

(iv) a CD28 transmembrane region comprising the amino acid sequence of SEQ ID NO:6, and
(v) an intracellular signaling region comprising a 4-1BB intracellular signaling sequence comprising the amino acid sequence of SEQ ID NO:7 and a CD3zeta intracellular signaling sequence comprising the amino acid sequence of SEQ ID NO:9.

[00278] The present disclosure provides a host cell, or a population of host cells, which harbors an expression vector operably linked to a nucleic acid that encodes a second polypeptide chain comprising two regions ordered from the amino terminus to the carboxyl terminus: (i) a CD38 antibody light chain variable region comprising the amino acid sequence of SEQ ID NO:3, and (ii) a CD38 antibody light chain constant region comprising the amino acid sequence of SEQ ID NO:4.

[00279] In one embodiment, the vector is operably linked to a nucleic acid that encodes the first and second polypeptide chains (SEQ ID NOS:6 and 7).

[00280] In one embodiment, the vector is operably linked to a nucleic acid that encodes the first polypeptide chain (SEQ ID NO:6), a T2A cleavage sequence (SEQ ID NO:12), and the second polypeptide chain (SEQ ID NO:7).

[00281] The present disclosure provides a vector operably linked to a nucleic acid that encodes a precursor polypeptide, comprising the amino acid sequence of SEQ ID NO:15.

[00282] In one embodiment, the host cell expresses the first polypeptide chain (SEQ ID NO:13 or 16) and the second polypeptide chain (SEQ ID NOS: 14 or 17). In one embodiment, the host cell expresses the precursor polypeptide of SEQ ID NO: 15 or 18).

[00283] In one embodiment, the first polypeptide chain (SEQ ID NO:13 or 16) includes or lacks the leader sequence underlined in Figure 35B or C. In one embodiment, the second polypeptide chain (SEQ ID NO:14 or 17) includes or lacks the leader sequence underlined in Figure 35B or C.

[00284] The present disclosure provides a host cell, or a population of host cells, which harbors an expression vector operably linked to a nucleic acid that encodes a Version 1 (e.g., V1) dimeric antigen receptors (DAR) construct comprising a first polypeptide chain carrying heavy chain variable (VH) and heavy chain constant regions (CH), and a second polypeptide chain carrying light chain variable (VL) and light chain constant regions (CL) (e.g., Figure 1), wherein the host cell, or a population of host cells harbor (a) a first vector is operably linked to a first nucleic acid that encodes the first polypeptide chain comprising five regions ordered from the

(TCL), acute myeloid leukemia (AML), hairy cell leukemia (HCL), Hodgkin's Lymphoma (HL), chronic myeloid leukemia (CML) and multiple myeloma (MM).

[00338] EXAMPLES

[00339] The following examples are meant to be illustrative and can be used to further understand embodiments of the present disclosure and should not be construed as limiting the scope of the present teachings in any way.

[00340] Example 1: Isolation of human PBMC Cells and primary T cells

[00341] Primary human T cells were isolated from healthy human donors either from buffy coats (San Diego blood bank), fresh blood or leukapheresis products (StemCell). Peripheral blood mononuclear cells were isolated by density gradient centrifugation. T cells were isolated from PBMCs by magnetic negative selection using EasySep™ Human T Cell Isolation Kit (STEMCELL) according to manufacturer's instructions.

[00342] Example 2: Primary T cell culture

[00343] Primary T cells were cultured in CTS™ OpTmizer™ T Cell Expansion SFM supplemented with 5% CTS™ Immune Cell SR (Thermo Fisher Scientific) with 300U/mL IL-2 (Proleukin) at a density of 10^6 cells per mL. Isolated T cells were stimulated freshly or from the frozen tank. Cells were activated with T Cell TransAct (Miltenyi) 3uL/ 10^6 cells per mL for two to three days. Following transfection, T cells were cultured in media with IL-2 at 300U/mL.

[00344] Example 3: Tumor Cell lines

[00345] Multiple myeloma cell line RPMI 8226 was obtained from ATCC and were transduced using a lentivirus carrying luciferase and GFP genes. A single cell clone with luciferase and GFP expression was selected (RPMI8226-FLuc). K562/RPE cells were made similarly by transducing the K562 cells with lentivirus carrying RPE genes. Both cell lines were cultured in RPMI1640 medium (ATCC) supplemented with 10% fetal bovine serum (Sigma).

[00346] Example 4: Preparation of CAR and DAR T cells

[00347] Activated T cells were introduced with nucleic acids encoding either a CAR or DAR construct.

[00348] The nucleic acid encoding the anti-CD38 CAR polypeptide included a heavy chain signal peptide (SEQ ID NO:10) followed by 2 additional amino acid residues Asp and Ile, a myc tag EQKLISEEDL (SEQ ID NO: 24), the anti-CD38 heavy chain variable region (SEQ ID NO:1), 15 amino acid linker GGGGSGGGGSGGGGS (SEQ ID NO:23), the anti-CD38 light