104, wherein the cancer is selected from a group consisting of gastric cancer, ovarian cancer, renal cancer, breast~~

~~cancer, prostate cancer, liver cancer, brain cancer, lymphoma, leukemia, skin cancer, pancreatic cancer, colorectal cancer, glioblastoma and lung cancer.~~

~~106. Use of the composition any one of the claims 1-65, 78-94 or 99-101 or a pharmaceutical composition of any one of the claims 66-67, 71-73, or 95-96, or the cell of claim 68-70 or102 in making a medicament for treating a cancer in a subject, wherein the cancer is selected from a group consisting of gastric cancer, ovarian cancer, renal cancer, breast cancer, prostate cancer, liver cancer, brain cancer, lymphoma, leukemia, skin cancer, pancreatic cancer, colorectal cancer, glioblastoma and lung cancer.~~

~~107. The composition of any one of the claims 1, 3, 5, 7, 9, 11 or 13-22, wherein the intracellular signaling domain comprises an intracellular signaling domain having tyrosine residues comprise at least one immunoreceptor tyrosine-based activation motif (ITAM) domain.~~

6~~108~~. The composition of any one of claims 1-5~~-107~~, wherein the intracellular signaling domain comprises at least one immunoreceptor tyrosine-based activation motif (ITAM) domain, and wherein the at least one ITAM domain is from ~~the~~an intracellular domain of a protein or polypeptide selected from a group consisting of CD3 zeta TCR subunit, CD3 epsilon TCR subunit, CD3 gamma TCR subunit, CD3 delta TCR subunit, TCR zeta chain, Fc epsilon receptor 1 chain, Fc epsilon receptor 2 chain, Fc gamma receptor 1 chain, Fc gamma receptor 2a chain, Fc gamma receptor 2b 1 chain, Fc gamma receptor 2b2 chain, Fc gamma receptor 3a chain, Fc gamma receptor 3b chain, Fc beta receptor 1 chain, TYROBP (DAP12), CD5, CD16a, CD16b, CD22, CD23, CD32, CD64, CD79a, CD79b, CD89, CD278, and CD66d, or functional fragment~~s~~ thereof~~, and amino acid sequences thereof having at least one but not more than 20 modifications thereto~~.

7. The composition of any one of claims 1-6, wherein the transmembrane domain comprises a sequence SFCLVMVLLFAVDTGLYFSV (SEQ ID NO: 79).

8. The composition of any one of claims 1-7, wherein the CFP further comprises an extracellular hinge domain comprising a sequence GLAVSTISSFFPPGYQV (SEQ ID NO: 78); and an intracellular cytoplasmic domain comprising a sequence KTNIRSSTRDWKDHKFKWRKDPQDK (SEQ ID NO: 80).

9. The composition of any one of claims 1-6, wherein the transmembrane domain comprises a sequence LIRMAVAGLVLVALLAILV (SEQ ID NO: 83).

10. The composition of any one of claims 1-6 and 9, wherein the CFP further comprises an extracellular hinge domain comprising a sequence IHQDYTTQN (SEQ ID NO: 82); and an intracellular cytoplasmic domain comprising a sequence ENWHSHTALNKEASADVAEPSWSQQMCQPGLTFARTPSVCK (SEQ ID NO: 84).

11. The composition of any one of claims 1-10, wherein the CFP further comprises a signal peptide sequence comprising a sequence MWLQSLLLLGTVACSIS (SEQ ID NO: 7).
12. The composition of any one of claims 1-11, wherein the scFv comprises a sequence selected from the group consisting of SEQ ID NO: 34 and 35.
13. The composition of any one of claims 1-12, wherein the recombinant polynucleic acid is an mRNA.
14. The composition of any one of claims 1-13, wherein the recombinant polynucleic acid does not substantially express in a T cell.
15. The composition of any one of claims 1-14, further comprising a nanoparticle delivery vehicle, wherein the nanoparticle delivery vehicle encapsulates the recombinant polynucleic acid.
16. The composition of claim 15, wherein the nanoparticle delivery vehicle comprises a lipid nanoparticle.
17. The composition of claim 16, wherein the lipid nanoparticle delivery vehicle comprises at least one cationic lipid, at least one non-cationic lipid, at least one neutral lipid, or at least one PEGylated lipid.
18. The composition of any one of claims 15-17, wherein the nanoparticle delivery vehicle comprises one or more polymers.
19. A cell comprising the composition of any one of claims 1-18, wherein the cell is a CD14+ cell.
20. A pharmaceutical composition comprising (i) a lipid nanoparticle, encapsulating the recombinant nucleic acid of any one of claims 1-14.
21. Use of the composition of any one of the claims 1-18, the cell of claim 19, or the pharmaceutical composition of claim 20, in the manufacture of a medicament for treating a cancer in a subject, wherein the cancer is selected from a group consisting of gastric cancer, ovarian cancer, renal cancer, breast cancer, prostate cancer, liver cancer, brain cancer, lymphoma, leukemia, skin cancer, pancreatic cancer, colorectal cancer, glioblastoma and lung cancer.
22. A composition of any one of the claims 1-18, a cell of claim 19, or a pharmaceutical composition of claim 20 for use in therapy.

