

What is claimed is:

1. An antibody or antigen-binding fragment thereof that specifically binds to Nectin-4, comprising:

(1a)

the following three heavy chain CDRs ~~defined according to the Chothia numbering system~~:

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 3 ~~or a variant thereof~~,

CDR-H2 comprising the sequence as set forth in SEQ ID NO: 4 ~~or a variant thereof~~,

CDR-H3 comprising the sequence as set forth in SEQ ID NO: 5 ~~or a variant thereof~~; and/or

the following three light chain CDRs ~~defined according to the Chothia numbering system~~:

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 6 ~~or a variant thereof~~,

CDR-L2 comprising the sequence as set forth in SEQ ID NO: 7 ~~or a variant thereof~~,

CDR-L3 comprising the sequence as set forth in SEQ ID NO: 8 ~~or a variant thereof~~;

or

(1b)

the following three heavy chain CDRs ~~defined according to the Abm numbering system~~:

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 9 ~~or a variant thereof~~,

CDR-H2 comprising the sequence as set forth in SEQ ID NO: 10 ~~or a variant thereof~~,

CDR-H3 comprising the sequence as set forth in SEQ ID NO: 5 ~~or a variant thereof~~; and/or

the following three light chain CDRs ~~defined according to the Abm numbering system~~:

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 6 ~~or a variant thereof~~,

CDR-L2 comprising the sequence as set forth in SEQ ID NO: 7 ~~or a variant thereof~~,

CDR-L3 comprising the sequence as set forth in SEQ ID NO: 8 ~~or a variant thereof~~;

or

(1c)

the following three heavy chain CDRs ~~defined according to the Kabat numbering system~~:

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 11~~-or a variant thereof~~,
CDR-H2 comprising the sequence as set forth in SEQ ID NO: 12 or 63~~-or a variant thereof~~,
CDR-H3 comprising the sequence as set forth in SEQ ID NO: 5~~-or a variant thereof~~; and/or
the following three light chain CDRs~~defined according to the Kabat numbering system~~:

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 6~~-or a variant thereof~~,
CDR-L2 comprising the sequence as set forth in SEQ ID NO: 7~~-or a variant thereof~~,
CDR-L3 comprising the sequence as set forth in SEQ ID NO: 8~~-or a variant thereof~~;

or

(1d)

the following three heavy chain CDRs~~defined according to the IMGT numbering system~~:

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 13~~-or a variant thereof~~,
CDR-H2 comprising the sequence as set forth in SEQ ID NO: 14~~-or a variant thereof~~,
CDR-H3 comprising the sequence as set forth in SEQ ID NO: 15~~-or a variant thereof~~;

and/or

the following three light chain CDRs~~defined according to the IMGT numbering system~~:

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 16~~-or a variant thereof~~,
CDR-L2 comprising the sequence as set forth in SEQ ID NO: 17~~-or a variant thereof~~,
CDR-L3 comprising the sequence as set forth in SEQ ID NO: 8~~-or a variant thereof~~;

or

(2a)

the following three heavy chain CDRs~~defined according to the Chothia numbering system~~:

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 21 or 18~~-or a variant thereof~~,
CDR-H2 comprising the sequence as set forth in SEQ ID NO: 22~~-or a variant thereof~~,
CDR-H3 comprising the sequence as set forth in SEQ ID NO: 23~~-or a variant thereof~~;

and/or

the following three light chain CDRs~~defined according to the Chothia numbering system~~:

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 24 ~~or a variant thereof~~,
CDR-L2 comprising the sequence as set forth in SEQ ID NO: 25 ~~or a variant thereof~~,
CDR-L3 comprising the sequence as set forth in SEQ ID NO: 26 ~~or a variant thereof~~;

or

(2b)

the following three heavy chain CDRs ~~defined according to the Abm numbering system~~:

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 27 or 36 ~~or a variant thereof~~,

CDR-H2 comprising the sequence as set forth in SEQ ID NO: 28 ~~or a variant thereof~~,

CDR-H3 comprising the sequence as set forth in SEQ ID NO: 23 ~~or a variant thereof~~;

and/or

the following three light chain CDRs ~~defined according to the Abm numbering system~~:

