so the modified T-cells will attack cancer cells. Isolated T-cells are engineered to express a TCR specifically recognizes LMP2 on the patient's cancer cells. Large numbers of the TCR T-cells are grown in the laboratory and given to the patient, typically by infusion. The inventors have implementing next-generation immune cell therapy with antigen specificity-redirected T cells to shorten the time needed to generate T-cell populations that can be used in immunotherapy.

In one aspect, the present disclosure refers to a population of T-cells comprising an engineered T-cell receptor (TCR), wherein the engineered TCR activates T-cells in response to a Latent membrane protein 2 (LMP2) antigen, wherein the engineered TCR comprises an amino acid sequence that shares at least 90% identity to the amino acid sequence as set forth in SEQ ID NO:3. In one ~~aspect~~example, the present disclosure refers to a population of T-cells comprising an engineered T-cell receptor (TCR), wherein the engineered TCR activates T-cells in response to a Latent membrane protein 2 (LMP2) antigen. In certain examples, the engineered TCR comprises the amino acid sequence of SEQ ID NO:03. In some examples, the engineered TCR comprises the amino acid sequence of SEQ ID NO:09. In certain examples, the LMP2 antigen comprises the sequence of SSCSSCPLSK (SEQ ID NO:01).

In certain examples, the population of T-cells comprises a therapeutically effective amount of cells for the treatment of a cancer comprising LMP2 in a subject. In some examples, the subject expresses human leukocyte antigen subtype A11 (HLA-A11).

In certain examples, at least a portion of the population of T-cells produces or has the potential to produce one or more cytokines. In some examples, the one or more cytokines are selected from the group consisting of IL-2, IFN-gamma, TNF-alpha, Granzyme A, Granzyme B, and GM-CSF.

In certain examples, the cancer is selected from the group consisting of nasopharyngeal carcinoma (NPC), lymphoma, gastric cancer, lung cancer, melanoma, breast cancer, prostate cancer, colon cancer, renal cell carcinoma, ovarian cancer, neuroblastoma, rhabdomyosarcoma, and leukemia. In some examples, the cancer is an EBV-associated cancer. In certain examples, the cancer is nasopharyngeal carcinoma (NPC). In certain examples, the cancer is lymphoma. In certain examples, the cancer is gastric cancer.

In another aspect, the present disclosure refers to a pharmaceutical composition comprising a population of T-cells as disclosed herein, and a pharmaceutically acceptable carrier. In certain examples, the pharmaceutically acceptable carrier supports maintenance of a therapeutically effective amount of cells for the treatment of a cancer comprising LMP2. In some examples, the pharmaceutical composition further comprising at least one therapeutic agent.

In yet another example, the present disclosure provides a method of treating a subject suffering from a cancer comprising LMP2, wherein the method comprises administering to the subject a therapeutically effective amount of the population of T-cells as disclosed herein,

ID NO:1).

In an example, the present disclosure provides a pharmaceutical composition comprising a population of T-cells expressing the engineered TCRs as disclosed herein, and a pharmaceutically acceptable carrier.

In another example, the present disclosure provides a method of inducing a T-cell response in a subject suffering from a cancer comprising LMP2, wherein the method comprises administering to the subject a therapeutically effective amount of a population of T-cells comprising the engineered TCRs as disclosed herein, or the pharmaceutical compositions as disclosed here, wherein the administration induces an anti-tumor response to the cancer. In another aspect, the present disclosure refers to use of a population of T-cells as disclosed herein in the manufacture of a pharmaceutical composition suitable for ~~inducing~~ activating a T-cell in response to LMP2 in a subject suffering from a cancer expressing LMP2. In certain examples, the cancer is selected from group consisting of nasopharyngeal carcinoma (NPC), lymphoma, gastric cancer, lung cancer, melanoma, breast cancer, prostate cancer, colon cancer, renal cell carcinoma, ovarian cancer, neuroblastoma, rhabdomyosarcoma, and leukemia. In certain examples, the cancer is an EBV-associated cancer. In certain examples, the cancer is nasopharyngeal carcinoma (NPC). In certain examples, the cancer is lymphoma. In certain examples, the cancer is gastric cancer.

Another example of the present disclosure provides all that is described and illustrated herein.

BRIEF DESCRIPTION OF THE DRAWINGS

The foregoing aspects and other features of the disclosure are explained in the following description, taken in connection with the accompanying drawings, herein:

FIG. 1A-1B are flow cytometric results showing the expression and activity of candidate LMP2-A11 TCRs. (A) Candidate TCR sequences were cloned into retroviral vectors that were transduced into Jurkat cells, the percentages of TCRb-positive cells are indicated. (B) Jurkat cell lines in FIG. 1A were co-cultured with Ramos lymphoma cells engineered to express the HLA-A11-LMP2 peptide linker. T cell activation was quantified by measuring CD69 expression. The TCR identified as TCR-NPC-A11-03 was identified as LMP2-specific.

