

U.S. PATENT 9,987,308 CHALLENGED CLAIMS LISTING

Claim No.	Limitation
1	An adoptive cellular immunotherapy composition containing chimeric antigen receptor-modified CD4⁺ T lymphocytes and chimeric antigen receptor-modified CD8⁺ T lymphocytes, wherein: (a) the chimeric antigen receptor-modified CD4⁺ T lymphocytes contain a chimeric antigen receptor that specifically binds to an antigen and at least 50% of the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes in the composition are surface positive for CD62L and/or CD45RA, and (b) the chimeric antigen receptor-modified CD8⁺ T lymphocytes contain a chimeric antigen receptor that specifically binds to the antigen and at least 50% of CD8⁺ cytotoxic T lymphocytes in the composition are surface positive for CD62L and/or CD45RO.
2	The adoptive cellular immunotherapy composition according to claim 1, wherein the antigen is associated with a disease or disorder selected from a solid tumor, hematologic malignancy, melanoma, and infection with a pathogen.
3	The adoptive cellular immunotherapy composition according to claim 1, wherein the antigen is selected from ROR1, tEGFR, Her2, L1-CAM, CD19, CD20, CD22, mesothelin, and CEA.
4	The adoptive cellular immunotherapy composition according to claim 1, wherein the chimeric antigen receptor of (a) and/or (b) comprises an extracellular antibody variable domain or single-chain antibody fragment specific for the antigen and an intracellular signaling module.
5	The adoptive cellular immunotherapy composition according to claim 4, wherein each of the intracellular signaling module of the chimeric antigen receptor contained by the CD4⁺ T lymphocytes and the intracellular signaling module of the chimeric antigen receptor contained by the CD8⁺ T lymphocytes, individually, comprise (a) a CD28 costimulatory domain and a CD3 intracellular signaling domain, or (b) a 4-1BB costimulatory domain and a CD3 intracellular signaling domain.

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6	The adoptive cellular immunotherapy composition according to claim 1, wherein: (a) at least 60% of the chimeric antigen receptor-modified CD4⁺ T lymphocytes are surface positive for CD62L and/or CD45RA; (b) at least 60% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are surface positive for CD62L and/or CD45RO; (c) at least 80% of the chimeric antigen receptor-modified CD4⁺ T lymphocytes are surface positive for CD62L and/or CD45RA; and/or (d) at least 80% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes are surface positive for CD62L and/or CD45RO.
7	The adoptive cellular immunotherapy composition according to claim 1, wherein the intracellular signaling domain of the chimeric antigen receptor contained by the CD8⁺ T lymphocytes is the same as the intracellular signaling domain of the chimeric antigen receptor contained by the CD4⁺ T lymphocytes.
8	The adoptive cellular immunotherapy composition according to claim 1, wherein the CD4⁺ helper T lymphocytes and the CD8⁺ cytotoxic T lymphocytes are derived from a subject and wherein the CD4⁺ helper T lymphocytes secrete a greater amount of IL-2 and/or exhibit a greater degree of proliferation when cultured in the presence of the antigen as compared to a reference population of CD4⁺ T cells that has been expanded in vitro from an effector memory T cell-enriched CD4⁺ T cell population or a bulk CD4⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD4⁺ helper T lymphocytes.
9	The adoptive cellular immunotherapy composition of claim 1, wherein at least 50% of the chimeric antigen receptor-modified CD4⁺ helper T lymphocytes in the composition are surface positive for CD62L.
10	The adoptive cellular immunotherapy composition of claim 1, wherein at least 50% of the chimeric antigen receptor-modified CD8⁺ cytotoxic T lymphocytes in the composition are surface positive for CD62L.

