

CLAIMS

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,
wherein the modified cell is a human macrophage or a human monocyte and
wherein the modified cell comprises an Ad5f35 adenoviral component, and
wherein the binding of the antigen binding domain to an antigen on a target cell causes the modified cell to exhibit an activity selected from the group consisting of phagocytosis, targeted cellular cytotoxicity, antigen presentation, and cytokine secretion.
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 costimulatory molecule,
wherein the modified cell is a human macrophage or a human monocyte that expresses the CAR, and
wherein the modified cell comprises an Ad5f35 adenoviral component, and
wherein the binding of the antigen binding domain to an antigen on a target cell causes the modified cell to exhibit an activity selected from the group consisting of phagocytosis, targeted cellular cytotoxicity, antigen presentation, and cytokine secretion.
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 antigen-binding fragments 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 binding of the antigen binding domain to an antigen on a target cell causes the modified cell to exhibit an activity selected from the group consisting of phagocytosis, targeted cellular cytotoxicity, antigen presentation, and cytokine secretion.~~
76. 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, a growth factor, a cytokine, an enzyme, a protein, a peptide, a fusion protein, a synthetic molecule, an organic molecule, a carbohydrate, a lipid, a hormone, a microsome, and any combination thereof.
87. The modified cell of claim 1 or claim 2, wherein the modified cell is a modified human macrophage and has at least one upregulated M1 marker and at least one downregulated M2 marker.
98. The modified cell of claim 1 or claim 2, wherein the modified cell is genetically modified to express the CAR.
109. The modified cell of claim 1 or 26, wherein the phagocytosis, targeted cellular cytotoxicity, antigen presentation, or cytokine secretion is enhanced by inhibition of CD47 or SIRP α activity in the modified cell with a blocking anti-CD47 antibody, a blocking anti-SIRP α antibody, a CRISPR/Cas enzyme, or an siRNA.

- ~~1110~~. A pharmaceutical composition comprising the modified cell of claim 1 or 2 and a pharmaceutically acceptable carrier.
- ~~1211~~. 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, wherein the modified cell is a human macrophage or a human monocyte,
and wherein the tumor or cancer comprises a tumor associated antigen to which the antigen binding domain binds.
- ~~1312~~. A method of modifying a cell, comprising:
introducing a chimeric antigen receptor (CAR) into a 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 modified cell is a human macrophage or a human monocyte that expresses the CAR, ~~and~~
wherein introducing the nucleic acid sequence comprises transducing the cell with an Ad5f35 viral vector comprising the nucleic acid sequence encoding the CAR, ~~and~~.
- ~~14~~. ~~—The method of claim 1312,~~ wherein when the antigen binding domain contacts an antigen on a target cell, the modified cell exhibits an activity selected from the group consisting of phagocytosis, targeted cellular cytotoxicity, antigen presentation, and cytokine secretion.
- ~~1513~~. The method of claim ~~1412~~, wherein contacting the cell with a blocking anti-CD47 antibody, a blocking anti-SIRP α antibody, a CRISPR/Cas enzyme, or an siRNA increases phagocytosis, targeted cellular cytotoxicity, antigen presentation, or cytokine secretion.
- ~~1614~~. The method of claim ~~1312~~, wherein the intracellular domain of the CAR comprises dual signaling domains.
- ~~1715~~. The method of claim ~~1312~~, 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 any antigen-binding fragment thereof.

1816. The method of claim **1312**, wherein the antigen binding domain of the CAR is selected from the group consisting of an anti-CD19 antibody, an anti-HER2 antibody, and antigen-binding fragments thereof.

1917. The method of claim **1312**, 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, a growth factor, a cytokine, an enzyme, a protein, a peptide, a fusion protein, a synthetic molecule, an organic molecule, a carbohydrate, a lipid, a hormone, a microsome, and any combination thereof.

~~**20.** A composition comprising the cell modified according to claim 13.~~