

Claims

1. A $\gamma\delta$ T cell comprising at least one vector, the at least one vector directing the expression of a chimeric antigen receptor (CAR) and a survival factor, wherein the CAR comprises an extracellular domain comprising chlorotoxin, a transmembrane domain and at least one intracellular signaling domain; and wherein the survival factor is a polypeptide that confers resistance to a chemotherapeutic agent.
2. The $\gamma\delta$ T cell of claim 1, wherein the intracellular signaling comprises CD3 ζ , MB1 chain, B29, FcRIII, or FcRI, or a combination of the foregoing.
3. The $\gamma\delta$ T cell of claim 1 wherein the intracellular signaling domain comprises only CD3 ζ .
4. The $\gamma\delta$ T cell of any one of claims 1 to 2, wherein the intracellular signaling domain comprises a costimulatory domain.
5. The $\gamma\delta$ T cell of claim 4, wherein the costimulatory domain comprises a functional signaling domain of a polypeptide selected from the group consisting of: CD27, CD28, 4-1BB (CD137), OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LIGHT, NKG2C, B7-H3, a ligand that specifically binds with CD83, CDS, ICAM-1, GITR, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), CD160, CD19, CD4, CD8 α , CD8 β , IL2R β , IL2R γ , IL7R α , ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, NKp44, NKp30, NKp46, and NKG2D.
6. A $\gamma\delta$ T cell comprising at least one vector, the at least one vector directing the expression of a chimeric antigen receptor (CAR) and a survival factor, wherein the CAR comprises an extracellular domain comprising chlorotoxin, and a transmembrane domain, and wherein the survival factor is a polypeptide that confers resistance to a chemotherapeutic agent.
7. The $\gamma\delta$ T cell of any one of claims 1 to 6, wherein the transmembrane domain is selected from the group consisting of: T-cell receptor alpha chain, T-cell receptor beta chain, T-cell

receptor zeta chain, CD28, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, CD154, KIRDS2, OX40, CD2, CD27, LFA-1, ICOS, 4-1BB, GITR, CD40, BAFFR, HVEM, SLAMF7, NKp80, CD160, CD19, IL2R β , IL2R γ , IL7R α , ITGA1, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, TNFR2, DNAM1, SLAMF4, CD84, CD96, CEACAM1, CRTAM, Ly9, CD160, PSGL1, CD100, SLAMF6, SLAM, BLAME, SELPLG, LTBR, PAG/Cbp, NKp44, NKp30, NKp46, NKG2D, and NKG2C.

8. The $\gamma\delta$ T cell of any one of claims 1 to 7, wherein the CAR further comprises an extracellular spacer.
9. The $\gamma\delta$ T cell of claim 8, wherein the extracellular spacer comprises all or a portion of a hinge region of human IgD or human IgG1 and optionally all or a portion of an immunoglobulin heavy chain constant region from human IgG1.
10. The $\gamma\delta$ T cell of any one of claims 1 to 9, wherein the CAR further comprises a flexible linker.
11. The $\gamma\delta$ T cell of claim 10, wherein the flexible linker has the sequence of SEQ ID NO: 2 or SEQ ID NO: 3, present from 1 to 10 copies.
12. The $\gamma\delta$ T cell of any one of claims 1 to 7, wherein the CAR further comprises a flexible linker and an extracellular spacer.
13. The $\gamma\delta$ T cell of claim 12, wherein the flexible linker has the sequence of SEQ ID NO: 2 or SEQ ID NO: 3, present from 1 to 10 copies.
14. The $\gamma\delta$ T cell of any one of claims 1 to 13, wherein a single vector directs the expression of the CAR, the survival factor, and a stress-induced antigen receptor, wherein the stress-induced antigen receptor is NKG2D.
15. The $\gamma\delta$ T cell of any one of claims 1 to 13, wherein the $\gamma\delta$ T cell naturally expresses a stress-induced antigen receptor, wherein the stress-induced antigen receptor is NKG2D.
16. The $\gamma\delta$ T cell of any one of the preceding claims, wherein the chemotherapeutic agent is selected from the group consisting of: trimethotrexate, temozolomide, raltitrexed, S-(4-Nitrobenzyl)-6-thioinosine, 6-benzylguanine, nitrosoureas, fotemustine, cytarabine, camptothecin, doxorubicin, melphalan, and any combination of the foregoing.

17. The $\gamma\delta$ T cell of any one of claims 1 to 16, wherein the survival factor is selected from the group consisting of: *O*⁶-Methylguanine-DNA methyltransferase, multidrug resistance protein 1, 5' nucleotidase II, dihydrofolate reductase and thymidylate synthase.
18. The $\gamma\delta$ T cell of any one of claims 1 to 17, wherein the $\gamma\delta$ T cell is isolated.
19. The $\gamma\delta$ T cell of claim 6, wherein the $\gamma\delta$ T cell lacks an intracellular signaling domain.
20. A pharmaceutical composition comprising a $\gamma\delta$ T cell of any one of claims 1 to 19 and a pharmaceutically acceptable carrier.
21. The pharmaceutical composition of claim 20, wherein the $\gamma\delta$ T cells are present at greater than or equal to 60% of the total cell population of the composition as determined by flow cytometry.
22. The pharmaceutical composition of claim 20 or 21, wherein the extracellular domain comprises chlorotoxin and the survival factor is *O*⁶-Methylguanine-DNA methyltransferase.
23. The pharmaceutical composition of any one of claims 20 to 22 for use in treating cancer, wherein the composition is for administration concurrently with the chemotherapeutic agent, or after administration of the chemotherapeutic agent, or any combination thereof.
24. The pharmaceutical composition of 23, wherein the cancer is selected from the group consisting of glioma, melanoma, neuroblastoma, medulloblastoma, or small cell lung carcinoma.
25. The pharmaceutical composition of claim 24, wherein the cancer is glioblastoma.
26. The pharmaceutical composition of claim 22, wherein the chemotherapeutic agent is temozolomide.