

What is Claimed

1. Use of an effective dose of a plurality of T cells in the manufacture of a medicament for the treatment of a malignancy, wherein:
 - (a) the plurality of T cells comprises one or more chimeric antigen receptors (CARs); and
 - (b) the effective dose comprises a predetermined amount of polyfunctional T cells determined using the Polyfunctional Strength Index (PSI), wherein the PSI incorporates protein intensities and percentage of polyfunctional cells expressing those proteins, wherein the polyfunctional cells comprise CD4⁺ T cells that secrete IL-17alpha, IL-8, and/or IFN-gamma and/or CD8⁺ T cells that secrete Granzyme B, IFN-gamma, IL-8, and/or MIP-1alpha when stimulated by the antigen.
2. The use of claim 1, wherein the Polyfunctional Strength Index (PSI) is calculated by multiplying the percentage of polyfunctional cells by the sum of the mean fluorescence intensity of the proteins secreted by the polyfunctional cells.
3. The use of claim 2, wherein the Polyfunctional Strength Index (PSI) is obtained by a method comprising (i) determining a desired percentage of Polyfunctional T cells; and (ii) obtaining a pre-determined cytokine profile.
4. The use of anyof claims 1 to 3, wherein the effective dose is adjusted proportionally with tumor burden.
5. The use of any one of claims 1 to 4, wherein the predetermined amount of polyfunctional T cells is determined using a composite index.
6. The use of any one of claims 3-5, wherein obtaining the pre-determined cytokine profile comprises measuring at least one of Granzyme B, IFN-gamma, MIP1a, Perforin, TNFa, TNFb, GMCSF, IL-2, IL-5, IL-7, IL-8, IL-9, IL-12, IL-15, IL-21, CCI-11, IP-10, MIP1b, RANTES, IL-4, IL-10, IL-13, IL-22, TGF-b1, SCD137, SCD40L, IL-1b, IL-6, IL-17a, IL-17f, MCP-1, and MCP-4.
7. The use of claim 6, wherein obtaining the pre-determined cytokine profile comprises selecting at least one of Granzyme B, IFN-gamma, MIP1a, Perforin, TNFa, TNFb, GMCSF, IL-2, IL-5, IL-7, IL-8, IL-9, IL-12, IL-15, IL-21, CCI-11, IP-10, MIP1b,

RANTES, IL-4, IL-10, IL-13, IL-22, TGF- β 1, SCD137, SCD40L, IL-1b, IL-6, IL-17a, IL-17f, MCP-1, and MCP-4.

8. The use of any one of claims 1 to 7, wherein the one or more CARs target a tumor antigen.
9. The use of any one of claims 1 to 8, wherein the tumor associated antigen is a tumor-associated surface antigen, selected from 5T4, alphafetoprotein (AFP), B7-1 (CD80), B7-2 (CD86), BCMA, B-human chorionic gonadotropin, CA-125, carcinoembryonic antigen (CEA), carcinoembryonic antigen (CEA), CD123, CD133, CD138, CD19, CD20, CD22, CD23, CD24, CD25, CD30, CD33, CD34, CD4, CD40, CD44, CD56, CD8, CLL-1, c-Met, CMV-specific antigen, CS-1, CSPG4, CTLA-4, DLL3, disialoganglioside GD2, ductal-epithelial mucine, EBV-specific antigen, EGFR variant III (EGFRvIII), ELF2M, endoglin, ephrin B2, epidermal growth factor receptor (EGFR), epithelial cell adhesion molecule (EpCAM), epithelial tumor antigen, ErbB2 (HER2/neu), fibroblast associated protein (fap), FLT3, folate binding protein, GD2, GD3, glioma-associated antigen, glycosphingolipids, gp36, HBV-specific antigen, HCV-specific antigen, HER1-HER2, HER2-HER3 in combination, HERV-K, high molecular weight-melanoma associated antigen (HMW-MAA), HIV-1 envelope glycoprotein gp41, HPV-specific antigen, human telomerase reverse transcriptase, IGF1 receptor, IGF-II, IL-11R α , IL-13R α 2, Influenza Virus-specific antigen; CD38, insulin growth factor (IGF1)-1, intestinal carboxyl esterase, kappa chain, LAGA-1a, lambda chain, Lassa Virus-specific antigen, lectin-reactive AFP, CD3, MAGE, MAGE-A1 and all other lineage-specific or tissue specific antigens, major histocompatibility complex (MHC) molecule, major histocompatibility complex (MHC) molecule presenting a tumor-specific peptide epitope, M-CSF, melanoma-associated antigen, mesothelin, mesothelin, MN-CA IX, MUC-1, mut hsp70-2, mutated p53, mutated p53, mutated ras, neutrophil elastase, NKG2D, Nkp30, NY-ESO-1, p53, PAP, prostase, prostate specific antigen (PSA), prostate-carcinoma tumor antigen-1 (PCTA-1), prostate-specific antigen protein, STEAP1, STEAP2, PSMA, RAGE-1, ROR1, RU1, RU2 (AS), surface adhesion molecule, surviving and telomerase, TAG-72, the extra domain A (EDA) and extra domain B (EDB) of fibronectin and the A1 domain of tenascin-C (TnC A1), thyroglobulin, tumor stromal antigens, vascular endothelial growth factor receptor-2 (VEGFR2), virus-specific surface antigen such as an HIV-specific antigen (such as HIV gp120), as well as any derivate or variant of these surface markers.