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 24 ~~or a variant thereof~~,

CDR-L2 comprising the sequence as set forth in SEQ ID NO: 25 ~~or a variant thereof~~,

CDR-L3 comprising the sequence as set forth in SEQ ID NO: 26 ~~or a variant thereof~~;

or

(2c)

the following three heavy chain CDRs ~~defined according to the Kabat numbering system~~:

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 29 or 44 ~~or a variant thereof~~,

CDR-H2 comprising the sequence as set forth in SEQ ID NO: 30 ~~or a variant thereof~~,

CDR-H3 comprising the sequence as set forth in SEQ ID NO: 23 ~~or a variant thereof~~;

and/or

the following three light chain CDRs ~~defined according to the Kabat numbering system~~:

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 24 ~~or a variant thereof~~,

CDR-L2 comprising the sequence as set forth in SEQ ID NO: 25 ~~or a variant thereof~~,

CDR-L3 comprising the sequence as set forth in SEQ ID NO: 26 ~~or a variant thereof~~;

or

(2d)

the following three heavy chain CDRs ~~defined according to the IMGT numbering system:~~

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 31 or 54 ~~or a variant thereof,~~

CDR-H2 comprising the sequence as set forth in SEQ ID NO: 32 ~~or a variant thereof,~~

CDR-H3 comprising the sequence as set forth in SEQ ID NO: 33 ~~or a variant thereof;~~

and/or

the following three light chain CDRs ~~defined according to the IMGT numbering system:~~

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 34 ~~or a variant thereof,~~

CDR-L2 comprising the sequence as set forth in SEQ ID NO: 35 ~~or a variant thereof,~~

CDR-L3 comprising the sequence as set forth in SEQ ID NO: 26 ~~or a variant thereof;~~

or

(3a)

the following three heavy chain CDRs ~~defined according to the Chothia numbering system:~~

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 39 ~~or a variant thereof,~~

CDR-H2 comprising the sequence as set forth in SEQ ID NO: 40 ~~or a variant thereof,~~

CDR-H3 comprising the sequence as set forth in SEQ ID NO: 41 ~~or a variant thereof;~~

and/or

the following three light chain CDRs ~~defined according to the Chothia numbering system:~~

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 42 ~~or a variant thereof,~~

CDR-L2 comprising the sequence as set forth in SEQ ID NO: 43 ~~or a variant thereof,~~

CDR-L3 comprising the sequence as set forth in SEQ ID NO: 8 ~~or a variant thereof;~~

or

(3b)

the following three heavy chain CDRs ~~defined according to the Abm numbering system:~~

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 45 ~~or a variant thereof,~~

CDR-H2 comprising the sequence as set forth in SEQ ID NO: 46 ~~or a variant thereof,~~

CDR-H3 comprising the sequence as set forth in SEQ ID NO: 41~~-or a variant thereof~~;
and/or

the following three light chain CDRs~~defined according to the Abm numbering system~~:

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 42~~-or a variant thereof~~,

CDR-L2 comprising the sequence as set forth in SEQ ID NO: 43~~-or a variant thereof~~,

CDR-L3 comprising the sequence as set forth in SEQ ID NO: 8~~-or a variant thereof~~;

or

(3c)

the following three heavy chain CDRs~~defined according to the Kabat numbering system~~:

CDR-H1 comprising the sequence as set forth in NO: 47~~-or a variant thereof~~,

CDR-H2 comprising the sequence as set forth in SEQ ID NO: 48 or 64~~-or a variant thereof~~,

CDR-H3 comprising the sequence as set forth in SEQ ID NO: 41~~-or a variant thereof~~;

and/or

the following three light chain CDRs~~defined according to the Kabat numbering system~~:

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 42~~-or a variant thereof~~,

CDR-L2 comprising the sequence as set forth in SEQ ID NO: 43~~-or a variant thereof~~,

CDR-L3 comprising the sequence as set forth in SEQ ID NO: 8~~-or a variant thereof~~;

or

(3d)

the following three heavy chain CDRs~~defined according to the IMGT numbering system~~:

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 49~~-or a variant thereof~~,

CDR-H2 comprising the sequence as set forth in SEQ ID NO: 50~~-or a variant thereof~~,