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11	The adoptive cellular immunotherapy composition of claim 1, wherein at least 50% of the chimeric antigen receptor-modified CD4+ helper T lymphocytes in the composition are surface positive for CD62L and at least 50% of the chimeric antigen receptor-modified CD8+ cytotoxic T lymphocytes in the composition are surface positive for CD62L.
12	The adoptive cellular immunotherapy composition of claim 1, wherein at least 60% of the chimeric antigen receptor-modified CD4+ helper T lymphocytes in the composition are surface positive for CD62L and/or at least 60% of the chimeric antigen receptor-modified CD8+ cytotoxic T lymphocytes in the composition are surface positive for CD62L.
13	The adoptive cellular immunotherapy composition of claim 1, wherein at least 80% of the chimeric antigen receptor-modified CD4+ helper T lymphocytes in the composition are surface positive for CD62L and/or at least 80% of the chimeric antigen receptor-modified CD8+ cytotoxic T lymphocytes in the composition are surface positive for CD62L.
14	The adoptive cellular immunotherapy composition of claim 1, wherein the chimeric antigen receptor-modified CD4+ helper T lymphocytes in the composition and the chimeric antigen receptor-modified CD8+ cytotoxic T lymphocytes are present in the composition at a ratio of between about 2:1 to about 1:2.
15	The adoptive cellular immunotherapy composition of claim 1, wherein the chimeric antigen receptor-modified CD4+ helper T lymphocytes in the composition and the chimeric antigen receptor-modified CD8+ cytotoxic T lymphocytes are present in the composition at a ratio of about 2:1, 1:1, or 1:2.
16	The adoptive cellular immunotherapy composition of claim 1, wherein the chimeric antigen receptor contained by the CD8+ T lymphocytes is the same as the chimeric antigen receptor contained by the CD4+ T lymphocytes.
18	The adoptive cellular immunotherapy composition according to claim 1, wherein the antigen is ROR1.
19	The adoptive cellular immunotherapy composition according to claim 1, wherein the antigen is Her2.

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20	The adoptive cellular immunotherapy composition according to claim 1, wherein the antigen is LI-CAM.
21	The adoptive cellular immunotherapy composition according to claim 1, wherein the antigen is CD19.
22	The adoptive cellular immunotherapy composition according to claim 1, wherein the antigen is CD20.
23	The adoptive cellular immunotherapy composition according to claim 1, wherein the antigen is CD22.
24	The adoptive cellular immunotherapy composition according to claim 1, wherein the antigen is mesothelin.
25	The adoptive cellular immunotherapy composition according to claim 1, wherein the antigen is CEA.
26	The adoptive cellular immunotherapy composition according to claim 2, wherein the disease or disorder is a solid tumor, hematologic malignancy, or melanoma.
27	The adoptive cellular immunotherapy composition according to claim 2, wherein the disease or disorder is a hematologic malignancy.
28	The adoptive cellular immunotherapy composition according to claim 1, wherein the antigen is a tumor associated antigen associated with a cancer selected from the group consisting of melanoma, breast cancer, squamous cell carcinoma, colon cancer, leukemia, myeloma, prostate cancer, B cell lymphoma, breast cancer, prostate cancer, and leukemia.
29	The adoptive cellular immunotherapy composition according to claim 1, wherein a greater percentage of the chimeric antigen receptor-modified CD4 ⁺ helper T lymphocytes are surface positive for CD62L and/or CD45RA as compared to a reference population of CD4 ⁺ T cells that has been expanded in vitro from an effector memory-enriched CD4 ⁺ T cell population or a bulk CD4 ⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD4 ⁺ helper T lymphocytes.

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30	The adoptive cellular immunotherapy composition according to claim 1, wherein a greater percentage of the chimeric antigen receptor-modified CD8 ⁺ cytotoxic T lymphocytes are surface positive for CD62L, CD45RO and/or CCR7 as compared to a reference population of CD8 ⁺ T cells that has been expanded in vitro from an effector memory-enriched CD8 ⁺ T cell population or bulk CD8 ⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD8 ⁺ cytotoxic T lymphocytes.
31	The adoptive cellular immunotherapy composition according to claim 1, wherein the chimeric antigen receptor-modified CD8 ⁺ cytotoxic T lymphocytes proliferate when co-cultured in vitro with the CD4 ⁺ helper T lymphocytes in the presence of the antigen, to a greater degree as compared to the degree of proliferation of the CD8 ⁺ cytotoxic T lymphocytes when co-cultured, under the same conditions, with a reference population of CD4 ⁺ T cells expanded in vitro from an effector memory-enriched CD4 ⁺ T cell population or a bulk CD4 ⁺ T cell population from the subject and modified to contain the chimeric antigen receptor contained by the CD4 ⁺ helper T lymphocytes.