CLAIMS

1. A compound for use in treating, inhibiting or ameliorating a solid tumor in a subject:

wherein the compound comprises a phospholipid and a fluorescein or fluorescein derivative;

wherein the compound is capable of integrating into a plasma membrane of a target cell of the solid tumor;

wherein administration of the compound to the subject labels the target cell;

wherein the bloodstream of the subject comprises engineered T cells comprising a chimeric antigen receptor (CAR), wherein the CAR comprises a ligand binding domain capable of specifically binding to fluorescein or a fluorescein derivative;

wherein administration of the compound to the subject forms a complex comprising the CAR and the compound, wherein the CAR specifically binds the fluorescein or fluorescein derivative;

wherein the CAR comprises a spacer domain having a spacer length of 12-250 amino acids; and

wherein the ligand binding domain comprises an amino acid sequence having at least 95% sequence identity with the amino acid sequence selected from any one of SEQ ID NOs:01-06.

2. Use of a compound in the manufacture of a medicament for treating, inhibiting or ameliorating a solid tumor in a subject:

wherein the compound comprises a phospholipid and a fluorescein or fluorescein derivative;

wherein the compound is capable of integrating into a plasma membrane of a target cell of the solid tumor;

wherein administration of the compound to the subject labels the target cell;

wherein the bloodstream of the subject comprises engineered T cells comprising a chimeric antigen receptor (CAR), wherein the CAR comprises a ligand binding domain capable of specifically binding to fluorescein or a fluorescein derivative;

wherein administration of the compound to the subject forms a complex comprising the CAR and the compound, wherein the CAR specifically binds the fluorescein or fluorescein derivative;

wherein the CAR comprises a spacer domain having a spacer length of 12-250 amino acids; and

wherein the ligand binding domain comprises an amino acid sequence having at least 95% sequence identity with the amino acid sequence selected from any one of SEQ ID NOs:01-06.

3. The compound for use of claim 1 or use of claim 2, wherein the CAR comprises a spacer domain comprising an IgG4 hinge.

4. A compound for use in treating, inhibiting, or ameliorating a cancer in a subject, wherein:

the compound comprises a phospholipid and a fluorescein or a fluorescein derivative, wherein the compound is capable of integrating into a plasma membrane of a target cell of the cancer; and

the bloodstream of the subject in combination with a comprises a T cell comprising a chimeric antigen receptor (CAR), wherein the CAR comprises a ligand binding domain which specifically binds to fluorescein or a fluorescein derivative and a spacer domain comprising an IgG4 hinge.

5. Use of a compound in the manufacture of a medicament for treating, inhibiting, or ameliorating a cancer in a subject, wherein:

the compound comprises a phospholipid and a fluorescein or a fluorescein derivative, wherein the compound is capable of integrating into a plasma membrane of a target cell of the cancer; and

the bloodstream of the subject in combination with a comprises a T cell comprising a chimeric antigen receptor (CAR), wherein the CAR comprises a ligand binding domain which specifically binds to fluorescein or a fluorescein derivative and a spacer domain comprising an IgG4 hinge.

6. The compound for use of claim 4 or use of claim 5, wherein the ligand binding domain comprises an amino acid sequence having at least 95% sequence identity with an amino acid sequence selected from any one of SEQ ID NOs: 1-6.

7. The compound for use of any of claims 1, 3, 4 or 6 or use of any of claims 2, 3, 5 or 6, wherein the ligand binding domain comprises the amino acid sequence of any one of SEQ ID NOs:01-06

8. The compound for use of any of claims 1, 3, 4, 6 or 7 or use of any of claims 2, 3, or 5-7, wherein the ligand binding domain comprises the amino acid sequence of any one of SEQ ID NOs:01, 02 or 05.

9. The compound for use of any of claims 1, 3, 4, or 6-8 or use of any of claims 2, 3, or 5-8, wherein the CAR comprises a spacer comprising: an IgG4 hinge connected to a CH2 domain to a CH3 domain; or an IgG4 hinge connected to a CH3 domain.

