

WHAT IS CLAIMED IS:

1. An isolated nucleic acid sequence encoding
 - a) a chimeric antigen receptor (CAR), wherein the CAR comprises an antigen-binding domain specific for a cell surface antigen; and
 - b) an armoring molecule, wherein the armoring molecule comprises a TGF- β receptor type 2 dominant-negative (TGF β RIIDN), wherein the TGF β RIIDN comprises a wild-type TGF- β receptor type 2 truncated at residue 194, andwherein the antigen-binding domain is a single chain variable fragment (scFv) comprising the nucleic acid sequence of SEQ ID NO: 33.
2. The isolated nucleic acid sequence according to claim 1, further comprising a transmembrane domain, a costimulatory domain, and a signal domain.
3. The isolated nucleic acid sequence of claim 2, wherein the transmembrane domain comprises a CD28 transmembrane domain.
4. The isolated nucleic acid sequence of claim 2, wherein the costimulatory domain comprises one or more of CD28, 4-1BB, CD3zeta, OX-40, ICOS, CD27, GITR, and MyD88/CD40 costimulatory domains.
5. The isolated nucleic acid sequence of claim 2, wherein the costimulatory domain comprises one or more of CD28, 4-1BB, and CD3zeta costimulatory domains.
6. The isolated nucleic acid sequence of claim 2, wherein the signal domain comprises a sequence encoding a CSFR2 signal peptide.
7. The isolated nucleic acid sequence according to claim 5, further comprising a hinge/spacer domain.

8. The isolated nucleic acid sequence of claim 7, wherein the hinge/spacer domain is an IgG4P hinge/spacer.
9. The isolated nucleic acid sequence of claim 1, wherein the TGF- β receptor type 2 dominant-negative (TGF β RIIDN) counters immunosuppression of a cell in a tumor microenvironment when expressed on a surface of the cell.
10. The isolated nucleic acid sequence of claim 1, encoded by the nucleic acid sequence of SEQ ID NO: 46.
11. The isolated nucleic acid of claim 1, wherein the cell surface antigen comprises GPC3.
12. A vector, comprising a nucleic acid sequence encoding a chimeric antigen receptor (CAR), wherein the CAR comprises an antigen-binding domain specific for a cell surface antigen and an armoring molecule, wherein the nucleic acid sequence comprises SEQ ID NO: 46.
13. A cell comprising the vector of claim 12.
14. A cell, comprising:
 - a nucleic acid sequence encoding a chimeric antigen receptor (CAR), and
 - a TGF β RIIDN armoring molecule expressed on a surface of the cell, wherein the TGF β RIIDN comprises a wild-type TGF- β receptor type 2 truncated at residue 194,
 - wherein the CAR comprises an antigen-binding domain, a transmembrane domain, a costimulatory domain, and a signal domain, and
 - wherein the antigen-binding domain is a single chain variable fragment (scFv) comprising the nucleic acid sequence of SEQ ID NO: 33.
15. A cell, comprising:

an anti-GPC3 chimeric antigen receptor (CAR) comprising an antigen binding domain, wherein the antigen binding domain comprises an antibody, Fab, or an scFv comprising a heavy chain variable region (VH) and a light chain variable region (VL),

wherein the VH comprises a CDR1 comprising the amino acid sequence of SEQ ID NO: 37, a CDR2 comprising the amino acid sequence of SEQ ID NO: 38, and a CDR3 comprising the amino acid sequence of SEQ ID NO: 39, and

wherein the VL comprises a CDR1 comprising the amino acid sequence of SEQ ID NO: 40 or SEQ ID NO: 43, a CDR2 comprising the amino acid sequence of SEQ ID NO: 41 or SEQ ID NO: 44, and a CDR3 comprising the amino acid sequence of SEQ ID NO: 42 or SEQ ID NO: 45; and

a TGFβRIIDN armoring molecule comprising amino acids 478 to 671 of SEQ ID NO: 47.

16. The cell of claim 15, wherein the VH comprises the amino acid sequence of SEQ ID NO: 27 or SEQ ID NO: 29.

17. The cell of claim 15, wherein the VL comprises the amino acid sequence of SEQ ID NO: 28 or SEQ ID NO: 30.

18. The cell of claim 15, wherein the anti-GPC3 chimeric antigen receptor (CAR) and TGFβRIIDN armoring molecules comprise the amino acid sequence of SEQ ID NO: 47.

19. The cell of claim 13, wherein the cell is selected from the group consisting of a T cell, a Natural Killer (NK) cell, a cytotoxic T lymphocyte (CTL), and a regulatory T cell.

20. A cell, comprising:

an anti-GPC3 chimeric antigen receptor (CAR) comprising an antigen binding domain, wherein the antigen binding domain comprises a scFv comprising a heavy chain variable region (VH) and a light chain variable region (VL),

wherein the VH comprises a CDR1 comprising the amino acid sequence of SEQ ID NO: 37, a CDR2 comprising the amino acid sequence of SEQ ID NO: 38, and a CDR3 comprising the amino acid sequence of SEQ ID NO: 39, and

wherein the VL comprises a CDR1 comprising the amino acid sequence of SEQ ID NO: 40, a CDR2 comprising the amino acid sequence of SEQ ID NO: 41, and a CDR3 comprising the amino acid sequence of SEQ ID NO: 42; and

a TGFβRIIDN armoring molecule expressed on the surface of the cell comprising amino acids 478 to 671 of SEQ ID NO: 47.

21. The cell of claim 20, wherein the VH comprises the amino acid sequence of SEQ ID NO: 27 and the VL comprises the amino acid sequence of SEQ ID NO: 28.

22. The cell of claim 20, wherein the scFv comprises the amino acid sequence of SEQ ID NO: 1.

23. The cell of claim 20, wherein the CAR comprises the amino acid sequence of SEQ ID NO: 25.

24. The cell of claim 20, wherein the CAR and TGFβRIIDN armoring molecule comprise the amino acid sequence of SEQ ID NO: 47.