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 transmembrane domain, a costimulatory signaling region, and a CD3 zeta signaling domain, wherein the costimulatory signaling region comprises the CD2 signaling domain.

2. The isolated nucleic acid sequence of claim 1, comprising the nucleic acid sequence of SEQ ID NO: 1.

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

4. The isolated nucleic acid sequence of claim 1, wherein the antigen binding domain binds to a tumor antigen.

5. The isolated nucleic acid sequence of claim 1, wherein the costimulatory signaling region further comprises the intracellular domain of a costimulatory molecule selected from the group consisting of CD27, CD28, 4-1BB, OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD7, LIGHT, NKG2C, B7-H3, a ligand that specifically binds with CD83, and any combination thereof.

6. An isolated chimeric antigen receptor (CAR) comprising an antigen binding domain, a transmembrane domain, a costimulatory signaling region, and a CD3 zeta signaling domain, wherein the costimulatory signaling region comprises the CD2 signaling domain

7. The isolated CAR of claim 6, wherein the antigen binding domain is an antibody or an antigen-binding fragment thereof.

8. The isolated CAR of claim 6, wherein the antigen binding domain binds to a tumor antigen.

9. The isolated CAR of claim 6, wherein the costimulatory signaling region further comprises the intracellular domain of a costimulatory molecule selected from the group consisting of CD27, CD28, 4-1BB, OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD7, LIGHT, NKG2C, B7-H3, a ligand that specifically binds with CD83, and any combination thereof.

10. A cell comprising a nucleic acid sequence encoding a chimeric antigen receptor (CAR), the CAR comprising an antigen binding domain, a transmembrane domain, a costimulatory signaling region, and a CD3 zeta signaling domain, wherein the costimulatory signaling domain comprises the CD2 signaling domain.

11. The cell of claim 10, wherein the nucleic acid comprises the nucleic acid sequence of SEQ ID NO: 1.

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

13. The cell of claim 10, wherein the antigen binding domain binds to a tumor antigen.

14. The cell of claim 10, wherein the costimulatory signaling region further comprises the intracellular domain of a costimulatory molecule selected from the group consisting of CD27, CD28, 4-1BB, OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD7, LIGHT, NKG2C, B7-H3, a ligand that specifically binds with CD83, and any combination thereof.

15. The cell of claim 14, wherein the cell is selected from the group consisting of a T cell, a Natural Killer (NK) cell, a cytotoxic T lymphocyte (CTL), and a regulatory T cell.

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

17. A vector comprising a nucleic acid sequence encoding a chimeric antigen receptor (CAR), wherein the CAR comprises an antigen binding domain, a transmembrane domain, a costimulatory signaling region, and a CD3 zeta signaling domain, wherein the costimulatory signaling region comprises the CD2 signaling domain.

18. The vector of claim 17, wherein the isolated nucleic acid sequence encoding a CAR comprises the nucleic acid sequence of SEQ ID NO: 1.

19. The vector of claim 17, wherein the antigen binding domain is an antibody or an antigen-binding fragment thereof.

20. The vector of claim 17, wherein the antigen binding domain binds to a tumor antigen.

21. The vector of claim 17, wherein the costimulatory signaling region further comprises the intracellular domain of a costimulatory molecule selected from the group consisting of CD27, CD28, 4-1BB, OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD7, LIGHT, NKG2C, B7-H3, a ligand that specifically binds with CD83, and any combination thereof.

22. A method for stimulating a T cell-mediated immune response to a target cell population or tissue in a mammal, the method comprising administering to a mammal an effective amount of a cell genetically modified to express a CAR, wherein the CAR comprises an antigen binding domain, a transmembrane domain, a costimulatory signaling region comprising the CD2 signaling domain, and a CD3 zeta signaling domain, and wherein the antigen binding domain is selected to specifically recognize the target cell population or tissue.

23. A method of providing an anti-tumor immunity in a mammal, the method comprising administering to the mammal an effective amount of a cell

genetically modified to express a CAR, wherein the CAR comprises an antigen binding domain, a transmembrane domain, a costimulatory signaling region comprising the CD2 signaling domain, and a CD3 zeta signaling, thereby providing an anti-tumor immunity in the mammal.