10. The compound for use of any of claims 1, 3, 4, or 6-9 or use of any of claims 2, 3, or 5-9, wherein the CAR comprises a spacer domain having a spacer length of 1-22 amino acids, 23-50 amino acids, 51-100 amino acids, 100 to 150 amino acids or 151-250 amino acids.

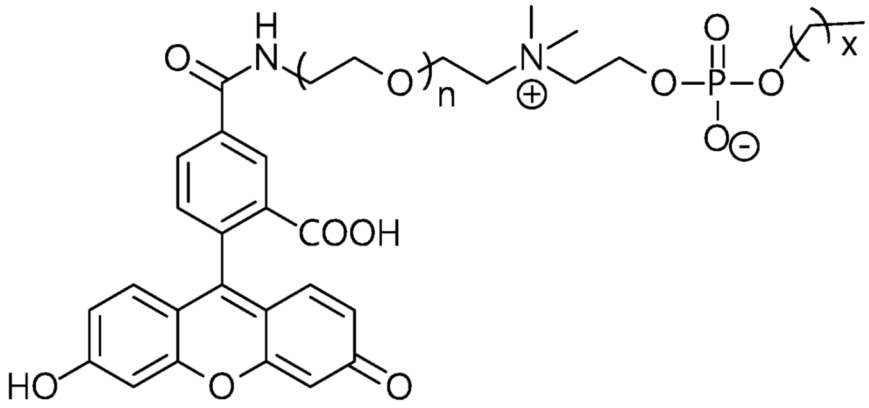
11. The compound for use of any of claims 1, 3, 4, or 6-10 or use of any of claims 2, 3, or 5-10, wherein the T cell is administered to the subject.

12. The compound for use of any of claims 1, 3, 4, or 6-12 or use of any of claims 2, 3, or 5-12, wherein the phospholipid comprises a polar head group, a hydrophobic group, and a linker between the polar head group and the fluorescein or fluorescein derivative.

13. The compound for use of any of claims 1, 3, 4, or 6-12 or use of any of claims 2, 3, or 5-12, wherein the compound comprises a phospholipid ether.

14. The compound for use of any of claims 1, 3, 4, or 6-13 or use of any of claims 2, 3, or 5-13, wherein the phospholipid is selected from the group consisting of a phosphatidylcholine, sphingomyelin, phosphoethanolamine, phosphatidyl serine, phosphatidyl inositol, phosphatidyl inositol, phosphocholine, and a trimethylarseno-ethyl-phosphate.

15. The compound for use of any of claims 1, 3, 4, or 6-14 or use of any of claims 2, 3, or 5-14, wherein the compound has the structure:



wherein:

n is 0 to 16; and

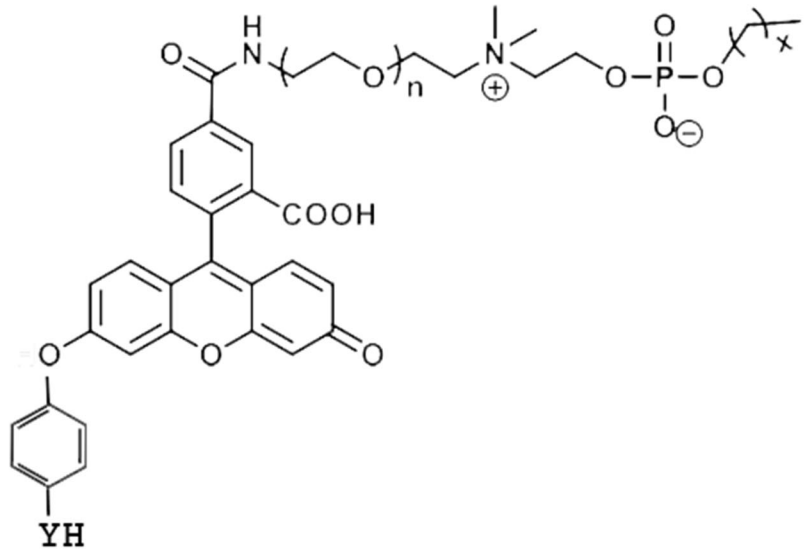
x is 10 to 20.

