

cell lymphoma and showed high reactivity. (WO2016-094304)

[0009] CD19 is expressed in both normal and cancer cells, so the CD19 antibody cannot accurately distinguish between normal cells and cancer cells, but the MVR antibody may accurately distinguish between normal and cancer cells, thereby ensuring high therapeutic effect and safety. (Han et al., 2018).

[0010] There has been a problem that CAR-T cells are not produced from particular HLA-DR type T cells having high affinity. In order to improve this, in this patent, antibodies having various binding affinities have been prepared, and finally, an antibody suitable as a CAR-T cell therapeutic was selected.

[0011] The present invention is a patent designed to have a variety of binding affinities to the antigen through the sequence variation of the murine MVR antibody; it is expected that the antibody itself may be used as a therapeutic agent, or that it may be used in therapeutic agents using the antibody (CAR-T cell therapeutics) and the like. In addition, the antibody of the present invention, by producing a humanized antibody with a murine MVR antibody to minimize immunogenicity. In addition, by discovering antibodies having various binding affinities, CAR-T production may be expected to be superior to the parent antibody when CAR-T is applied, and may be applied to CAR-T cell therapeutics for blood cancer treatment.

Summary

[0011a] In one aspect, the present disclosure refers to antigen-binding molecule comprising a heavy chain variable region represented by Sequence No. 7 and a light-chain variable region represented by Sequence No. 8~~comprising a heavy chain complementarity-determining region 1 (HCDR1) that comprises an amino acid sequence represented by Sequence No. 1, an HCDR2 that comprises an amino acid sequence represented by Sequence No. 2, an HCDR3 that comprises an amino acid sequence represented by Sequence No. 3; a light chain variable region comprising a light chain complementarity determining region 1 (LCDR1) that comprises an amino acid sequence represented by Sequence No. 4, an LCDR2 that comprises an amino acid sequence represented by Sequence No. 5, and an LCDR3 that comprises an amino acid sequence represented by Sequence No. 6;~~ wherein the antigen-binding molecule is a chimeric antigen receptor (CAR).

[0011b] In another aspect, the present disclosure refers to nucleic acid molecule encoding an antigen-binding molecule as disclosed herein.

[0011c] In another aspect, the present disclosure refers to expression vector comprising the nucleic acid molecule as disclosed herein.

[0011d] In another aspect, the present disclosure refers to cell comprising the nucleic acid molecule as disclosed herein.

[0011e] In another aspect, the present disclosure refers to use of a pharmaceutical composition comprising the cell as disclosed herein~~for treating cancer, comprising the cell as disclosed herein~~ as a pharmaceutically effective ingredient in the manufacture of a medicament for treating cancer.

[0011f] In another aspect, the present disclosure refers to use of a pharmaceutical composition comprising a T cell comprising a therapeutically effective quantity of the antigen-binding molecule as disclosed herein as a pharmaceutically effective ingredient in the manufacture of a medicament for treating cancer.

[0011g] In another aspect, the present disclosure refers to an *in vitro* method of manufacturing a T cell with a modified chimeric antigen receptor (CAR-T)~~for the treatment of cancer, comprising a step of infecting a T cell with nucleic acids that encode an antigen-binding molecule comprising a heavy chain variable region represented by Sequence No. 7 and a light-chain variable region represented by Sequence No. 8a heavy chain variable region comprising a heavy chain complementarity-determining region 1 (HCDR1) comprising an amino acid sequence represented by Sequence No. 1, an HCDR2 comprising an amino acid sequence represented by Sequence No. 2, and an HCDR3 comprising an amino acid sequence represented by Sequence No. 3; a light chain variable region comprising a light chain complementarity-determining region 1 (LCDR1) comprising an amino acid sequence represented by Sequence No. 4, an LCDR2 comprising an amino acid sequence represented by Sequence No. 5, and an LCDR3 comprising an amino acid sequence represented by Sequence No. 6; wherein the antigen-binding molecule is a chimeric antigen receptor (CAR).~~

~~[0011h] In another aspect, the present disclosure refers to therapeutic pharmaceutical composition for treating cancer, comprising as a pharmaceutically effective ingredient, T cells comprising the antigen-binding molecule as disclosed herein.~~

Detailed Description of the Invention

Problem to be solved

[0012] An object of the present invention is to provide an MVR that may be clinically applied, and to provide CAR-T cells having an excellent therapeutic effect. Specifically, the present invention provides a co-stimulatory domain that may be introduced into various CAR-T cells as an co-stimulatory domain that plays a major role in its function in second-generation CAR-T cells. Moreover, it is an object of the present invention to provide various antigen-binding domains that are able to bind to antigens expressed on the surface of particular cancer cells and are capable of forming CAR-T cells.

Means of solving the problem

[0013] 1. An antigen-binding molecule comprising a heavy chain variable region comprising a heavy-chain complementarity-determining region 1 (HCDR1) comprising an amino acid sequence represented by Sequence No. 1, an HCDR2 comprising an amino acid sequence represented by Sequence No. 2, and an HCDR3 comprising an amino acid sequence represented by Sequence No. 3; a light-chain variable region comprising a light-chain complementarity-

Claims

[Claim 1]

Antigen-binding molecule comprising a heavy chain variable region represented by Sequence No. 7 and a light-chain variable region represented by Sequence No. 8 ~~comprising a heavy chain complementarity-determining region 1 (HCDR1) that comprises an amino acid sequence represented by Sequence No. 1, an HCDR2 that comprises an amino acid sequence represented by Sequence No. 2, an HCDR3 that comprises an amino acid sequence represented by Sequence No. 3; a light-chain variable region comprising a light-chain complementarity-determining region 1 (LCDR1) that comprises an amino acid sequence represented by Sequence No. 4, an LCDR2 that comprises an amino acid sequence represented by Sequence No. 5, and an LCDR3 that comprises an amino acid sequence represented by Sequence No. 6; wherein the antigen-binding molecule is a chimeric antigen receptor (CAR).~~

~~[Claim 2]~~

~~Antigen-binding molecule according to Claim 1, comprising a heavy chain variable region represented by Sequence No. 7 and a light-chain variable region represented by Sequence No. 8.~~

[Claim 23]

Antigen-binding molecule according to Claim 1, comprising an amino acid sequence represented by Sequence No. 9.