24. A method of treating a mammal having a disease, disorder or condition associated with an elevated expression of a tumor antigen, the method comprising administering to the mammal an effective amount of a cell genetically modified to express a CAR, wherein the CAR comprises an antigen binding domain a transmembrane domain, a costimulatory signaling region comprising the CD2 signaling domain, and a CD3 zeta signaling domain, thereby treating the mammal.

25. The method of claim 24, wherein the cell is an autologous T cell.

26. The method of claim 24, wherein the tumor antigen is selected from the group consisting of CD19, CD20, CD22, ROR1, mesothelin, CD33/IL3Ra, c-Met, PSMA, Glycolipid F77, EGFRvIII, GD-2, NY-ESO-1 TCR, MAGE A3 TCR, and any combination thereof.

27. A method of treating a human with cancer, the method comprising administering to the human a T cell genetically engineered to express a CAR, wherein the CAR comprises an antigen binding domain, a transmembrane domain, a costimulatory signaling region comprising the CD2 signaling domain, and a CD3 zeta signaling domain.

28. The method of claim 27, wherein the human is resistant to at least one chemotherapeutic agent.

29. A method of generating a persisting population of genetically engineered T cells in a human diagnosed with cancer, the method comprising administering to the human a T cell genetically engineered to express a CAR, wherein the CAR comprises an antigen binding domain a transmembrane domain, a costimulatory signaling region comprising the CD2 signaling domain, and a CD3 zeta

signaling domain, wherein the persisting population of genetically engineered T cells persists in the human for at least one month after administration.

30. The method of claim 29, wherein the persisting population of genetically engineered T cells comprises at least one cell selected from the group consisting of a T cell that was administered to the human, a progeny of a T cell that was administered to the human, and a combination thereof.

31. The method of claim 29, wherein the persisting population of genetically engineered T cells comprises a memory T cell.

32. The method of claim 29, wherein the persisting population of genetically engineered T cells persists in the human for at least three months after administration.

33. The method of claim 29, wherein the persisting population of genetically engineered T cells persists in the human for at least four months, five months, six months, seven months, eight months, nine months, ten months, eleven months, twelve months, two years, or three years after administration.

34. The method of claim 29, wherein the cancer is treated.

35. A method of expanding a population of genetically engineered T cells in a human diagnosed with cancer, the method comprising administering to the human a T cell genetically engineered to express a CAR, wherein the CAR comprises an antigen binding domain, a transmembrane domain, a costimulatory signaling region comprising the CD2 signaling domain, and a CD3 zeta signaling domain, wherein the administered genetically engineered T cell produces a population of progeny T cells in the human.

36. The method of claim 35, wherein the progeny T cells in the human comprise a memory T cell.

37. The method of claim 35, wherein the T cell is an autologous T cell.

38. The method of claim 35, wherein the population of progeny T cells persists in the human for at least three months after administration.

39. The method of claim 35, wherein the population of progeny T cells persist in the human for at least four months, five months, six months, seven months, eight months, nine months, ten months, eleven months, twelve months, two years, or three years after administration.

40. A method of modulating the amount of cytokine secreted by a T cell, said method comprising genetically engineering the T cell to express a CAR, wherein the CAR comprises an antigen binding domain, a transmembrane domain, a costimulatory domain region comprising CD2, and a CD3 zeta signaling domain.

41. The method of claim 40, wherein modulating the amount of cytokine secreted by a T cell reduces the proliferation of T regulatory cells.

42. A method of reducing the amount of activation-induced calcium influx into a T cell, said method comprising genetically engineering the T cell to express a CAR, wherein the CAR comprises an antigen binding domain, a transmembrane domain, a costimulatory domain region comprising CD2, and a CD3 zeta signaling domain.

43. The method of claim 42, wherein reducing the amount of activation-induced calcium influx into a T cell prevents the activation-induced cell death of the T cell.

CLAIMS

1. An isolated nucleic acid sequence encoding a chimeric antigen receptor (CAR), wherein the CAR comprises an antigen binding domain, a transmembrane domain, a costimulatory signaling region, and a CD3 zeta signaling domain, wherein the costimulatory signaling region comprises the CD2 signaling domain.