16. The compound for use of any of claims 1, 3, 4, or 6-15 or use of any of claims 2, 3, or 5-15, wherein the compound comprises a masking moiety, optionally wherein the masking moiety is linked to the target moiety via a cleavable moiety.

17. The compound for use or use of claim 16, wherein the cleavable moiety is configured to be cleavable by a reactive oxygen species (ROS), or by an acidic environment present in a tumor microenvironment of a solid tumor.

18. The compound for use or use of claim 16 or 17, wherein the masking moiety comprises a phenolic hydroxyl group bound to a hydroxyl on a xanthene moiety.

19. The compound for use of any of claims 1, 3, 4, or 6-18 or use of any of claims 2, 3, or 5-19, wherein the compound has the structure:



wherein:

Y is O or NH;

n is 0 to 16; and

x is 10 to 20.

20. The compound for use of any of claims 1, 3, 4, or 6-19 or use of any of claims 2, 3, or 5-19, wherein the T 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.

21. The compound for use of any of claims 1, 3, 4, or 6-20 or use of any of claims 2, 3, or 5-20, wherein the T cell is a CD4+ T helper lymphocyte cell that is 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.

22. The compound for use of any of claims 1, 3, 4, or 6-21 or use of any of claims 2, 3, or 5-21, wherein the spacer domain has a length of 151-250 amino acids.

23. The compound for use of any of claims 1, 3, 4, or 6-22 or use of any of claims 2, 3, or 5-22, wherein the spacer domain comprises the amino acid sequence of SEQ ID NO:07.

24. The compound for use of any of claims 1, 3, 4, or 6-23 or use of any of claims 2, 3, or 5-23, wherein the solid tumor is selected from colon cancer, breast cancer, ovarian cancer, lung cancer, pancreatic cancer, prostate cancer, melanoma, renal cancer, pancreatic

cancer, brain cancer, glioblastoma, neuroblastoma, medulloblastoma, sarcoma, bone cancer, or liver cancer.

25. A system comprising (i) a compound comprising a phospholipid ether and fluorescein or a fluorescein derivative (FL-PLE), wherein the compound is capable of integrating into a plasma membrane of a cancer cell; and (ii) a T cell comprising a chimeric antigen receptor (CAR), wherein the CAR comprises a ligand binding domain which specifically binds to the fluorescein or fluorescein derivative, and a spacer domain comprising an IgG4 hinge.

26. The system of claim 25, wherein the ligand binding domain comprises an amino acid sequence having at least 95% sequence identity with an amino acid sequence selected from any one of SEQ ID NOs: 1-6.

27. A system comprising (i) a compound comprising a phospholipid ether and fluorescein or a fluorescein derivative (FL-PLE), wherein the compound is capable of integrating into a plasma membrane of a cancer cell; and (ii) a T cell comprising a chimeric antigen receptor (CAR), wherein the CAR comprises a ligand binding domain comprising an amino acid sequence having at least 95% sequence identity with an amino acid sequence selected from any one of SEQ ID NOs: 1-6.

28. The system of any one of claims 25-27, wherein the ligand binding domain comprises an amino acid sequence selected from any one of SEQ ID NOs: 1, 2 and 5.

29. The system of any one of claims 25-28, wherein the spacer domain comprises an IgG4 hinge connected to a CH2 domain and a CH3 domain, an IgG4 hinge connected to a CH3 domain.

30. The system of any one of claims 25-28, wherein the spacer domain comprises an amino acid sequence having at least 95% sequence identity with the amino acid sequence of SEQ ID NO:07.