CDR-H3 comprising the sequence as set forth in SEQ ID NO: 51~~-or a variant thereof~~;

and/or

the following three light chain CDRs~~defined according to the IMGT numbering system~~:

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 52~~-or a variant thereof~~,

CDR-L2 comprising the sequence as set forth in SEQ ID NO: 53~~-or a variant thereof~~,

CDR-L3 comprising the sequence as set forth in SEQ ID NO: 8 ~~or a variant thereof;~~
~~wherein, the variant has a substitution, deletion or addition of one or more amino acids~~
~~(e.g., a substitution, deletion or addition of 1, 2 or 3 amino acids) as compared to the sequence~~
~~from which it is derived; preferably, the substitution is a conservative substitution;~~

preferably, the antibody or antigen-binding fragment further comprises a framework region derived from a human or murine immunoglobulin;

preferably, the antibody or antigen-binding fragment binds to human Nectin-4.

2. The antibody or antigen-binding fragment thereof according to claim 1, comprising:

(a) the following six CDRs for heavy and light chains ~~defined according to the Chothia numbering system:~~

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 3 ~~or a variant thereof,~~

CDR-H2 comprising the sequence as set forth in SEQ ID NO: 4 ~~or a variant thereof,~~

CDR-H3 comprising the sequence as set forth in SEQ ID NO: 5 ~~or a variant thereof,~~

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 6 ~~or a variant thereof,~~

CDR-L2 comprising the sequence as set forth in SEQ ID NO: 7 ~~or a variant thereof,~~

CDR-L3 comprising the sequence as set forth in SEQ ID NO: 8 ~~or a variant thereof;~~ or

(b) the following six CDRs for heavy and light chains ~~defined according to the Abm numbering system:~~

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 9 ~~or a variant thereof,~~

CDR-H2 comprising the sequence as set forth in SEQ ID NO: 10 ~~or a variant thereof,~~

CDR-H3 comprising the sequence as set forth in SEQ ID NO: 5 ~~or a variant thereof,~~

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 6 ~~or a variant thereof,~~

CDR-L2 comprising the sequence as set forth in SEQ ID NO: 7 ~~or a variant thereof,~~

CDR-L3 comprising the sequence as set forth in SEQ ID NO: 8 ~~or a variant thereof;~~ or

(c) the following six CDRs for heavy and light chains ~~defined according to the Kabat numbering system:~~

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 11 ~~or a variant thereof~~,
CDR-H2 comprising the sequence as set forth in SEQ ID NO: 12 or 63 ~~or a variant thereof~~,
CDR-H3 comprising the sequence as set forth in SEQ ID NO: 5 ~~or a variant thereof~~,
CDR-L1 comprising the sequence as set forth in SEQ ID NO: 6 ~~or a variant thereof~~,
CDR-L2 comprising the sequence as set forth in SEQ ID NO: 7 ~~or a variant thereof~~,
CDR-L3 comprising the sequence as set forth in SEQ ID NO: 8 ~~or a variant thereof~~; or
(d) the following six CDRs for heavy and light chains ~~defined according to the IMGT numbering system~~:

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 13 ~~or a variant thereof~~,
CDR-H2 comprising the sequence as set forth in SEQ ID NO: 14 ~~or a variant thereof~~,
CDR-H3 comprising the sequence as set forth in SEQ ID NO: 15 ~~or a variant thereof~~,
CDR-L1 comprising the sequence as set forth in SEQ ID NO: 16 ~~or a variant thereof~~,
CDR-L2 comprising the sequence as set forth in SEQ ID NO: 17 ~~or a variant thereof~~,
CDR-L3 comprising the sequence as set forth in SEQ ID NO: 8 ~~or a variant thereof~~;
~~wherein the variant has a substitution, deletion or addition of one or more amino acids (e.g., a substitution, deletion or addition of 1, 2 or 3 amino acids) as compared to the sequence from which it is derived; preferably, the substitution is a conservative substitution.~~

3. The antibody or antigen-binding fragment thereof according to claim 1, comprising:

(a) the following six CDRs for heavy and light chains ~~defined according to the Chothia numbering system~~:

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 21 or 18 ~~or a variant thereof~~,
CDR-H2 comprising the sequence as set forth in SEQ ID NO: 22 ~~or a variant thereof~~,
CDR-H3 comprising the sequence as set forth in SEQ ID NO: 23 ~~or a variant thereof~~,
CDR-L1 comprising the sequence as set forth in SEQ ID NO: 24 ~~or a variant thereof~~,
CDR-L2 comprising the sequence as set forth in SEQ ID NO: 25 ~~or a variant thereof~~,
CDR-L3 comprising the sequence as set forth in SEQ ID NO: 26 ~~or a variant thereof~~; or

(b) the following six CDRs for heavy and light chains ~~defined according to the Abm numbering system:~~

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 27 or 36 ~~or a variant thereof,~~

CDR-H2 comprising the sequence as set forth in SEQ ID NO: 28 ~~or a variant thereof,~~

CDR-H3 comprising the sequence as set forth in SEQ ID NO: 23 ~~or a variant thereof,~~

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 24 ~~or a variant thereof,~~

CDR-L2 comprising the sequence as set forth in SEQ ID NO: 25 ~~or a variant thereof,~~

CDR-L3 comprising the sequence as set forth in SEQ ID NO: 26 ~~or a variant thereof;~~ or

(c) the following six CDRs for heavy and light chains ~~defined according to the Kabat numbering system:~~

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 29 or 44 ~~or a variant thereof,~~

CDR-H2 comprising the sequence as set forth in SEQ ID NO: 30 ~~or a variant thereof,~~

CDR-H3 comprising the sequence as set forth in SEQ ID NO: 23 ~~or a variant thereof,~~

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 24 ~~or a variant thereof,~~

CDR-L2 comprising the sequence as set forth in SEQ ID NO: 25 ~~or a variant thereof,~~

CDR-L3 comprising the sequence as set forth in SEQ ID NO: 26 ~~or a variant thereof;~~ or

(d) the following six CDRs for heavy and light chains ~~defined according to the IMGT numbering system:~~

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 31 or 54 ~~or a variant thereof,~~

CDR-H2 comprising the sequence as set forth in SEQ ID NO: 32 ~~or a variant thereof,~~

CDR-H3 comprising the sequence as set forth in SEQ ID NO: 33 ~~or a variant thereof,~~

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 34 ~~or a variant thereof,~~

CDR-L2 comprising the sequence as set forth in SEQ ID NO: 35 ~~or a variant thereof,~~

CDR-L3 comprising the sequence as set forth in SEQ ID NO: 26 ~~or a variant thereof;~~

~~wherein the variant has a substitution, deletion or addition of one or more amino acids (e.g., a substitution, deletion or addition of 1, 2 or 3 amino acids) as compared to the sequence from which it is derived; preferably, the substitution is a conservative substitution.~~

4. The antibody or antigen-binding fragment thereof according to claim 1, comprising:

(a) the following six CDRs for heavy and light chains ~~defined according to the Chothia numbering system:~~

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 39 ~~or a variant thereof,~~

CDR-H2 comprising the sequence as set forth in SEQ ID NO: 40 ~~or a variant thereof,~~

CDR-H3 comprising the sequence as set forth in SEQ ID NO: 41 ~~or a variant thereof,~~

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 42 ~~or a variant thereof,~~

CDR-L2 comprising the sequence as set forth in SEQ ID NO: 43 ~~or a variant thereof,~~

CDR-L3 comprising the sequence as set forth in SEQ ID NO: 8 ~~or a variant thereof;~~ or

(b) the following six CDRs for heavy and light chains ~~defined according to the Abm numbering system:~~

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 45 ~~or a variant thereof,~~

CDR-H2 comprising the sequence as set forth in SEQ ID NO: 46 ~~or a variant thereof,~~

CDR-H3 comprising the sequence as set forth in SEQ ID NO: 41 ~~or a variant thereof,~~

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 42 ~~or a variant thereof,~~

CDR-L2 comprising the sequence as set forth in SEQ ID NO: 43 ~~or a variant thereof,~~

CDR-L3 comprising the sequence as set forth in SEQ ID NO: 8 ~~or a variant thereof;~~ or

(c) the following six CDRs for heavy and light chains ~~defined according to the Kabat numbering system:~~