2. The isolated nucleic acid sequence of claim 1, comprising the nucleic acid sequence of SEQ ID NO: 1.

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

4. The isolated nucleic acid sequence of claim 1, wherein the antigen binding domain binds to a tumor antigen.

5. The isolated nucleic acid sequence of claim 1, wherein the costimulatory signaling region further comprises the intracellular domain of a costimulatory molecule selected from the group consisting of CD27, CD28, 4-1BB, OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD7, LIGHT, NKG2C, B7-H3, a ligand that specifically binds with CD83, and any combination thereof.

6. An isolated chimeric antigen receptor (CAR) comprising an antigen binding domain, a transmembrane domain, a costimulatory signaling region, and a CD3 zeta signaling domain, wherein the costimulatory signaling region comprises the CD2 signaling domain

7. The isolated CAR of claim 6, wherein the antigen binding domain is an antibody or an antigen-binding fragment thereof.

8. The isolated CAR of claim 6, wherein the antigen binding domain binds to a tumor antigen.

9. The isolated CAR of claim 6, wherein the costimulatory signaling region further comprises the intracellular domain of a costimulatory molecule selected from the group consisting of CD27, CD28, 4-1BB, OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD7, LIGHT, NKG2C, B7-H3, a ligand that specifically binds with CD83, and any combination thereof.

10. A cell comprising a nucleic acid sequence encoding a chimeric antigen receptor (CAR), the CAR comprising an antigen binding domain, a transmembrane domain, a costimulatory signaling region, and a CD3 zeta signaling domain, wherein the costimulatory signaling domain comprises the CD2 signaling domain.

11. The cell of claim 10, wherein the nucleic acid comprises the nucleic acid sequence of SEQ ID NO: 1.

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

13. The cell of claim 10, wherein the antigen binding domain binds to a tumor antigen.

14. The cell of claim 10, wherein the costimulatory signaling region further comprises the intracellular domain of a costimulatory molecule selected from the group consisting of CD27, CD28, 4-1BB, OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD7, LIGHT, NKG2C, B7-H3, a ligand that specifically binds with CD83, and any combination thereof.

15. The cell of claim 14, wherein the cell is selected from the group consisting of a T cell, a Natural Killer (NK) cell, a cytotoxic T lymphocyte (CTL), and a regulatory T cell.

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

17. A vector comprising a nucleic acid sequence encoding a chimeric antigen receptor (CAR), wherein the CAR comprises an antigen binding domain, a transmembrane

domain, a costimulatory signaling region, and a CD3 zeta signaling domain, wherein the costimulatory signaling region comprises the CD2 signaling domain.

18. The vector of claim 17, wherein the isolated nucleic acid sequence encoding a CAR comprises the nucleic acid sequence of SEQ ID NO: 1.

19. The vector of claim 17, wherein the antigen binding domain is an antibody or an antigen-binding fragment thereof.

20. The vector of claim 17, wherein the antigen binding domain binds to a tumor antigen.

21. The vector of claim 17, wherein the costimulatory signaling region further comprises the intracellular domain of a costimulatory molecule selected from the group consisting of CD27, CD28, 4-1BB, OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD7, LIGHT, NKG2C, B7-H3, a ligand that specifically binds with CD83, and any combination thereof.

22. An effective amount of a cell genetically modified to express a CAR for use as a medicament for the therapeutic and/or prophylactic treatment of stimulating a T cell-mediated immune response to a target cell population or tissue in a mammal, wherein the CAR comprises an antigen binding domain, a transmembrane domain, a costimulatory signaling region comprising the CD2 signaling domain, and a CD3 zeta signaling domain, and wherein the antigen binding domain is selected to specifically recognize the target cell population or tissue.

23. An effective amount of a cell genetically modified to express a CAR for use as a medicament for the therapeutic and/or prophylactic treatment of providing an anti-tumor immunity in a mammal, wherein the CAR comprises an antigen binding domain, a transmembrane domain, a costimulatory signaling region comprising the CD2 signaling domain, and a CD3 zeta signaling.

