

CLAIMS

What is claimed is:

1. A modified cell comprising a chimeric antigen receptor (CAR), wherein the CAR comprises an antigen binding domain, a transmembrane domain and an intracellular domain of a stimulatory and/or co-stimulatory molecule, and wherein cell is a monocyte, macrophage, or dendritic cell that possesses targeted effector activity.
2. A modified cell comprising a nucleic acid sequence encoding a chimeric antigen receptor (CAR), wherein nucleic acid sequence comprises a nucleic acid sequence encoding an antigen binding domain, a nucleic acid sequence encoding a transmembrane domain and a nucleic acid sequence encoding an intracellular domain of a stimulatory and/or co-stimulatory molecule, and wherein the cell is a monocyte, macrophage, or dendritic cell that expresses the CAR and possesses targeted effector activity.
3. The modified cell of claim 1 or 2, wherein the antigen binding domain of the CAR comprises an antibody selected from the group consisting of a monoclonal antibody, a polyclonal antibody, a synthetic antibody, human antibody, humanized antibody, single domain antibody, single chain variable fragment, and antigen-binding fragments thereof.
4. The modified cell of claim 1 or 2, wherein the antigen binding domain of the CAR is selected from the group consisting of an anti-CD19 antibody, an anti-HER2 antibody, and a fragment thereof.
5. The modified cell of claim 1 or claim 2, wherein the intracellular domain of the CAR comprises dual signaling domains.
6. The modified cell of claim 1 or 2, wherein the targeted effector activity is directed against an antigen on a target cell that specifically binds the antigen binding domain of the CAR.
7. The modified cell of claim 1 or 2, wherein the targeted effector activity is selected from the group consisting of phagocytosis, targeted cellular cytotoxicity, antigen presentation, and cytokine secretion.

8. The modified cell of claim 1 or 2 further comprising an agent selected from the group consisting of a nucleic acid, an antibiotic, an anti-inflammatory agent, an antibody or antibody fragments thereof, a growth factor, a cytokine, an enzyme, a protein, a peptide, a fusion protein, a synthetic molecule, an organic molecule, a carbohydrate or the like, a lipid, a hormone, a microsome, a derivative or a variation thereof, and any combination thereof.
9. The modified cell of claim 1 or claim 2, wherein the modified cell has at least one upregulated M1 marker and at least one downregulated M2 marker.
10. The modified cell of claim 1 or claim 2, wherein the modified cell is genetically modified to express the CAR.
11. The modified cell of claim 1 or claim 2, wherein the targeted effector activity is enhanced by inhibition of CD47 or SIRP α activity.
12. A pharmaceutical composition comprising the cell of claim 1 or 2 and a pharmaceutically acceptable carrier.
13. Use of the modified cell of claim 1 or 2 in the manufacture of a medicament for the treatment of an immune response in a subject in need thereof.
14. Use of the modified cell of claim 1 or 2 in the manufacture of a medicament for the treatment of a tumor or cancer in a subject in need thereof.
15. A method of treating a disease or condition associated with a tumor or cancer in a subject comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising the modified cell of claim 1 or 2.
16. A method of treating a tumor in a subject, comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising the modified cell of claim 1 or 2.
17. A method for stimulating an immune response to a target tumor cell or tumor tissue in a subject comprising administering to a subject a therapeutically effective amount of a pharmaceutical composition comprising the modified cell of claim 1 or 2.

18. A method of modifying a cell, comprising:
introducing a chimeric antigen receptor (CAR) into the monocyte, macrophage, or dendritic cell, wherein the CAR comprises an antigen binding domain, a transmembrane domain and an intracellular domain of a stimulatory and/or co-stimulatory molecule, and wherein the cell is a monocyte, macrophage, or dendritic cell that expresses the CAR and possesses targeted effector activity.
19. The method of claim 18, wherein introducing the CAR into the cell comprises introducing a nucleic acid sequence encoding the CAR.
20. The method of claim 19, wherein introducing the nucleic acid sequence comprises electroporating a mRNA encoding the CAR.
21. The method of claim 19, wherein introducing the nucleic acid sequence comprises transducing the cell with a viral vector comprising the nucleic acid sequence encoding the CAR.
22. The method of claim 18, wherein the targeted effector activity is directed against an antigen on a target cell that specifically binds the antigen binding domain of the CAR.
23. The method of claim 18, wherein the targeted effector activity is selected from the group consisting of phagocytosis, targeted cellular cytotoxicity, antigen presentation, and cytokine secretion.
24. The method of claim 18 further comprising inhibiting CD47 or SIRP α activity to enhance the targeted effector activity.
25. The method of claim 24, wherein inhibiting CD47 or SIRP α activity comprises contacting the cell with a blocking anti-CD47 or a blocking anti-SIRP α antibody.
26. The method of claim 18, wherein the intracellular domain of the CAR comprises dual signaling domains.
27. The method of claim 18, wherein the antigen binding domain of the CAR comprises an antibody selected from the group consisting of a synthetic antibody, human antibody, humanized antibody, single domain antibody, single chain variable fragment, and antigen-binding fragments thereof.

28. The method of claim 18, wherein the antigen binding domain of the CAR is selected from the group consisting of an anti-CD19 antibody, an anti-HER2 antibody, and a fragment thereof.
29. The method of claim 18 further comprising modifying the cell to deliver an agent to a target, wherein the agent is selected from the group consisting of a nucleic acid, an antibiotic, an anti-inflammatory agent, an antibody or antibody fragments thereof, a growth factor, a cytokine, an enzyme, a protein, a peptide, a fusion protein, a synthetic molecule, an organic molecule, a carbohydrate or the like, a lipid, a hormone, a microsome, a derivative or a variation thereof, and any combination thereof.
30. A composition comprising the cell modified according to claim 18.