CLAIMS

What is claimed is:

1. An isolated nucleic acid sequence encoding a chimeric antigen receptor (CAR), wherein the CAR comprises an antigen binding domain, a hinge domain, a transmembrane domain, a costimulatory signaling region, and a CD3 zeta signaling domain, and further wherein when the CAR is transduced into a T cell, the CAR contributes to at least one of: increased antigen-independent activation of the transduced T cell, increased mean cell volume (MCV) of the transduced T cell, increased cell population expansion of the transduced T cell, increased proliferation of the transduced T cell, increased numbers of progeny of the transduced T cell, increased effector cytokine secretion, sustained expression of granzyme, increased persistence of the transduced T cell population in vitro, or increased persistence of the transduced T cell population in vivo.

2. The isolated nucleic acid sequence of claim 1, wherein the hinge domain is an IgG4 hinge domain.

3. The isolated nucleic acid sequence of claim 1, wherein the antigen binding domain is an anti-cMet binding domain, the hinge domain is IgG4, the transmembrane domain is a CD28 transmembrane domain, and the costimulatory signaling region is a CD28 signaling region.

4. The isolated nucleic acid sequence of claim 3, wherein the CAR comprises the amino acid sequence of SEQ ID NO: 1.

5. The isolated nucleic acid sequence of claim 1, wherein the antigen binding domain is an anti-mesothelin binding domain, the hinge domain is an IgG4 hinge domain, the transmembrane domain is a CD28 transmembrane domain, and the costimulatory signaling region is a CD28 signaling region.

6. The isolated nucleic acid sequence of claim 5, wherein the CAR comprises the amino acid sequence of SEQ ID NO: 2.

7. The isolated nucleic acid sequence of claim 1, wherein the antigen binding domain is an anti-CD19 binding domain, the hinge domain is an IgG4 hinge domain, the transmembrane domain is an CD28 transmembrane domain, and the costimulatory signaling region is a CD28 signaling region.

8. The isolated nucleic acid sequence of claim 7, wherein the CAR comprises the amino acid sequence of SEQ ID NO: 3.

9. The isolated nucleic acid sequence of claim 1, wherein the antigen binding domain is an antibody or an antigen-binding fragment thereof.

10. A T cell comprising a nucleic acid sequence encoding a chimeric antigen receptor (CAR), the CAR comprising an antigen binding domain, a hinge domain, a transmembrane domain, a costimulatory signaling region, and a CD3 zeta signaling domain, and wherein when the CAR is transduced into a T cell, the CAR contributes to at least one of: increased antigen-independent activation of the transduced T cell, increased mean cell volume (MCV) of the transduced T cell, increased cell population expansion of the transduced T cell, increased proliferation of the transduced T cell, increased effector cytokine secretion, increased expression of granzyme, increased numbers of progeny of the transduced T cell, increased persistence of the transduced T cell population in vitro, or increased persistence of the transduced T cell population in vivo.

11. The T cell of claim 10, wherein the hinge domain is an IgG4 hinge domain.

12. The T cell of claim 10, wherein the antigen binding domain is an anti-cMet binding domain, the hinge domain is an IgG4 hinge domain, the transmembrane domain is a CD28 transmembrane domain, and the costimulatory signaling region is a CD28 signaling region.

13. The T cell of claim 12, wherein the CAR comprises the amino acid sequence of SEQ ID NO: 1.

14. The T cell of claim 10, wherein the antigen binding domain is an anti-mesothelin binding domain, the hinge domain is an IgG4 hinge domain, the transmembrane domain is an CD28 transmembrane domain, and the costimulatory signaling region is a CD28 signaling region.

15. The T cell of claim 14, wherein the CAR comprises the amino acid sequence of SEQ ID NO: 2.

16. The T cell of claim 10, wherein the antigen binding domain is an anti-CD19 binding domain, the hinge domain is an IgG4 hinge domain, the transmembrane domain is a CD28 transmembrane domain, and the costimulatory signaling region is a CD28 signaling region.