24. An effective amount of a cell genetically modified to express a CAR for use as a medicament for the therapeutic and/or prophylactic treatment of treating a mammal having a disease, disorder or condition associated with an elevated expression of a

tumor antigen, wherein the CAR comprises an antigen binding domain a transmembrane domain, a costimulatory signaling region comprising the CD2 signaling domain, and a CD3 zeta signaling domain, thereby treating the mammal.

25. The cell of claim 24, wherein the cell is an autologous T cell to the mammal.

26. The cell of claim 24, wherein the tumor antigen is selected from the group consisting of CD19, CD20, CD22, ROR1, mesothelin, CD33/IL3Ra, c-Met, PSMA, Glycolipid F77, EGFRvIII, GD-2, NY-ESO-1 TCR, MAGE A3 TCR, and any combination thereof.

27. A T cell genetically engineered to express a CAR for use as a medicament for the therapeutic and/or prophylactic treatment of treating a human with cancer, wherein the CAR comprises an antigen binding domain, a transmembrane domain, a costimulatory signaling region comprising the CD2 signaling domain, and a CD3 zeta signaling domain.

28. The T cell of claim 27, wherein the human is resistant to at least one chemotherapeutic agent.

29. A T cell genetically engineered to express a CAR for use as a medicament for the therapeutic and/or prophylactic treatment of generating a persisting population of genetically engineered T cells in a human diagnosed with cancer, wherein the CAR comprises an antigen binding domain a transmembrane domain, a costimulatory signaling region comprising the CD2 signaling domain, and a CD3 zeta signaling domain.

30. The T cell of claim 29, wherein the persisting population of genetically engineered T cells comprises at least one cell selected from the group consisting of a T cell that was administered to the human, a progeny of a T cell that was administered to the human, and a combination thereof.

31. The T cell of claim 29, wherein the persisting population of genetically engineered T cells comprises a memory T cell.

32. The T cell of claim 29, wherein the persisting population of genetically engineered T cells persists in the human for at least three months after administration.

33. The T cell of claim 29, wherein the persisting population of genetically engineered T cells persists in the human for at least four months, five months, six months, seven months, eight months, nine months, ten months, eleven months, twelve months, two years, or three years after administration.

34. The T cell of claim 29, wherein the cancer is treated.

35. A T cell genetically engineered to express a CAR for use as a medicament for the therapeutic and/or prophylactic treatment of expanding a population of genetically engineered T cells in a human diagnosed with cancer, wherein the CAR comprises an antigen binding domain, a transmembrane domain, a costimulatory signaling region comprising the CD2 signaling domain, and a CD3 zeta signaling domain, wherein the administered genetically engineered T cell produces a population of progeny T cells in the human.

36. The T cell of claim 35, wherein the progeny T cells in the human comprise a memory T cell.

37. The T cell of claim 35, wherein the T cell is an autologous T cell.

38. The T cell of claim 35, wherein the population of progeny T cells persists in the human for at least three months after administration.

39. The T cell of claim 35, wherein the population of progeny T cells persist in the human for at least four months, five months, six months, seven months, eight months, nine months, ten months, eleven months, twelve months, two years, or three years after administration.

40. A T cell to express a CAR for use as a medicament for the therapeutic and/or prophylactic treatment of modulating the amount of cytokine secreted by the T cell,

wherein the CAR comprises an antigen binding domain, a transmembrane domain, a costimulatory domain region comprising CD2, and a CD3 zeta signaling domain.

41. The T cell of claim 40, wherein modulating the amount of cytokine secreted by a T cell reduces the proliferation of T regulatory cells.

42. A T cell to express a CAR for use as a medicament for the therapeutic and/or prophylactic treatment of reducing the amount of activation-induced calcium influx into the T cell, wherein the CAR comprises an antigen binding domain, a transmembrane domain, a costimulatory domain region comprising CD2, and a CD3 zeta signaling domain.

43. The T cell of claim 42, wherein the reduced amount of activation-induced calcium influx into the T cell prevents the activation-induced cell death of the T cell.