~~109. The composition of claim 107, wherein the at least one ITAM domain comprises a Src-family kinase phosphorylation site.~~

~~110. The composition of claim 107, wherein the at least one ITAM domain comprises a Syk recruitment domain.~~

111. The composition of any one of the claims 107-110, wherein the intracellular signaling subunit further comprises a DAP12 recruitment domain.

112. The composition of any one of the claims 107-111, wherein the intracellular domain comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 ITAM domains.

113. A composition comprising one or more recombinant nucleic acid sequences comprising:

(A) a first nucleic acid sequence encoding an exogenous polypeptide;

(B) a second nucleic acid sequence encoding a chimeric antigen receptor fusion protein (CFP),

wherein the CFP comprises:

(a) an intracellular signaling subunit comprising an intracellular signaling domain having one or more tyrosine residues that are phosphorylated upon antigen binding by the receptor;

(b) a transmembrane domain,

(c) an extracellular binding domain having binding specificity for a component on the surface of a target cell, wherein the extracellular binding domain is operably linked to the transmembrane domain and the intracellular signaling subunit; and

(d) a transcription activator domain operably linked to the intracellular signaling subunit by a protease cleavage sequence, wherein the transcription activator domain promotes transcription of the first nucleic acid sequence encoding the exogenous polypeptide; and

(C) a third nucleic acid sequence encoding (i) a protease that cleaves the protease cleavage sequence that operably links the transcription activator domain to the intracellular signaling subunit; (ii) a domain that binds to the tyrosine residues that are phosphorylated upon activation of the CFP; wherein the protease that cleaves the protease cleavage sequence and the domain that binds to the tyrosine residues are operably linked.

114. The composition of claim 113, wherein the third nucleic acid sequence further encodes (iii) a stimulus responsive element.

115. The composition of claim 114, wherein the stimulus responsive element (iii) is fused to the domain that binds to the phosphorylated tyrosine residues.

116. The composition of claim 114 or 115, wherein the stimulus responsive element (iii) is responsive to the microenvironment of the cell that expresses the nucleic acid sequence.

117. The composition of claim 116, wherein the one or more recombinant nucleic acid is expressed in a myeloid cell.

118. The composition of claim 113, wherein the transcription activator domain further

~~comprises a DNA binding domain.~~

~~119. The composition of claim 118, wherein the DNA binding domain is selected from the DNA binding domain (DB) of Gal4, ZFHD1 or tet-R.~~

~~120. The composition of claim 113, wherein the transcription activator domain comprises a VP64 transactivation domain.~~

~~121. The composition of any one of the claims 113-120, wherein the protease that cleaves the protease cleavage sequence that operably links the transcription activator domain to the intracellular signaling subunit is a hepatitis C virus (HCV) NS3 protease.~~

~~122. The composition of any one of the claims 113-121, wherein the domain that binds to the tyrosine residues that are phosphorylated upon activation of the CFP is a phosphotyrosine binding (PTB) domain.~~

~~123. The composition of claim 122, wherein the PTB is an Shc PTB.~~

~~124. The composition of any one of the claims 113-117, wherein (c) is a degron, operably linked with (b).~~

~~125. The composition of claim 124, wherein the degron is an HIF-1a degron.~~

~~126. A pharmaceutical composition comprising the composition of any one of claims 113-125 and a pharmaceutically acceptable excipient.~~

~~127. A cell comprising the composition of any one of the claims 113-125.~~

~~128. The cell of claim 128, wherein the cell is CD14+.~~

~~129. A method of treating a disease in a subject, comprising, administering to the subject any one of: (i) the pharmaceutical composition of claim 126; or~~

~~(ii) the cell of claim 127 or claim 128.~~