FIG. 2A-2B are flow cytometric results showing the expression and activity of candidate LMP2-A11 TCRs. (A) Candidate TCR sequences were cloned into retroviral vectors that were transduced into Jurkat cells, the percentages of TCRb-positive cells are indicated. (B) Jurkat cell lines in 1A were co-cultured with Ramos lymphoma cells engineered to express the HLA-A11-LMP2 peptide linker. T cell activation was quantified

CLAIMS

We claim:

1. A population of T-cells comprising an engineered T-cell receptor (TCR), wherein the engineered TCR activates T-cells in response to a Latent membrane protein 2 (LMP2) antigen, wherein the engineered TCR comprises an amino acid sequence that shares at least 90% identity to the amino acid sequence as set forth in SEQ ID NO:3.

2. The population of T-cells of claim 1, wherein the engineered TCR comprises the amino acid sequence as set forth in SEQ ID NO:5 and the amino acid sequence as set forth in SEQ ID NO:7.

3. The population of T-cells of claim 2, wherein the engineered TCR comprises the amino acid sequence as set forth in SEQ ID NO:4 and the amino acid sequence as set forth in SEQ ID NO:6.

4. The population of T-cells of claim ~~2 or 3~~1, wherein the engineered TCR comprises the amino acid sequence as set forth in SEQ ID NO:3.

~~5. The population of T-cells of claim 1, wherein the engineered TCR comprises an amino acid sequence that shares at least 90% identity to the amino acid sequence as set forth in SEQ ID NO:3.~~

~~6. The population of T-cells of claim 1, wherein the engineered TCR comprises the amino acid sequence as set forth in SEQ ID NO:11 and the amino acid sequence as set forth in SEQ ID NO:13.~~

~~7. The population of T-cells of claim 6, wherein the engineered TCR comprises the amino acid sequence as set forth in SEQ ID NO:10 and the amino acid sequence as set forth in SEQ ID NO:12.~~

~~8. The population of T-cells of claim 6 or 7, wherein the engineered TCR comprises the amino acid sequence as set forth in SEQ ID NO:9.~~

~~9. The population of T-cells of claim 1, wherein the engineered TCR comprises an amino acid sequence that shares at least 90% identity to the amino acid sequence as set forth in SEQ ID NO:9.~~

~~10~~5. The population of T-cells of claim 1, wherein the LMP2 antigen comprises the amino acid sequence as set forth in SEQ ID NO:1.

~~11~~6. The population of T-cells of any of claims 1-~~10~~5, wherein the population of T-cells comprises a therapeutically effective amount of cells for the treatment of a cancer comprising LMP2 in a subject, and wherein the subject expresses human leukocyte antigen subtype A11 (HLA-A11).

~~12~~7. The population of T-cells of claim 1, wherein at least a portion of the population of T-cells produces or has the potential to produce one or more cytokines.

~~13~~8. The population of T-cells of claim ~~12~~7, wherein the one or more cytokines are selected from the group consisting of IL-2, IFN-gamma, TNF-alpha, Granzyme A, Granzyme B, and GM-CSF.

~~14~~9. A pharmaceutical composition comprising a population of T-cells according to any of claims 1-~~13~~8, and a pharmaceutically acceptable carrier.

~~15~~10. Use of a population of T-cells according to any of claims 1-~~13~~ 8 in the manufacture of a pharmaceutical composition for treating a subject suffering from a cancer expressing LMP2.

~~16~~11. Use of a population of T-cells according to any of claims 1-~~13~~ 8 in the manufacture of a pharmaceutical composition for inhibiting the growth of a tumor expressing LMP2 in a subject in need thereof.

~~17~~12. Use of a population of T-cells according to any of claims 1-~~13~~ 8 in the manufacture of a pharmaceutical composition suitable for ~~inducing~~ activating a T-cell in response to LMP2 in a subject suffering from a cancer expressing LMP2.

~~18~~13. The use of claim ~~15~~10, ~~16~~11, or ~~17~~12, wherein the cancer is selected from group consisting of nasopharyngeal carcinoma (NPC), lymphoma, gastric cancer, lung cancer, melanoma, breast cancer, prostate cancer, colon cancer, renal cell carcinoma, ovarian cancer, neuroblastoma, rhabdomyosarcoma, and leukemia.

~~19~~14. The use of claim ~~18~~13, wherein the cancer is an EBV-associated cancer.

~~20~~15. The use of claim ~~19~~14, wherein the cancer is EBV-positive nasopharyngeal carcinoma (NPC), EBV-positive lymphoma, or EBV-positive gastric cancer.