

CLAIMS

1. A pharmaceutical composition, wherein the pharmaceutical composition comprises modified T cells comprising a first nucleic acid encoding a chimeric antigen receptor (CAR) and a second nucleic acid encoding therapeutic agents IL-6 and IFN γ and comprising SEQ ID NO: 469.
2. The pharmaceutical composition of claim 1, wherein the modified T cells express and secrete the therapeutic agents IL-6 and IFN γ in response to activation of the modified T cells.
3. The pharmaceutical composition of claim 1, wherein the modified T cells comprise nucleic acid sequences encoding SEQ ID NOS: 287 and 328.
4. The pharmaceutical composition of claim 1, wherein the CAR comprises an extracellular domain, a transmembrane domain, and an intracellular domain, the extracellular domain binding an antigen.
5. The pharmaceutical composition of claim 4, wherein the intracellular domain comprises a co-stimulatory domain that comprises an intracellular domain of a co-stimulatory molecule selected from the group consisting of CD27, CD28, 4-1BB, OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LIGHT, NKG2C, B7-H3, and a combination thereof.
6. The pharmaceutical composition of claim 4, wherein the antigen is CD19.
7. The pharmaceutical composition of claim 1, wherein the therapeutic agents IL-6 and IFN γ are present in the modified T cells in a recombinant DNA construct, in an mRNA, or in a viral vector.
8. The pharmaceutical composition of claim 1, wherein the modified T cells further comprises a nucleic acid sequence comprising a binding site for a transcription modulator that modulates secretion of therapeutic agents IL-6 or IFN γ .
9. The pharmaceutical composition of claim 1, wherein SEQ ID NO: 469 drives expression and secretion of the therapeutic agents IL6 and IFN γ .
10. The pharmaceutical composition of claim 1, wherein the CAR and the therapeutic agents IL6 and IFN γ are produced in the form of a polyprotein, which is cleaved to generate separate CAR and therapeutic agent molecules, and there is a cleavable moiety between the CAR and the therapeutic agents IL-6 and IFN γ , the cleavable moiety comprising a 2A peptide, and the 2A peptide comprising P2A or T2A.
11. The pharmaceutical composition of claim 1, wherein the modified T cells comprise an additional CAR, and the additional CAR binds a solid tumor antigen.
12. The pharmaceutical composition of claim 11, wherein the solid tumor antigen is TSHR.
13. The pharmaceutical composition of claim 11, wherein the modified T cells comprise a dominant negative PD-1.