17. The T cell of claim 16, wherein the CAR comprises the amino acid sequence of SEQ ID NO: 3.

18. The T cell of claim 10, wherein the antigen binding domain is an antibody or an antigen-binding fragment thereof.

19. The T cell of claim 10, wherein the cell exhibits an anti-tumor immunity when the antigen binding domain binds to its corresponding antigen.

20. A vector comprising a nucleic acid sequence encoding a chimeric antigen receptor (CAR), the CAR comprising an antigen binding domain, a hinge domain, a transmembrane domain, a costimulatory signaling region, and a CD3 zeta signaling domain, and wherein when the CAR is transduced into a T cell, the CAR contributes to at least one of: increased antigen-independent activation of the transduced T cell, increased mean cell volume (MCV) of the transduced T cell, increased cell population expansion of the transduced T cell, increased proliferation of the transduced T cell, increased numbers of progeny of the transduced T cell, increased persistence of the transduced T cell population in vitro, or increased persistence of the transduced T cell population in vivo.

21. The vector of claim 20, wherein the hinge domain is an IgG4 hinge domain.

22. The vector of claim 20, wherein the antigen binding domain is an anti-cMet binding domain, the hinge domain is an IgG4 hinge domain, the transmembrane domain is a CD28 transmembrane domain, and the costimulatory signaling region is a CD28 signaling region.

23. The vector of claim 22, wherein the CAR comprises the amino acid sequence of SEQ ID NO: 1.

24. The vector of claim 20, wherein the antigen binding domain is an anti-mesothelin binding domain, the hinge domain is an IgG4 hinge domain, the transmembrane domain is a CD28 transmembrane domain, and the costimulatory signaling region is a CD28 signaling region.

25. The vector of claim 24, wherein the CAR comprises the amino acid sequence of SEQ ID NO: 2.

26. The vector of claim 20, wherein the antigen binding domain is an anti-CD19 binding domain, the hinge domain is an IgG4 hinge domain, the transmembrane domain is a CD28 transmembrane domain, and the costimulatory signaling region is a CD28 signaling region.

27. The vector of claim 26, wherein the CAR comprises the amino acid sequence of SEQ ID NO: 3.

28. The vector of claim 20, wherein the antigen binding domain is an antibody or an antigen-binding fragment thereof.

29. A persisting population of genetically modified T cells, wherein the T cells comprise a nucleic acid sequence encoding a chimeric antigen receptor (CAR), the CAR comprising an antigen binding domain, a hinge domain, a transmembrane domain, a costimulatory signaling region, and a CD3 zeta signaling domain, and wherein when the CAR is transduced into a T cell, the CAR contributes

to at least one of: increased antigen-independent activation of the transduced T cell, increased mean cell volume (MCV) of the transduced T cell, increased cell population expansion of the transduced T cell, increased proliferation of the transduced T cell, increased numbers of progeny of the transduced T cell, increased persistence of the transduced T cell population in vitro, or increased persistence of the transduced T cell population in vivo.

30. The persisting population of genetically modified T cells of claim 29, wherein the genetically modified T cells exhibit an anti-tumor immunity when the antigen binding domain binds to its corresponding antigen.

31. The persisting population of genetically modified T cells of claim 29, wherein the T cells exhibit a cytokine signature comprising at least one cytokine selected from the group consisting of IFN-γ, TNF-α, IL-17A, IL-2, IL-3, IL-4, GM-CSF, IL-10, IL-13, Granzyme B, Perforin, and any combination thereof.

32. The persisting population of genetically modified T cells of claim 29, wherein the T cells proliferate in the absence of exogenous cytokine or feeder cells.

CLAIMS

1. An isolated nucleic acid sequence encoding a chimeric antigen receptor (CAR), wherein the CAR comprises an anti-cMet binding domain, a hinge domain, a transmembrane domain, a costimulatory signaling region, and a CD3 zeta signaling domain.

