

CLAIMS:

1. A method of inducing expansion of a chimeric antigen receptor (CAR) T cell comprising:
incubating the CAR T cell with a hapten antigen presenting cell (H-APC),
wherein the CAR T cell comprises a CAR which specifically binds to a hapten attached to the H-APC.
2. The method of claim 1, wherein the hapten is selected from a hapten listed in TABLE 1.
3. The method of claim 1 or 2, wherein the hapten is selected from fluorescein, urushiol, quinone, biotin, dinitrophenol, or a derivative thereof; and/or the CAR comprises an scFv comprising an amino acid sequence having at least 95% sequence identity to any one of SEQ ID NOs 01-06, 08 or 10.
4. The method of any one of claims 1-3, further comprising attaching *ex vivo* the hapten to an extracellular surface of the H-APC.
5. The method of claim 4, wherein the hapten is attached to the H-APC via a phospholipid ether (PLE).
6. The method of any one of claims 1-5, wherein the incubating is performed *ex vivo*.
7. The method of any one of claims 1-6, wherein the CAR T cell comprises an additional CAR which specifically binds to a cancer antigen.
8. The method of any one of claims 1-7, wherein the CAR T cell and the H-APC are derived from a single subject.
9. Use of a chimeric antigen receptor (CAR) T cell in the preparation of a medicament for treating, inhibiting, or ameliorating a cancer in a subject, wherein:
the CAR T cell comprises a first CAR which specifically binds to a tumor specific antigen of the cancer and a second CAR which specifically binds to a hapten;
and
the CAR T cell is stimulated or restimulated by a hapten antigen presenting cell (H-APC), comprising the hapten, to be administered to the subject.
10. The use of claim 9, wherein the stimulating or restimulating is repeated.

11. The use of claim 9 or claim 10, wherein wherein the CAR T cell and the H-APC are derived from the subject.

12. The use of any one of claims 9-11, wherein the tumor specific antigen is selected from the group consisting of CD19, CD22, HER2, CD7, CD30, B cell maturation antigen (BCMA), GD2, glypican-3, MUC1, CD70, CD33, epithelial cell adhesion molecule (EpCAM), Epidermal Growth Factor variant III, receptor tyrosine kinase-like orphan receptor 1 (ROR1), CD123, Prostate Stem Cell Antigen (PSCA), CD5, Lewis Y antigen, B7H3, CD20, CD43, HSP90, and IL13; and/or the hapten is selected from a hapten listed in TABLE 1.

13. The use of any one of claims 9-12, wherein the hapten is selected from fluorescein, urushiol, quinone, biotin, or dinitrophenol, or a derivative thereof; and/or the second CAR comprises an scFv comprising an amino acid sequence having at least 95% sequence identity to any one of SEQ ID NOs 01-06, 08 or 10.

14. The use of any one of claims 9-13, wherein the hapten is covalently attached to the extracellular surface of the H-APC.

15. The use of any one of claims 9-14, wherein the hapten is attached to the H-APC via a phospholipid ether (PLE).

16. The use of any one of claims 9-15, wherein the CAR T cell is derived from a CD4⁺ cell, a CD8⁺ cell, a precursor T cell, or a hematopoietic stem cell; and wherein the H-APC is derived from a T cell or a B cell.

17. The use of any one of claims 9-16, wherein the CD8⁺ cell is a CD8⁺ T cytotoxic 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; the CD4⁺ cell is a CD4⁺ T helper 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 use of any one of claims 9-17, wherein the subject is mammalian.

19. A composition comprising:

a hapten antigen presenting cell (H-APC) comprising a hapten; and

a chimeric antigen receptor (CAR) T cell comprising a first CAR which is capable of specifically binding to a cancer antigen, and a second CAR which is specifically bound to the hapten.

20. The composition of claim 19, wherein the hapten is selected from fluorescein, urushiol, quinone, biotin, dinitrophenol, or a derivative thereof; and/or the second CAR comprises an scFv comprising an amino acid sequence having at least 95% sequence identity to any one of SEQ ID NOs 01-06, 08 or 10; and/or further comprising a cancer cell comprising the cancer antigen.