

CLAIMS:

1. A nucleic acid encoding a chimeric antigen receptor (CAR), wherein the CAR comprises:

a ligand binding domain which specifically binds to a dinitrophenol (DNP) moiety, wherein the ligand binding domain comprises a variable heavy chain domain (VH) comprising an amino acid sequence having at least 95% sequence identity to SEQ ID NO:01 and a variable light chain domain (VL) comprising an amino acid sequence having at least 95% sequence identity to SEQ ID NO:02;

a spacer comprising an IgG4 hinge -CH2-CH3 domain;

a transmembrane domain; and

an intracellular signaling domain.

2. The nucleic acid of claim 1, wherein the ligand binding domain comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NOs:09 or 10.

3. The nucleic acid of claim 1 or claim 2, wherein the spacer has a length of at least 229 consecutive amino acid residues.

4. The nucleic acid of any one of claims 1-3, wherein the spacer comprises the amino acid sequence of SEQ ID NO:20.

5. The nucleic acid of any one of claims 1-4, wherein the transmembrane domain comprises a CD28 transmembrane domain; and the intracellular signaling domain comprises a portion of CD3 zeta and/or a portion of 4-1BB.

6. The nucleic acid of any one of claims 1-5, wherein the transmembrane domain comprises a CD28 transmembrane domain set forth in SEQ ID NO:23 and the intracellular signaling domain comprises a portion of CD3 zeta set forth in SEQ ID NO:25 and/or a portion of 4-1BB set forth in SEQ ID NO:24.

7. The nucleic acid of any one of claims 1-6, further comprising a polynucleotide encoding (i) a selectable gene that is a dihydrofolate reductase double mutant (DHFRdm); (ii) a cell surface selectable marker selected from the group consisting of a truncated EGFR (EGFRt), a truncated Her2 (Her2tG), and a truncated CD19 (CD19t); and/or (iii) a cleavable

linker comprising a ribosome skip sequence selected from the group consisting of P2A, T2A, E2A and F2A.

8. A vector comprising the nucleic acid of any one of claims 1-7.
9. The vector of claim 8, wherein the vector comprises a lentiviral vector.
10. A method suitable for preparing a population of cells for an infusion, comprising:
 - introducing the nucleic acid of any one of claims 1-7 or the vector of claim 8 or claim 9 into a cell; and
 - culturing the cell under conditions suitable to obtain a population of cells sufficient for an infusion.
11. A chimeric antigen receptor (CAR) encoded by the nucleic acid of any one of claims 1-7.
12. A cell comprising the nucleic acid of any one of claims 1-7, or a chimeric antigen receptor (CAR) encoded by the nucleic acid, wherein the cell is derived from a CD4⁺ T cell, a CD8⁺ T cell, a precursor T cell, or a hematopoietic stem cell.
13. The cell of claim 12, wherein the CD8⁺ T cell is a CD8⁺ cytotoxic T lymphocyte cell selected from the group consisting of a naïve CD8⁺ T cell, a central memory CD8⁺ T cell, an effector memory CD8⁺ T cell, and a bulk CD8⁺ T cell; or the CD4⁺ cell is a CD4⁺ helper T lymphocyte cell selected from the group consisting of a naïve CD4⁺ T cell, a central memory CD4⁺ T cell, an effector memory CD4⁺ T cell, and a bulk CD4⁺ T cell.
14. Use of the nucleic acid of any one of claims 1-7, the vector of claim 8 or claim 9, the CAR of claim 11 or the cell of claim 12 or claim 13, in the manufacture of a medicament for treating, inhibiting or ameliorating a cancer in a subject, wherein the nucleic acid, vector, CAR or cell is to be administered to the subject in combination with a composition comprising a dinitrophenol (DNP) moiety, wherein the DNP moiety is covalently linked to a phospholipid that integrates into the plasma membrane of a cell of the cancer.
15. The use of claim 14, wherein the composition comprising the DNP moiety is to be administered subsequent to the nucleic acid, vector, CAR, or cell.
16. The use of claim 14, wherein the central memory CD8⁺ T cell is positive for CD45RO and CD62L, or the naïve CD4⁺ T cell is positive for CD45RA and CD62L, and negative for CD45RO.

17. The use of any one of claims 14-16, wherein the DNP is attached to a phospholipid that is a phospholipid ether (PLE).

18. The use of any one of claims 14-17, wherein the cancer comprises a cell selected from the group consisting of a breast cancer cell, brain cancer cell, colon cancer cell, renal cancer cell, pancreatic cancer cell, and ovarian cancer cell.

19. The use of any one of claims 14-18, wherein the subject is human.