

CLAIMS

1. A nucleic acid encoding a chimeric receptor comprising:
 - a) a polynucleotide encoding an extracellular ligand binding domain, wherein the ligand binding domain binds specifically to CD171;
 - b) a polynucleotide encoding an extracellular polypeptide spacer comprising the amino acid sequence set forth in SEQ ID NO:01, wherein the polypeptide spacer has a length of 119 consecutive amino acids or less;
 - c) a polynucleotide encoding a transmembrane domain; and
 - d) a polynucleotide encoding an intracellular signaling domain;wherein the polypeptide spacer is located between the ligand binding domain and the transmembrane domain.
2. The nucleic acid of claim 1, wherein the chimeric receptor comprises an extracellular domain consisting of the ligand binding domain and the extracellular polypeptide spacer.
3. The nucleic acid of claim 1 or 2, wherein the polypeptide spacer is selected from the group consisting of:
 - a polypeptide spacer having a length less than or equal to 15 amino acids;
 - a polypeptide spacer comprising the amino acid sequence set forth in SEQ ID NO: 59; and
 - a polypeptide spacer comprising the amino acid sequence set forth in SEQ ID NO: 21.
4. The nucleic acid of claim 1 or 2, wherein the polypeptide spacer is selected from the group consisting of:
 - a polypeptide spacer comprising the amino acid sequence set forth in SEQ ID NO: 59 and having a length of 119 consecutive amino acids; and
 - a polypeptide spacer comprising the amino acid sequence set forth in SEQ ID NO: 21 and having a length of 12 consecutive amino acids.
5. The nucleic acid of any one of claims 1-4, wherein the polypeptide spacer comprises a portion of a hinge region of a human antibody.

6. The nucleic acid of any one of claims 1-5, wherein the ligand binding domain comprises an antibody fragment.

7. The nucleic acid of any one of claims 1-6, wherein the ligand binding domain is a single chain variable fragment.

8. The nucleic acid of any one of claims 1-7, wherein the polynucleotide encoding a ligand binding domain comprises the nucleotide sequence of residues 2150 to 2875 set forth in SEQ ID NO:54.

9. The nucleic acid of any one of claims 1-8, wherein the intracellular signaling domain comprises all of or a portion of CD3 zeta in combination with a costimulatory domain selected from the group consisting of CD27, CD28, 4-1BB, OX-40, CD30, CD40, PD-1, ICOS, LFA-1, CD2, CD7, NKG2C, B7-H3, and a combination thereof.

10. The nucleic acid of claim 9, wherein the intracellular signaling domain comprises a portion of CD3 zeta and a portion of 4-1BB.

11. The nucleic acid of any one of claims 1-10, further comprising a polynucleotide encoding a selectable marker.

12. The nucleic acid of any one of claims 1-11, wherein the nucleic acid comprises at least 95% sequence identity to the nucleotide sequence of residues 2084 to 3778 of SEQ ID NO:55, residues 2084 to 3457 of SEQ ID NO:56, or residues 2084 to 3580 of SEQ ID NO:57.

13. The nucleic acid of any one of claims 1-12, wherein the nucleic acid comprises the nucleotide sequence of residues 2084 to 3778 of SEQ ID NO:55, residues 2084 to 3457 of SEQ ID NO:56, or residues 2084 to 3580 of SEQ ID NO:57.

14. A chimeric receptor polypeptide encoded by the nucleic acid of any one of claims 1-13.

15. An expression vector comprising the nucleic acid of any one of claims 1-13.

16. A host cell comprising the nucleic acid of any one of claims 1-13 or the expression vector of claim 15.

17. The host cell of claim 16, wherein the host 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 wherein the host 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.

18. The host cell of claim 15, wherein the host cell is a precursor T cell, or a hematopoietic stem cell.

19. A pharmaceutical composition comprising the host cell of any one of claims 16-18 and a pharmaceutically acceptable excipient.

20. A method for preparing the host cell of any one of claims 16-18 comprising:

a) introducing the nucleic acid of any one of claims 1-13 into a lymphocyte population that has a CD45RA-, CD45RO+, and CD62L+ phenotype; and

b) culturing the cells in the presence of anti-CD3 and/or anti CD28, and at least one homeostatic cytokine until the cells expand sufficiently for use as a cell infusion.

21. The method of claim 20, wherein the lymphocyte population is CD8+ or CD4+.

22. Use of the host cell of any one of claims 16-18 in the manufacture of a medicament for treating or inhibiting a cancer or a solid tumor expressing CD171.

23. The use of claim 22, wherein the cancer is a neuroblastoma.

24. The use of claim 22, wherein the cancer is selected from the group consisting of a breast cancer, a brain cancer, a colon cancer, a renal cancer, a pancreatic cancer, and an ovarian cancer.

25. Use of the host cell of any one of claims 16-18 in the manufacture of a medicament for performing cellular immunotherapy in a subject having a cancer or a tumor.

26. The use of claim 25, wherein the cancer is neuroblastoma.

27. The use of claim 25, wherein the cancer is selected from the group consisting of a breast cancer, brain cancer, colon cancer, renal cancer, pancreatic cancer, and ovarian cancer.