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 47 ~~or a variant thereof,~~

CDR-H2 comprising the sequence as set forth in SEQ ID NO: 48 or 64 ~~or a variant thereof,~~

CDR-H3 comprising the sequence as set forth in SEQ ID NO: 41 ~~or a variant thereof,~~

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 42 ~~or a variant thereof,~~

CDR-L2 comprising the sequence as set forth in SEQ ID NO: 43 ~~or a variant thereof,~~

CDR-L3 comprising the sequence as set forth in SEQ ID NO: 8 ~~or a variant thereof;~~ or

(d) the following six CDRs for heavy and light chains ~~defined according to the IMGT numbering system:~~

CDR-H1 comprising the sequence as set forth in SEQ ID NO: 49 ~~or a variant thereof,~~

CDR-H2 comprising the sequence as set forth in SEQ ID NO: 50 ~~or a variant thereof,~~

CDR-H3 comprising the sequence as set forth in SEQ ID NO: 51 ~~or a variant thereof,~~

CDR-L1 comprising the sequence as set forth in SEQ ID NO: 52 ~~or a variant thereof,~~

CDR-L2 comprising the sequence as set forth in SEQ ID NO: 53 ~~or a variant thereof,~~

CDR-L3 comprising the sequence as set forth in SEQ ID NO: 8 ~~or a variant thereof;~~

~~wherein the variant has a substitution, deletion or addition of one or more amino acids (e.g., a substitution, deletion or addition of 1, 2 or 3 amino acids) as compared to the sequence from which it is derived; preferably, the substitution is a conservative substitution.~~

5. The antibody or antigen-binding fragment thereof according to any one of claims 1 to 4, comprising:

a VH having the sequence as set forth in SEQ ID NO: 1 or SEQ ID NO: 55 or a variant thereof and/or a VL having the sequence as set forth in SEQ ID NO: 2 or SEQ ID NO: 56 or a variant thereof; or

a VH having the sequence as set forth in SEQ ID NO: 19 or SEQ ID NO: 57 or a variant thereof and/or a VL having the sequence as set forth in SEQ ID NO: 20 or SEQ ID NO: 58 or a variant thereof; or

a VH having the sequence as set forth in SEQ ID NO: 37 or SEQ ID NO: 59 or a variant thereof and/or a VL having the sequence as set forth in SEQ ID NO: 38 or SEQ ID NO: 60 or a variant thereof;

wherein the variant has a sequence identity of at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% as compared to the sequence from which it is derived, or has a substitution, deletion or addition of one or more amino acids ~~(e.g., a substitution, deletion or addition of 1, 2, 3, 4 or 5 amino acids)~~ as compared to the sequence from which it is derived; preferably, the substitution is a conservative substitution.

6. The antibody or antigen-binding fragment thereof according to any one of claims 1 to 5, comprising:

(1) a VH having the sequence as set forth in SEQ ID NO: 1 or a variant thereof and/or a VL having the sequence as set forth in SEQ ID NO: 2 or a variant thereof; or

(2) a VH having the sequence as set forth in SEQ ID NO: 19 or a variant thereof and/or a VL having the sequence as set forth in SEQ ID NO: 20 or a variant thereof; or

(3) a VH having the sequence as set forth in SEQ ID NO: 37 or a variant thereof and/or a VL having the sequence as set forth in SEQ ID NO: 38 or a variant thereof; or

(4) a VH having the sequence as set forth in SEQ ID NO: 55 or a variant thereof and/or a VL having the sequence as set forth in SEQ ID NO: 56 or a variant thereof; or

(5) a VH having the sequence as set forth in SEQ ID NO: 57 or a variant thereof and/or a VL having the sequence as set forth in SEQ ID NO: 58 or a variant thereof; or

(6) a VH having the sequence as set forth in SEQ ID NO: 59 or a variant thereof and/or a VL having the sequence as set forth in SEQ ID NO: 60 or a variant thereof;

wherein the variant has a sequence identity of at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% as compared to the sequence from which it is derived, or has a substitution, deletion or addition of one or more amino acids (~~e.g., a substitution, deletion or addition of 1, 2, 3, 4 or 5 amino acids~~) as compared to the sequence from which it is derived; preferably, the substitution is a conservative substitution.

