

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 Centyrin that specifically binds prostate specific membrane antigen (PSMA);
 - (b) a transmembrane domain, and
 - (c) an endodomain comprising at least one costimulatory domain

wherein the at least one Centyrin that specifically binds PSMA comprises the amino acid sequence of SEQ ID NO: 18002.
2. The CAR of claim 1, wherein the ectodomain of (a) further comprises a signal peptide.
3. The CAR of claim 1 or claim 2, wherein the ectodomain of (a) further comprises a hinge between the antigen recognition region and the transmembrane domain.
4. The CAR of claim 2 or claim 3, 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 any one of claims 1 to 6, 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 any one of claims 1 to 9, wherein the endodomain comprises a human CD3 ζ endodomain.
11. The CAR of any one of claims 1 to 10, 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 any one of claims 10 to 12, wherein the human CD3 ζ endodomain ~~domain~~ comprises an amino acid sequence of SEQ ID NO: 18008.
14. The CAR of any one of claims 11 to 13, wherein the human 4-1BB costimulatory domain comprises an amino acid sequence of SEQ ID NO: 18012.
15. The CAR of any one of claims 3 to 14, 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.~~
- 21.18. The CAR of any one of claims 1 to 17, wherein the at least one Centyrin that

specifically binds PSMA is encoded by a nucleic acid sequence comprising SEQ ID NO: 18003.

~~22.19.~~ A composition comprising the CAR of any one of claims 1 to 18 and at least one pharmaceutically acceptable carrier.

~~23.20.~~ A transposon comprising a nucleic acid sequence encoding the CAR of any one of claims 1 to 18.

~~24.21.~~ A composition comprising the transposon of claim ~~20~~23.

~~25.22.~~ A vector comprising a nucleic acid sequence encoding the CAR of any one of claims 1 to 18.

~~26.23.~~ A composition comprising the vector of claim ~~22~~25.

~~27.24.~~ A cell comprising the CAR of any one of claims 1 to 18.

~~28.25.~~ A cell comprising the transposon of claim ~~20~~23.

~~29.26.~~ A cell comprising the vector of claim ~~22~~25.

~~30.27.~~ The cell of any one of claims 24 to 2627, wherein the cell is an immune cell.

~~31.28.~~ The cell of claim ~~27~~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.

~~32.29.~~ The cell of any one of claims 24 to 2827, wherein the cell is autologous.

~~33.30.~~ A composition comprising a population of cells, wherein the plurality of cells of the population comprises the cell of any one of claims 24 to 2827.

~~34.31.~~ 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.~~

~~36.32. The CAR of claim 1, comprising the amino acid sequence of SEQ ID NO: 18070.~~

~~37.33. 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,

wherein the at least one Centyrin that specifically binds PSMA comprises the amino acid sequence of SEQ ID NO: 18002.

~~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.~~

~~39.34. The CAR of claim 3337, 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.