10. The use of any one of claims 1 to 9, wherein the malignancy is a solid tumor, sarcoma, carcinoma, lymphoma, multiple myeloma, Hodgkin's Disease, non-Hodgkin's lymphoma (NHL), primary mediastinal large B cell lymphoma (PMBC), diffuse large B cell lymphoma (DLBCL), follicular lymphoma (FL), transformed follicular lymphoma, splenic marginal zone lymphoma (SMZL), chronic or acute leukemia, acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia (ALL) (including non T cell ALL), chronic lymphocytic leukemia (CLL), T-cell lymphoma, one or more of B-cell acute lymphoid leukemia ("BALL"), T-cell acute lymphoid leukemia ("TALL"), acute lymphoid leukemia (ALL), chronic myelogenous leukemia (CML), B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, Marginal zone lymphoma, myelodysplasia and myelodysplastic syndrome, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, a plasma cell proliferative disorder (*e.g.*, asymptomatic myeloma (smoldering multiple myeloma or indolent myeloma), monoclonal gammopathy of undetermined significance (MGUS), plasmacytomas (*e.g.*, plasma cell dyscrasia, solitary myeloma, solitary plasmacytoma, extramedullary plasmacytoma, and multiple plasmacytoma), systemic amyloid light chain amyloidosis, POEMS syndrome (also known as Crow-Fukase syndrome, Takatsuki disease, and PEP syndrome), or a combination thereof.

11. The use of any one of claims 1 to 10, wherein the proteins or cytokines comprises one or more of Granzyme B, IFN-gamma, MIP1a, Perforin, TNFa, TNFb, GMCSF, IL-2, IL-5, IL-7, IL-8, IL-9, IL-12, IL-15, IL-21, CCI-11, IP-10, MIP1b, RANTES, IL-4, IL-10, IL-13, IL-22, TGF-b1, SCD137, SCD40L, IL-1b, IL-6, IL-17a, IL-17f, MCP-1, and MCP-4.

12. The use of any one of claims 1 to 11 further comprising modulating the total dose to adjust the total number of polyfunctional cells.

13. The use of any one of claims 1 to 12 further comprising modulating the total dose to adjust the total Polyfunctional Strength Index (PSI).

14. The use of any one of claims 1 to 13 further comprising treating a malignancy in a patient comprising:

- (a) obtaining a plurality of T cells comprising one or more chimeric receptors;
- (b) measuring the Polyfunctional Strength Index (PSI) of the T cells;
- (c) preparing an effective dose comprising a predetermined amount of polyfunctional T cells; and
- (d) administering to the patient the effective dose comprising a predetermined amount of polyfunctional T cells.

15. The use of any one of claims 1 to 14 further comprising:

- (a) determining the amount of polyfunctional T cells in the plurality of T cells; and
- (b) determining if patient will respond to chimeric receptor treatment based on the amount of polyfunctional T cells.

16. The use of any one of claims 1 to 14 further comprising :

- (a) obtaining a plurality of T cells comprising one or more chimeric receptors;
- (b) preparing an effective dose comprising a predetermined amount of polyfunctional T cells; and
- (c) administering to the patient the effective dose comprising a predetermined amount of polyfunctional T cells.