7. The antibody or antigen-binding fragment thereof according to any one of claims 1 to 6, which is a murine antibody, a chimeric antibody, or a humanized antibody.

8. The antibody or antigen-binding fragment thereof according to any one of claims 1 to 7, further comprising:

a human immunoglobulin heavy chain constant region or a variant thereof, and a light chain constant region or a variant thereof, wherein the variant has a substitution, deletion or addition of one or more amino acids (~~e.g., a substitution, deletion or addition of up to 20, up to~~

~~15, up to 10, or up to 5 amino acids; for example, a substitution, deletion or addition of 1, 2, 3, 4 or 5 amino acids)~~ compared to the wild-type sequence from which it is derived;

preferably, the heavy chain constant region is an IgG heavy chain constant region, such as an IgG1, IgG2, IgG3 or IgG4 heavy chain constant region; the light chain constant region is selected from κ or λ light chain constant region;

more preferably, the heavy chain constant region is an IgG1 heavy chain constant region;

most preferably, the heavy chain constant region has the sequence as set forth in SEQ ID NO: 61; the light chain constant region is a κ light chain constant region; and/or the light chain constant region has the sequence as set forth in SEQ ID NO: 62.

9. The antibody or antigen-binding fragment thereof according to any one of claims 1 to 8, comprising a heavy chain and a light chain, wherein:

(a) the heavy chain comprises: a VH having the sequence as set forth in SEQ ID NO: 1, and a heavy chain constant region having the sequence as set forth in SEQ ID NO: 61, and the light chain comprises: a VL having the sequence as set forth in SEQ ID NO: 2, and a light chain constant region having the sequence as set forth in SEQ ID NO: 62; or

(b) the heavy chain comprises: a VH having the sequence as set forth in SEQ ID NO: 19, and a heavy chain constant region having the sequence as set forth in SEQ ID NO: 61, and the light chain comprises: a VL having the sequence as set forth in SEQ ID NO: 20, and a light chain constant region having the sequence as set forth in SEQ ID NO: 62; or

(c) the heavy chain comprises: a VH having the sequence as set forth in SEQ ID NO: 37, and a heavy chain constant region having the sequence as set forth in SEQ ID NO: 61, and the light chain comprises: a VL having the sequence as set forth in SEQ ID NO: 38, and a light chain constant region having the sequence as set forth in SEQ ID NO: 62; or

(d) the heavy chain comprises: a VH having the sequence as set forth in SEQ ID NO: 55, and a heavy chain constant region having the sequence as set forth in SEQ ID NO: 61, and the light chain comprises: a VL having the sequence as set forth in SEQ ID NO: 56, and a light chain constant region having the sequence as set forth in SEQ ID NO: 62; or

(e) the heavy chain comprises: a VH having the sequence as set forth in SEQ ID NO: 57, and a heavy chain constant region having the sequence as set forth in SEQ ID NO: 61, and the

light chain comprises: a VL having the sequence as set forth in SEQ ID NO: 58, and a light chain constant region having the sequence as set forth in SEQ ID NO: 62; or

(f) the heavy chain comprises: a VH having the sequence as set forth in SEQ ID NO: 59, and a heavy chain constant region having the sequence as set forth in SEQ ID NO: 61, and the light chain comprises: a VL having the sequence as set forth in SEQ ID NO: 60, and a light chain constant region having the sequence as set forth in SEQ ID NO: 62.

10. The antibody or antigen-binding fragment thereof according to any one of claims 1 to 9, which is selected from the group consisting of scFv, Fab, Fab', F(ab')₂, Fv fragment, disulfide-stabilized Fv (dsFv), diabody, bispecific antibody and multispecific antibody.

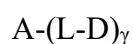
11. The antibody or antigen-binding fragment thereof according to any one of claims 1 to 10, which binds to the IgV domain of Nectin-4.

12. The antibody or antigen-binding fragment thereof according to any one of claims 1 to 11, which is conjugated to at least one label; preferably, the label is selected from the group consisting of enzyme, fluorescent dye, radioisotope, biotin and colloidal gold.

