

WHAT IS CLAIMED IS:

1. An immune cell comprising:
 - a chimeric antigen receptor (CAR), wherein the CAR comprises an extracellular antigen-binding domain that binds specifically to glypican-3 (GPC3), wherein the extracellular antigen-binding domain comprises:
 - a light chain variable domain comprising VL CDRs 1, 2, and 3 and a heavy chain variable domain comprising VH CDRs 1, 2, and 3, wherein
 - a. the VL CDRs 1, 2, and 3 comprise SEQ ID NOs: 1, 2, and 3, and
 - b. the VH CDRs 1, 2, and 3 comprise SEQ ID NOs: 4, 5, and 6, and
 - a transmembrane domain, and an intracellular signaling domain; and
 - an exogenous nucleic acid comprising a sequence encoding interleukin-18.
2. The immune cell of claim 1, wherein the light chain variable domain comprises a sequence that is at least 80% identical to SEQ ID NO: 10.
3. The immune cell of claim 2, wherein the light chain variable domain comprises a sequence that is at least 90% identical to SEQ ID NO: 10.
4. The immune cell of claim 3, wherein the light chain variable domain comprises a sequence that is at least 96% identical to SEQ ID NO: 10.
5. The immune cell of any one of claims 1-4, wherein the heavy chain variable domain comprises a sequence that is at least 80% identical to SEQ ID NO: 8.
6. The immune cell of claim 5, wherein the heavy chain variable domain comprises a sequence that is at least 90% identical to SEQ ID NO: 8.
7. The immune cell of claim 6, wherein the heavy chain variable domain comprises a sequence that is at least 96% identical to SEQ ID NO: 8.

8. The immune cell of any one of claims 1-7, wherein the interleukin-18 is a human interleukin-18.
9. The immune cell of claim 8, wherein the human interleukin-18 comprises a sequence that
5 is at least 80% identical to SEQ ID NO: 11 or 12.
10. The immune cell of claim 9, wherein the human interleukin-18 comprises a sequence that is at least 90% identical to SEQ ID NO: 11 or 12.
- 10 11. The immune cell of claim 10, wherein the human interleukin-18 comprises a sequence that is at least 96% identical to SEQ ID NO: 11 or 12.
12. The immune cell of any one of claims 1-11, wherein the sequence encoding interleukin-18 further includes a sequence encoding a secretion signal sequence.
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13. The immune cell of claim 12, wherein the secretion signal sequence is an interleukin-2 secretion signal sequence.
14. The immune cell of claim 13, wherein the interleukin-2 secretion signal sequence
20 comprises a sequence of SEQ ID NO: 13 or 14.
15. The immune cell of any one of claims 1-14, wherein the exogenous nucleic acid further comprises a promoter operably linked to the sequence encoding interleukin-18.
- 25 16. The immune cell of claim 15, wherein the promoter is a constitutive promoter.
17. The immune cell of claim 15, wherein the promoter is an inducible promoter.
18. The immune cell of claim 15, wherein the promoter is an NFAT promoter.
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19. The immune cell of any one of claims 1-18, wherein the antigen-binding domain is humanized.
20. The immune cell of any one of claims 1-18, wherein the antigen-binding domain is human.
21. The immune cell of any one of claims 1-20, wherein the antigen-binding domain is an scFv.
22. The immune cell of any one of claims 1-21, wherein the transmembrane domain is a transmembrane domain selected from a protein selected from the group consisting of: 4-1BB/CD137, an activating NK cell receptor, an immunoglobulin protein, B7-H3, BAFFR, BLAME (SLAMF8), BTLA, CD100 (SEMA4D), CD103, CD160 (BY55), CD18, CD19, CD19a, CD2, CD247, CD27, CD276 (B7-H3), CD28, CD29, CD3delta, CD3 epsilon, CD3 gamma, CD3 zeta, CD30, CD4, CD40, CD49a, CD49D, CD49f, CD69, CD7, CD84, CD8, CD8alpha, CD8beta, CD96 (Tactile), CD11a, CD11b, CD11c, CD11d, CDS, CEACAM1, CRT AM, cytokine receptor, DAP-10, DNAM1 (CD226), Fc gamma receptor, GADS, GITR, HVEM (LIGHTR), IA4, ICAM-1, Ig alpha (CD79a), IL-2R beta, IL-2R gamma, IL-7R alpha, inducible T cell costimulator (ICOS), an integrin, ITGA4, ITGA6, ITGAD, ITGAE, ITGAL, ITGAM, ITGAX, ITGB2, ITGB7, ITGB1, KIRDS2, LAT, LFA-1, a ligand that specifically binds with CD83, LIGHT, LTBR, Ly9 (CD229), lymphocyte function-associated antigen-1 (LFA-1), an MHC class 1 molecule, NKG2C, NKG2D, NKp30, NKp44, NKp46, NKp80 (KLRF1), OX-40, PAG/Cbp, programmed death-1 (PD-1), PSGL1, SELPLG (CD162), a Signaling Lymphocytic Activation Molecule (a SLAM protein), SLAM (SLAMF1), SLAMF4 (CD244), SLAMF6 (NTB-A), SLAMF7, SLP-76, a TNF receptor protein, TNFR2, TNFSF14, a Toll ligand receptor, TRANCE/RANKL, VLA1, and VLA-6.
23. The immune cell of claim 22, wherein the transmembrane domain is a transmembrane domain from CD8alpha.

