

CLAIMS

What is claimed is:

1. A chimeric antigen receptor (CAR) comprising:
 - (a) an ectodomain comprising an antigen recognition region, wherein the antigen recognition region comprises at least one Centryn that specifically binds prostate specific membrane antigen (PSMA);
 - (b) a transmembrane domain, and
 - (c) an endodomain comprising at least one costimulatory domain.
2. The CAR of claim 1, wherein the ectodomain of (a) further comprises a signal peptide.
3. The CAR of claim 1, wherein the ectodomain of (a) further comprises a hinge between the antigen recognition region and the transmembrane domain.
4. The CAR of claim 2, wherein the signal peptide comprises an amino acid sequence encoding a human CD2, CD3 δ , CD3 ϵ , CD3 γ , CD3 ζ , CD4, CD8 α , CD19, CD28, 4-1BB or GM-CSFR signal peptide.
5. The CAR of claim 4, wherein the signal peptide comprises an amino acid sequence encoding a human CD8 α signal peptide.
6. The CAR of claim 5, wherein the human CD8 α signal peptide comprises an amino acid sequence of SEQ ID NO: 18004.
7. The CAR of claim 1, wherein the transmembrane domain comprises an amino acid sequence encoding a human CD2, CD3 δ , CD3 ϵ , CD3 γ , CD3 ζ , CD4, CD8 α , CD19, CD28, 4-1BB or GM-CSFR transmembrane domain.
8. The CAR of claim 7, wherein the transmembrane domain comprises an amino acid sequence encoding a human CD8 α transmembrane domain.

9. The CAR of claim 8, wherein the human CD8 α transmembrane domain comprises an amino acid sequence of SEQ ID NO: 18006.
10. The CAR of claim 1, wherein the endodomain comprises a human CD3 ζ endodomain.
11. The CAR of claim 1, wherein the at least one costimulatory domain comprises a human 4-1BB, CD28, CD40, ICOS, MyD88, OX-40 intracellular segment, or any combination thereof.
12. The CAR of claim 11, wherein the at least one costimulatory domain comprises a human 4-1BB costimulatory domain.
13. The CAR of claim 10, wherein the human CD3 ζ endodomain domain comprises an amino acid sequence of SEQ ID NO: 18008.
14. The CAR of claim 11, wherein the human 4-1BB costimulatory domain comprises an amino acid sequence of SEQ ID NO: 18012.
15. The CAR of claim 3, wherein the hinge comprises an amino acid sequence derived from a human CD8 α , IgG4, CD4 sequence or any combination thereof.
16. The CAR of claim 15, wherein the hinge comprises an amino acid sequence derived from a human CD8 α .
17. The CAR of claim 16, wherein the sequence derived from a human CD8 α comprises an amino acid sequence of SEQ ID NO: 18014.
18. The CAR of claim 1, wherein the at least one Centyrin that specifically binds PSMA comprises an amino acid sequence of SEQ ID NO: 18000.

19. The CAR of claim 1, wherein the at least one Centyrin that specifically binds PSMA is encoded by a nucleic acid sequence comprising SEQ ID NO: 18001.
20. The CAR of claim 1, wherein the at least one Centyrin that specifically binds PSMA comprises an amino acid sequence of SEQ ID NO: 18002.
21. The CAR of claim 1, wherein the at least one Centyrin that specifically binds PSMA is encoded by a nucleic acid sequence comprising SEQ ID NO: 18003.
22. A composition comprising the CAR of claim 1 and at least one pharmaceutically acceptable carrier.
23. A transposon comprising a nucleic acid sequence encoding the CAR of claim 1.
24. A composition comprising the transposon of claim 23.
25. A vector comprising a nucleic acid sequence encoding the CAR of claim 1.
26. A composition comprising the vector of claim 25.
27. A cell comprising the CAR of claim 1.
28. A cell comprising the transposon of claim 23.
29. A cell comprising the vector of claim 25.
30. The cell of claim 27, wherein the cell is an immune cell.
31. The cell of claim 30, wherein the immune cell is a T-cell, a Natural Killer (NK) cell, a Natural Killer (NK)-like cell, a Cytokine Induced Killer (CIK) cell, a hematopoietic progenitor cell, a peripheral blood (PB) derived T cell or an umbilical cord blood (UCB) derived T-cell.

32. The cell of claim 27, wherein the cell is autologous.
33. A composition comprising a population of cells, wherein the plurality of cells of the population comprises the cell of claim 27.
34. A method of producing a population of modified T-cells comprising:
- (a) introducing into a plurality of T-cells a composition comprising a nucleic acid sequence encoding the CAR of claim 1 thereby generating a modified T-cell population;
 - (b) culturing the modified T-cell population under conditions suitable for integration of the nucleic acid sequence encoding the CAR; and
 - (c) expanding and/or selecting at least one cell from the modified T-cell population that expresses the CAR on the cell surface.
35. The CAR of claim 1, comprising the amino acid sequence of SEQ ID NO: 18063.
36. The CAR of claim 1, comprising the amino acid sequence of SEQ ID NO: 18070.
37. A chimeric antigen receptor (CAR) comprising:
- (a) an ectodomain comprising a human CD8 α signal peptide and an antigen recognition region, wherein the antigen recognition region comprises at least one Centyrin that specifically binds PSMA;
 - (b) a hinge domain comprising a human CD8 α hinge domain;
 - (c) a transmembrane domain comprising a human CD8 α transmembrane domain; and
 - (d) an endodomain comprising a human 4-1BB costimulatory domain and a human CD3 ζ endodomain.
38. The CAR of claim 37, wherein the at least one Centyrin that specifically binds PSMA comprises the amino acid sequence of SEQ ID NO: 18000, wherein the human CD8 α signal peptide comprises the amino acid sequence of SEQ ID NO: 18004, wherein the human CD8 α hinge domain comprises the amino acid sequence of SEQ ID NO: 18014, wherein the human CD8 α transmembrane domain comprises the amino acid sequence of SEQ ID NO: 18006, wherein the human 4-1BB costimulatory domain comprises the amino acid sequence of SEQ ID

NO: 18012, and wherein the human CD3 ζ endodomain comprises the amino acid sequence of SEQ ID NO: 18008.

39. The CAR of claim 37, wherein the at least one Centyrin that specifically binds PSMA comprises the amino acid sequence of SEQ ID NO: 18002, wherein the human CD8 α signal peptide comprises the amino acid sequence of SEQ ID NO: 18004, wherein the human CD8 α hinge domain comprises the amino acid sequence of SEQ ID NO: 18014, wherein the human CD8 α transmembrane domain comprises the amino acid sequence of SEQ ID NO: 18006, wherein the human 4-1BB costimulatory domain comprises the amino acid sequence of SEQ ID NO: 18012, and wherein the human CD3 ζ endodomain comprises the amino acid sequence of SEQ ID NO: 18008.