2. The isolated nucleic acid sequence of claim 1, wherein the hinge domain is an IgG4 hinge domain.

3. The isolated nucleic acid sequence of claim 1, wherein the hinge domain is IgG4, the transmembrane domain is a CD28 transmembrane domain, and the costimulatory signaling region is a CD28 signaling region.

4. The isolated nucleic acid sequence of claim 3 encoding an amino acid sequence comprising SEQ ID NO: 1.

5. A T cell comprising a nucleic acid sequence encoding a chimeric antigen receptor (CAR), the CAR comprising an anti-cMet binding domain, a hinge domain, a transmembrane domain, a costimulatory signaling region, and a CD3 zeta signaling domain.

6. The T cell of claim 5, wherein the hinge domain is an IgG4 hinge domain.

7. The T cell of claim 5, wherein the hinge domain is an IgG4 hinge domain, the transmembrane domain is a CD28 transmembrane domain, and the costimulatory signaling region is a CD28 signaling region.

8. The T cell of claim 7, wherein the nucleic acid sequence encodes an amino acid sequence comprising SEQ ID NO: 1.

9. The T cell of claim 5, wherein the cell exhibits an anti-tumor immunity when the antigen binding domain binds to its corresponding antigen.

10. A vector comprising a nucleic acid sequence encoding a chimeric antigen receptor (CAR), the CAR comprising an anti-cMet binding domain, a hinge domain, a transmembrane domain, a costimulatory signaling region, and a CD3 zeta signaling domain.

11. The vector of claim 10, wherein the hinge domain is an IgG4 hinge domain.

12. The vector of claim 10, wherein the hinge domain is an IgG4 hinge domain, the transmembrane domain is a CD28 transmembrane domain, and the costimulatory signaling region is a CD28 signaling region.

13. The vector of claim 12, wherein the nucleic acid sequence encodes an amino acid sequence comprising SEQ ID NO: 1.

14. A persisting population of genetically modified T cells, wherein the T cells comprise a nucleic acid sequence encoding a chimeric antigen receptor (CAR), the CAR comprising an anti-cMet binding domain, a hinge domain, a transmembrane domain, a costimulatory signaling region, and a CD3 zeta signaling domain.

15. The persisting population of genetically modified T cells of claim 14, wherein the genetically modified T cells exhibit an anti-tumor immunity when the antigen binding domain binds to its corresponding antigen.

16. The persisting population of genetically modified T cells of claim 14, wherein the T cells exhibit a cytokine signature comprising at least one cytokine selected from the group consisting of IFN-γ, TNF-α, IL-17A, IL-2, IL-3, IL-4, GM-CSF, IL-10, IL-13, Granzyme B, Perforin, and any combination thereof.

17. The persisting population of genetically modified T cells of claim 14, wherein the T cells proliferate in the absence of exogenous cytokine or feeder cells.

18. The T cell of claim 5, wherein the CAR is transduced into the T cell and the CAR contributes to at least one property selected from the group consisting of: increased antigen-independent activation of the transduced T cell, increased mean cell volume (MCV) of the transduced T cell, increased cell population expansion of the transduced T cell, increased proliferation of the transduced T cell, increased numbers of progeny of the transduced T cell, increased effector cytokine secretion, sustained expression of granzyme, increased persistence of the transduced T cell in vitro, and increased persistence of the transduced T cell in vivo.

19. The persisting population of genetically modified T cells of claim 14, wherein the CAR is transduced into the modified T cells and the CAR contributes to at least one property selected from the group consisting of: increased antigen-independent activation of the transduced T cells, increased mean cell volume (MCV) of the transduced T cells, increased cell population expansion of the transduced T cells, increased proliferation of the transduced T cells, increased numbers of progeny of the transduced T cells, increased effector cytokine secretion, sustained expression of granzyme, increased persistence of the transduced T cells in vitro, and increased persistence of the transduced T cells in vivo.