[Claim 34]

Antigen-binding molecule according to Claim 1, further comprising the amino acid sequence represented by Sequence No. 13.

[Claim 45]

Antigen-binding molecule according to Claim 1, further comprising an amino acid sequence represented by Sequence No. 14.

[Claim 56]

Antigen-binding molecule according to Claim 1, further comprising a transmembrane domain and an intracellular signaling domain for activating T cells.

[Claim ~~67~~]

Antigen-binding molecule according to Claim ~~56~~, in which the said transmembrane domain is selected from the group made up of an alpha chain of a T cell receptor, a beta chain of a T cell receptor, a zeta chain of a T cell receptor, CD28, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137 and CD154, wherein the said intracellular signaling domain is a CD3zeta signaling domain and a co-stimulatory signaling domain.

[Claim ~~78~~]

Antigen-binding molecule according to Claim ~~67~~, wherein the co-stimulatory signaling domain is selected from the group made up of CD28, OX~~40~~40, CD27, ICAM-1, CD278, and CD137.

[Claim ~~89~~]

Nucleic acid molecule encoding an antigen-binding molecule according to ~~one of Claims 1 to Claim 78~~.

[Claim ~~94~~]

Expression vector comprising the nucleic acid molecule of Claim ~~89~~.

[Claim ~~104~~]

Cell comprising the nucleic acid molecule of Claim ~~89~~.

[Claim ~~114~~]

Cell according to Claim ~~104~~ that is a T cell.

[Claim ~~124~~]

Cell according to Claim ~~114~~, wherein the T cells are CD8+ T cells and/or CD4+ T cells.

[Claim ~~134~~]

Cell according to Claim ~~104~~ that is a chimeric antigen receptor-modified T cell (CAR-T).

[Claim ~~145~~]

Use of a pharmaceutical composition ~~comprising the cell of Claim 10 for treating cancer,~~
~~comprising the cell of Claim 11~~ as a pharmaceutically effective ingredient in the manufacture of

a medicament for treating cancer.

[Claim 1516]

~~Pharmaceutical composition~~The use according to Claim 1415, wherein the cancer is esophageal adenocarcinoma, colorectal cancer, melanoma, ocular melanoma, small cell lung cancer, neuroblastoma, teratoma, fetal cancer, squamous cell carcinoma, head and neck squamous cell carcinoma, thymoma, lymphocytic leukemia, B-cell lymphoma, diffuse large B-cell lymphoma, leukemia, acute myeloid leukemia, or the like.

[Claim 1617]

Use of a pharmaceutical composition comprising a T cell comprising a therapeutically effective quantity of the antigen-binding molecule of ~~any of Claims 1 to~~Claim 87 as a pharmaceutically effective ingredient in the manufacture of a medicament for treating cancer.

[Claim 1718]

The use according to Claim 1617, in which the pharmaceutical composition either comprises CD8+ T cells, or comprises CD4+ T cells and CD8+ T cells.

[Claim 1819]

The use according to Claim 1718, wherein the proportion of the cell counts of CD4+ T cells to CD8+ T cells is substantially 1:1.

[Claim 1920]

~~An in vitro Method-method~~ of manufacturing a T cell with a modified chimeric antigen receptor (CAR-T)~~for the treatment of cancer~~, comprising a step of infecting a T cell with nucleic acids that encode an antigen-binding molecule comprising a heavy chain variable region represented by Sequence No. 7 and a light-chain variable region represented by Sequence No. 8~~a heavy chain variable region comprising a heavy chain complementarity determining region 1 (HCDR1) comprising an amino acid sequence represented by Sequence No. 1, an HCDR2 comprising an amino acid sequence represented by Sequence No. 2, and an HCDR3 comprising an amino acid sequence represented by Sequence No. 3; a light chain variable region comprising a light chain complementarity determining region 1 (LCDR1) comprising an amino acid sequence represented by Sequence No. 4, an LCDR2 comprising an amino acid sequence represented by Sequence No.~~

~~5, and an LCDR3 comprising an amino acid sequence represented by Sequence No. 6; wherein the antigen-binding molecule is a chimeric antigen receptor (CAR).~~

~~[Claim 21]~~

~~Therapeutic pharmaceutical composition for treating cancer, comprising as a pharmaceutically effective ingredient, T cells comprising the antigen-binding molecule according to any of Claims 1 to 8.~~

~~[Claim 22] Therapeutic pharmaceutical composition according to Claim 21, in which the pharmaceutical composition either comprises CD8+ T cells or comprises CD4+ T cells and CD8+ T cells.~~

~~[Claim 23]~~

~~Therapeutic pharmaceutical composition according to Claim 18, in which the proportion of the cell counts of CD4+ T cells to CD8+ T cells is substantially 1:1.~~