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(54) Title: GAMMA DELTA T CELL COMPOSITIONS AND METHODS OF USE

(57) Abstract: The present disclosure provides genetically modified iPSC-derived γδT cells and their precursors. A double genomic disruption in the suppressor of cytokine signaling 1 (SOCS1) gene and the cytokine-inducible sh2-containing protein (CISH) gene are provided, as is a triple genomic disruption in genes for SOCS1, CISH, and Bcl-2 interacting mediator of cell death (BIM), as is a quadruple genomic disruption in genes for SOCS1, CISH, BIM, and cell surface death receptor (FAS), as is a quintuple genomic disruption in genes for SOCS1, CISH, BIM, β-2-Microglobulin (B2M), and class II transactivator (CIITA), as is a sextuple genomic disruption in genes for SOCS1, CISH, BIM, B2M, CIITA, and FAS. Also provided is genetically modified iPSC-derived γδT cells and their precursors with improved proliferation and tumor killing activity. Also provided are genetically modified iPSC-derived γδT cells and their precursors further comprising CD19 CAR. The present disclosure further provides methods making and using such cells, as well as gene editing systems.

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