(NPL 20).

**[Citation List]**

**[Patent Literature]**

[0008]

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[PTL 3] WO2012/003956
[PTL 4] WO2012/156018
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[PTL 6] WO2014/075697
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**[Summary ~~of Invention~~]**

[0009a] In one aspect, the present disclosure provides an antigen-binding molecule that comprises: a first antigen-binding site that has binding activity towards CLDN6, and a second antigen-binding site that has binding activity towards T-cell receptor complex, wherein the first antigen-binding site is formed by (a) a first heavy chain variable region comprising HVR-H1, HVR-H2, and HVR-H3 amino acid sequences shown in SEQ ID NOs: 113, 117, and 118, respectively; and (b) a first light chain variable region comprisingHVR-L1, HVR-L2, and HVR-L3 amino acid sequences shown in SEQ ID NOs: 119, 120, and 121, respectively.

[0009b] In another aspect, the present disclosure provides an antigen-binding molecule that comprises: a first antigen-binding site that has binding activity towards CLDN6, and a second antigen-binding site that has binding activity towards T-

cell receptor complex, wherein the first antigen-binding site comprises a first heavy chain variable region comprising an amino acid sequence selected from SEQ ID NOs: 85, 1, 33, 84, and 83, and a first light chain variable region comprising an amino acid sequence selected from SEQ ID NOs: 87, 2, 43, 86, and 88.

[0009c] In another aspect, the present disclosure provides an antigen-binding molecule that comprises: a first antigen-binding site that has binding activity towards CLDN6, and a second antigen-binding site that has binding activity towards T-cell receptor complex, wherein the first antigen-binding site is formed by a first heavy chain comprising an amino acid sequence selected from SEQ ID NOs: 104, 105, 106, and 107 and a first light chain comprising an amino acid sequence shown in SEQ ID NO: 112.

[0009d] In another aspect, the present disclosure provides an isolated nucleic acid encoding the antigen binding molecule as described herein. In yet another aspect, the present disclosure provides a host cell comprising the nucleic acid as described herein. In yet another aspect, the present disclosure provides a pharmaceutical composition comprising the antigen-binding molecule as described herein, and a pharmaceutically acceptable carrier.

[0009e] In a further aspect, the present disclosure provides a pharmaceutical composition as described herein for use as a medicament. In a further aspect, the present disclosure provides a use of the antigen-binding molecule as described herein or the pharmaceutical composition as described herein in the manufacture of a medicament for treating and/or preventing cancer.

**[Technical Problem]**

[0010] As mentioned above, bispecific sc(Fv)$_2$ is a modified low-molecular-weight antibody molecule without an Fc region and shows significantly shorter blood half-life compared with IgG-type antibodies, which would cause inconvenience for their use as

[CLAIMS]

[Claim 1]
An antigen-binding molecule that comprises:
a first antigen-binding site that has binding activity towards CLDN6, and
a second antigen-binding site that has binding activity towards T-cell receptor complex,
wherein the first antigen-binding site is formed by
(a) a first heavy chain variable region comprising HVR-H1, HVR-H2, and HVR-H3 amino acid sequences shown in SEQ ID NOs: 113, 117, and 118, respectively; and
(b) a first light chain variable region comprising HVR-L1, HVR-L2, and HVR-L3 amino acid sequences shown in SEQ ID NOs: 119, 120, and 121, respectively.
An isolated antibody that comprises:
a first heavy chain variable region comprising HVR-H1, HVR-H2 and HVR-H3 amino acid sequences of SEQ ID NOs: 113, 117, and 118, respectively;
a first light chain variable region comprising HVR-L1, HVR-L2 and HVR-L3 amino acid sequences of SEQ ID NOs: 119, 120, and 121, respectively;
a second heavy chain variable region comprising HVR-H1, HVR-H2 and HVR-H3 amino acid sequences of SEQ ID NOs: 122, 123, and 124, respectively; and
a second light chain variable region comprising HVR-L1, HVR-L2 and HVR-L3 amino acid sequences of SEQ ID NOs: 114, 115, and 116, respectively.

[Claim 2]
An antigen-binding molecule that comprises:
a first antigen-binding site that has binding activity towards CLDN6, and
a second antigen-binding site that has binding activity towards T-cell receptor complex,
wherein the first antigen-binding site comprises a first heavy chain variable region comprising an amino acid sequence selected from SEQ ID NOs: 85, 1, 33, and 84, and 83, and a first light chain variable region comprising an amino acid sequence selected from SEQ ID NOs: 87, 2, 43, 86, and 88.
An isolated antibody that comprises:
a first heavy chain variable region comprising an amino acid sequence selected from SEQ ID NOs: 85, 1, 33 and 84; and a first light chain variable region comprising an amino acid sequence selected from SEQ ID NOs: 87, 2, 43, 86 and 88;
a second heavy chain variable region comprising an amino acid sequence selected from SEQ ID NOs: 60 and 70; and a second light chain variable region comprising an amino acid sequence selected from SEQ ID NOs: 61 and 71.