24. The immune cell of any one of claims 1-23, wherein the intracellular signaling domain comprises an intracellular signaling domain from a protein selected from the group consisting of: 4-1BB/CD137, an activating NK cell receptor, an immunoglobulin protein, B7-H3, BAFFR, BLAME (SLAMF8), BTLA, CD100 (SEMA4D), CD103, CD160
5 (BY55), CD18, CD19, CD19a, CD2, CD247, CD27, CD276 (B7-H3), CD28, CD29, CD3delta, CD3epsilon, CD3gamma, CD3zeta, CD30, CD4, CD40, CD49a, CD49D, CD49f, CD69, CD7, CD84, CD8, CD8alpha, CD8beta, CD96 (Tactile), CD11a, CD11b, CD11c, CD11d, CDS, CEACAM1, CRTAM, a cytokine receptor, DAP-10, DNAM1
10 (CD226), Fc gamma receptor, GADS, GITR, HVEM (LIGHTR), IA4, ICAM-1, Ig alpha (CD79a), IL-2Rbeta, IL-2R gamma, IL-7R alpha, inducible T cell costimulator (ICOS), an integrin, ITGA4, ITGA6, ITGAD, ITGAE, ITGAL, ITGAM, ITGAX, ITGB2, ITGB7, ITGB1, KIRDS2, LAT, ligand that specifically binds with CD83, LIGHT, LTBR, Ly9 (CD229), Ly108, lymphocyte function-associated antigen-1 (LFA-1), a MHC class I molecule, NKG2C, NKG2D, NKp30, NKp44, NKp46, NKp80 (KLRF1), OX-40,
15 PAG/Cbp, programmed death-1 (PD-1), PSGL1, SELPLG (CD162), a Signaling Lymphocytic Activation Molecules (SLAM protein), SLAM (SLAMF1), SLAMF4 (CD244), SLAMF6 (NTB-A), SLAMF7, SLP-76, a TNF receptor protein, TNFR2, TNFSF14, a Toll ligand receptor, TRANCE/RANKL, VLA1, and VLA-6, or any combination thereof.
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25. The immune cell of claim 24, wherein the intracellular signaling domain is from 4-1BB and CD3zeta.
26. The immune cell of any one of claims 1-25, wherein the immune cell is a human immune
25 cell.
27. The immune cell of claim 26, wherein the human immune cell is an autologous human immune cell.
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28. The immune cell of claim 26, wherein the human immune cell is an allogeneic human immune cell.

29. The immune cell of any one of claims 1-28, wherein the immune cell is a T cell.

30. The immune cell of any one of claims 1-28, wherein the immune cell is an NK cell.

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31. The immune cell of any one of claims 1-30, wherein the immune cell secretes the IL-18 encoded by the exogenous nucleic acid.

32. A pharmaceutical composition comprising an immune cell of any one of claims 1-31 and a pharmaceutically acceptable carrier.

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33. A kit comprising a pharmaceutical composition of claim 32.

34. A method of treating a subject having a glypican-3-associated cancer, the method comprising administering to the subject an immune cell of any one of claims 1-31 or a pharmaceutical composition of claim 32.

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