

CHIMERIC ANTIGEN RECEPTORS AND THEIR USES

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This patent application claims the benefit of U.S. Provisional Patent Application No. 62/506,268, filed May 15, 2017, which is incorporated by reference herein in its entirety.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH AND DEVELOPMENT

[0002] This invention was made with Government support under project number Z01 BC011565 by the National Institutes of Health, National Cancer Institute. The Government has certain rights in the invention.

INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ELECTRONICALLY

[0003] Incorporated by reference in its entirety herein is a computer-readable nucleotide/amino acid sequence listing submitted concurrently herewith and identified as follows: one 180,939 Byte ASCII (Text) file named “739267_ST25.TXT” dated May 15, 2018.

BACKGROUND OF THE INVENTION

[0004] Cancer is a public health concern. Despite advances in treatments such as chemotherapy, the prognosis for many cancers, including hematological malignancies, may be poor. Accordingly, there exists an unmet need for additional treatments for cancer, particularly hematological malignancies.

BRIEF SUMMARY

[0004a] In one aspect, the present disclosure provides for a chimeric antigen receptor (CAR) amino acid construct comprising the amino acid sequence of SEQ ID NO: 48, 49, 50, 51, or 52 .

[0004b] In another aspect, the present disclosure provides for a nucleic acid comprising a nucleotide sequence encoding the CAR amino acid construct as described herein.

[0004c] In another aspect, the present disclosure provides for an isolated host cell comprising a recombinant expression vector comprising the nucleic acid as described herein.

[0004d] In another aspect, the present disclosure provides for a pharmaceutical composition comprising the CAR amino acid construct as described herein, the nucleic acid as described herein, the host cell as described herein or a population of cells thereof, and a pharmaceutically acceptable carrier.

[0004e] In another aspect, the present disclosure provides for the use of the host cell as described herein or a population of cells thereof in the manufacture of a medicament for the treatment of cancer in a mammal, wherein the host cell is a T cell or an NK cell.

[0005] An example of the disclosure provides a chimeric antigen receptor (CAR) amino acid construct comprising (a) a cleavable domain; (b) a first CAR comprising a first antigen binding domain, a first transmembrane domain, and a first intracellular T cell signaling domain; and (c) a second CAR comprising a second antigen binding domain, a second transmembrane domain, and a second intracellular T cell signaling domain; wherein the first and second CARs are linked through the cleavable domain, wherein the first antigen binding domain comprises an antigen binding domain of the m971 antibody, wherein when the first CAR is cleaved from the construct, the first antigen binding domain has antigenic specificity for CD22.

[0006] Another example of the disclosure provides a chimeric antigen receptor (CAR) amino acid construct comprising (a) a cleavable domain; (b) a first CAR comprising a first antigen

Claims

1. A chimeric antigen receptor (CAR) amino acid construct comprising the amino acid sequence of SEQ ID NO: 48, 49, 50, 51, or 52.
2. The CAR amino acid construct according to claim 1, wherein the CAR amino acid construct comprises the amino acid sequence of SEQ ID NO: 48.
3. The CAR amino acid construct according to claim 1, wherein the CAR amino acid construct comprises the amino acid sequence of SEQ ID NO: 49.
4. The CAR amino acid construct according to claim 1, wherein the CAR amino acid construct comprises the amino acid sequence of SEQ ID NO: 50.
5. The CAR amino acid construct according to claim 1, wherein the CAR amino acid construct comprises the amino acid sequence of SEQ ID NO: 51.
6. The CAR amino acid construct according to claim 1, wherein the CAR amino acid construct comprises the amino acid sequence of SEQ ID NO: 52.
7. A nucleic acid comprising a nucleotide sequence encoding the CAR amino acid construct of any one of claims 1-6.
8. An isolated host cell comprising a recombinant expression vector comprising the nucleic acid of claim 7.
9. A pharmaceutical composition comprising the CAR amino acid construct of any one of claims 1-6, the nucleic acid of claim 7, the host cell of claim 8 or a population of cells thereof, and a pharmaceutically acceptable carrier.

10. Use of the host cell of claim 8 or a population of cells thereof in the manufacture of a medicament for the treatment of cancer in a mammal, wherein the host cell is a T cell or an NK cell.
11. The use of claim 10, wherein the host cell is a T cell.
12. The use of claim 10 or 11, wherein the cancer is a hematological malignancy.