

CLAIMS

We claim:

- 5 1. A chimeric antigen receptor (CAR), wherein the CAR comprises:
 - (1) an extracellular binding domain that specifically binds to LYPD3;
 - (2) a transmembrane domain; and
 - (3) at least one cytoplasmic signaling domain.
- 10 2. The CAR of claim 1, wherein the extracellular binding domain comprises a single chain variable fragment (scFv) that specifically binds to LYPD3.
3. The CAR of claim 2, wherein the scFv comprises an amino acid sequence sharing at least 95% sequence identity to the amino acid sequence of SEQ ID NO:10.
- 15 4. The CAR of any of claims 1-3, wherein the transmembrane domain comprises an amino acid sequence derived from a molecule that is the alpha chain of the T-cell receptor, the beta chain of the T-cell receptor, the zeta chain of the T-cell receptor, CD3-epsilon, CD3-zeta, CD4, CD5, CD8, CD9, CD16, CD22, CD28, CD33, CD37, CD45, CD64, CD80, CD86,
 - 20 CD134, CD137, or CD154.
5. The CAR of any of claims 1-4, wherein the transmembrane domain comprises an amino acid sequence derived from CD8.
- 25 6. The CAR of any of claims 1-5, wherein the transmembrane domain comprises an amino acid sequence sharing at least 95% sequence identity to the amino acid sequence of SEQ ID NO:11.
7. The CAR of any of claims 1-6, wherein the at least one cytoplasmic signaling domain
 - 30 comprises at least one amino acid sequence derived from a molecule that is CD2, CD3-zeta, CD3-gamma, CD3-delta, CD3-epsilon, CD5, CD7, CD22, CD27, CD28, CD30, CD40, CD66d, CD79a, CD79b, 4-1BB (CD137), OX40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), LIGHT, NKG2C, B7-H3, FcR-gamma, FcR-beta, or TCR-zeta.

8. The CAR of any of claims 1-7, wherein the at least one cytoplasmic signaling domain comprises an amino acid sequence derived from CD3-zeta.
- 5 9. The CAR of any of claims 1-8, wherein the at least one cytoplasmic signaling domain comprises an amino acid sequence sharing at least 95% sequence identity to the amino acid sequence of SEQ ID NO:14.
- 10 10. The CAR of any of claims 1-7, wherein the at least one cytoplasmic signaling domain comprises an amino acid sequence derived from CD28.
11. The CAR of any of claims 1-7 and 10, wherein the at least one cytoplasmic signaling domain comprises an amino acid sequence sharing at least 95% sequence identity to the amino acid sequence of SEQ ID NO:12.
- 15 12. The CAR of any of claims 1-7, wherein the at least one cytoplasmic signaling domain comprises an amino acid sequence derived from 4-1BB.
13. The CAR of any of claims 1-7 and 12, wherein the at least one cytoplasmic signaling domain comprises an amino acid sequence sharing at least 95% sequence identity to the amino acid sequence of SEQ ID NO:13.
- 20 14. The CAR of any of claims 1-13, wherein the CAR comprises three cytoplasmic signaling domains, wherein the first cytoplasmic signaling domain is derived from CD28, wherein the second cytoplasmic signaling domain is derived from CD3, and wherein the third cytoplasmic signaling domain is derived from 4-1BB.
- 25 15. The CAR of claim 14, wherein the first cytoplasmic signaling comprises an amino acid sequence sharing at least 95% sequence identity to the amino acid sequence of SEQ ID NO:14, wherein the second cytoplasmic signaling domain comprises an amino acid sequence sharing at least 95% sequence identity to the amino acid sequence of SEQ ID NO:12, and wherein the third cytoplasmic signaling domain comprises an amino acid sequence sharing at least 95% sequence identity to the amino acid sequence of SEQ ID NO:13 .
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16. A population of activated T-cells comprising the chimeric antigen receptor (CAR) of any of claims 1-15.
17. The population of claim 16, wherein the population of activated T-cells is present in a therapeutically effective amount for treatment of a cancer expressing LYPD3.
18. A pharmaceutical composition comprising a population of activated T-cells expressing the CAR according to any of claims 1-15, and a pharmaceutically acceptable carrier.
19. The pharmaceutical composition of claim 18, wherein the pharmaceutically acceptable carrier supports maintenance of the population of activated T-cells.
20. The pharmaceutical composition of claim 18 or 19, further comprising at least one therapeutic agent.
21. An isolated nucleic acid comprising a nucleotide sequence encoding the CAR of any of claims 1-15.
22. A method of inducing a T-cell response in a subject suffering from a cancer expressing LYPD3, wherein the method comprises administering to the subject a therapeutically effective amount of the population of activated T-cells of claim 16 or 17, or the pharmaceutical composition of any of claims 18-20, wherein the administration induces an anti-tumor response to the cancer.
23. The method of claim 22, wherein the cancer is selected from the group consisting of lung cancer, head and neck cancer, cervical cancer, urothelial cancer, melanoma, breast cancer, prostate cancer, colon cancer, renal cell carcinoma, ovarian cancer, neuroblastoma, rhabdomyosarcoma, leukemia, and lymphoma.
24. A method of preparing a population of activated T-cells expressing the chimeric antigen receptor (CAR) of any of claims 1-15, wherein the method comprises:
- (1) transfecting or transducing isolated T-cells with a nucleic acid encoding the CAR of any of claims 1-15; and
 - (2) expanding the CAR-expressing T-cells following transfection or transduction,

wherein the T-cells are expanded by culturing in the presence of IL-2, and/or CD3 and CD28 antibodies.

25. The method of claim 24, wherein the isolated T-cells are isolated from a mammal.

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26. The method of claim 25, wherein the mammal is a human.

27. The method of claim 26, wherein the human is a subject suffering from a cancer expressing LYPD3.

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28. The method of any of claims 24-28, wherein the isolated T-cells are autologous to the subject suffering from a cancer expressing LYPD3.