[Claim 3]
The antigen-binding molecule of claim 1 or 2, wherein the second antigen-binding site has binding activity towards CD3.

[Claim 4]
The antigen-binding molecule of any one of claim 1 to 3, wherein the first antigen binding site is included in a single-chain Fv (scFv), Fv or Fab.

[Claim 53]
The antigen-binding moleculeantibody of any one of claim 1 toor 32, wherein the first heavy chain variable region is linked to a first CH1 domain shown in SEQ ID NO: 95, the first light chain variable region is linked to a first CL domain shown in SEQ ID NO:

63~~, the second heavy chain variable region is linked to a second CH1 domain shown in SEQ ID NO: 97, and the second light chain variable region is linked to a second CL domain shown in SEQ ID NO: 62~~.

[Claim 6]

The antigen-binding molecule of any one of claim 1 to 5, wherein the antigen binding molecule further comprises an antibody Fc region.

[Claim 7~~4~~]

The antigen-binding molecule of claim 6~~antibody of any one of claims 1 to 3~~, wherein the ~~antibody~~ antigen-binding molecule further comprises any one of the Fc region combinations selected from:

(1) a first Fc region shown in SEQ ID NO: 72 and a second Fc region shown in SEQ ID NO: 73;

(2) a first Fc region shown in SEQ ID NO: 74 and a second Fc region shown in SEQ ID NO: 75;

(3) a first Fc region shown in SEQ ID NO: 76 and a second Fc regionshown in SEQ ID NO: 77; and

(4) a first Fc region shown in SEQ ID NO: 78 and a second Fc region shown in SEQ ID NO: 79.

[Claim 8~~5~~]

The antigen-binding molecule~~antibody~~ of claim 7~~4~~, wherein the first Fc region is in the same polypeptide chain with the first heavy chain variable region, and the second Fc region is in the same polypeptide chain with the second heavy chain variable region.

[Claim 9~~6~~]

An antigen-binding molecule that comprises:

a first antigen-binding site that has binding activity towards CLDN6, and

a second antigen-binding site that has binding activity towards T-cell receptor complex,

wherein the first antigen-binding site is formed by

~~An isolated antibody that comprises:~~

a first heavy chain comprising an amino acid sequence selected from SEQ ID NOs: 104, 105, 106, and 107 and a first light chain comprising an amino acid sequence shown in SEQ ID NO: 112.~~;~~

~~a second heavy chain comprising an amino acid sequence selected from SEQ ID NOs: 108, 109, 110, and 111 and a second light chain comprising an amino acid sequence shown in SEQ ID NO: 98.~~

[Claim 10~~7~~]

An isolated nucleic acid encoding the ~~antibody~~ antigen binding molecule of any one of claims 1 to 9~~6~~.

[Claim 11~~8~~]

A host cell comprising the nucleic acid of claim 10~~7~~.

[Claim 12~~9~~]

A method of producing an antibody comprising culturing the host cell of claim 11~~8~~ so that the ~~antibody~~ antigen-binding molecule is produced.

[Claim 13~~10~~]

A pharmaceutical composition comprising the ~~antibody~~ antigen-binding molecule of any one of claims 1 to 9~~6~~, and a pharmaceutically acceptable carrier.

[Claim 14~~11~~]

The pharmaceutical composition of claim 13~~10~~, which induces Tcell-dependent cytotoxicity.

[Claim 15~~12~~]

~~The~~ A pharmaceutical composition of claim 13~~10~~ or 14~~11, which is a pharmaceutical composition used for treatment and/or prevention of cancer~~ for use as a medicament.

~~[Claim 13]~~

~~The composition of any one of claims 10 to 12, which is a pharmaceutical composition used for treatment and/or prevention of ovarian cancer, non-small cell lung cancer, gastric cancer, or liver cancer.~~

[Claim 16~~14~~]

Use of the antigen-binding molecule~~antibody~~ of any one of claims 1 to ~~6~~9 or the pharmaceutical composition of any one of claims 13 to 14 in the manufacture of a medicament for treating and/or preventing cancer.

[Claim 17]

The use of claim 16, wherein the cancer is ovarian cancer, non-small cell lung cancer, gastric cancer, or liver cancer.

~~[Claim 15]~~

~~A method of treating an individual having cancer comprising administering to the individual an effective amount of the antibody of any one of claims 1 to 6.~~