13. An antibody-drug conjugate, comprising the antibody or antigen-binding fragment thereof according to any one of claims 1 to 11 and at least one therapeutic agent.

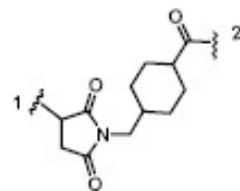
14. The antibody-drug conjugate according to claim 13, wherein the therapeutic agent is a cytotoxic agent.

15. The antibody-drug conjugate according to claim 13 or 14, which has the structure shown in Formula (I),



(I);

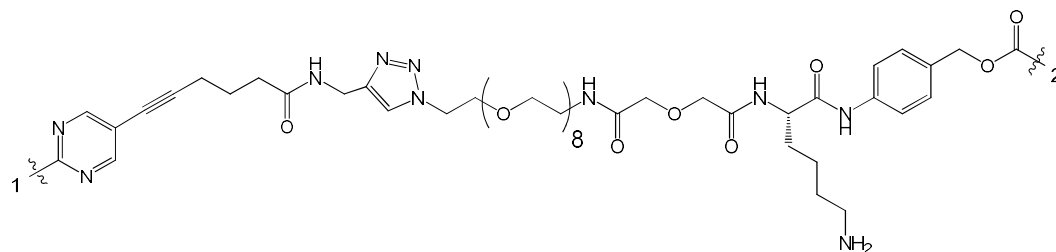
L comprises an amino acid or a peptide consisting of 2-10 amino acids; further preferably,



The image displays 12 chemical structures of building blocks, arranged in a 4x3 grid. Each structure is labeled with a number (1-12) and has wavy lines indicating attachment points. The structures are as follows:

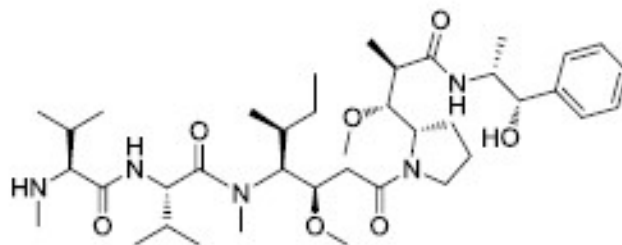
- 1: CCCC(=O)C1=CC=CC=C1 (4-iodobutan-1-one)
- 2: CCCC(=O)C1=CC=CC=C1 (4-iodobutan-1-one)
- 3: CCCC(=O)C1=CC=CC=C1 (4-iodobutan-1-one)
- 4: CCCC(=O)C1=CC=CC=C1 (4-iodobutan-1-one)
- 5: CCCC(=O)C1=CC=CC=C1 (4-iodobutan-1-one)
- 6: CCCC(=O)C1=CC=CC=C1 (4-iodobutan-1-one)
- 7: CCCC(=O)C1=CC=CC=C1 (4-iodobutan-1-one)
- 8: CCCC(=O)C1=CC=CC=C1 (4-iodobutan-1-one)
- 9: CCCC(=O)C1=CC=CC=C1 (4-iodobutan-1-one)
- 10: CCCC(=O)C1=CC=CC=C1 (4-iodobutan-1-one)
- 11: CCCC(=O)C1=CC=CC=C1 (4-iodobutan-1-one)
- 12: CCCC(=O)C1=CC=CC=C1 (4-iodobutan-1-one)

or

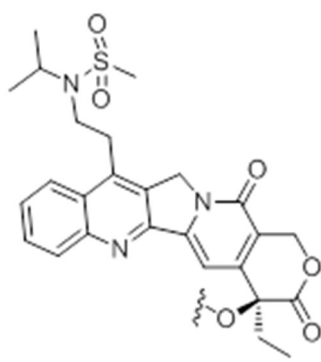
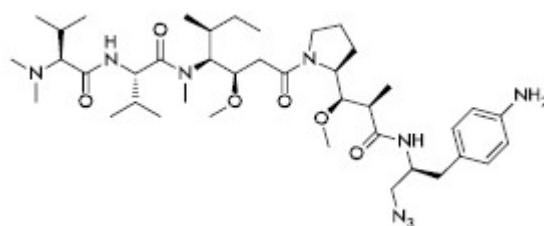
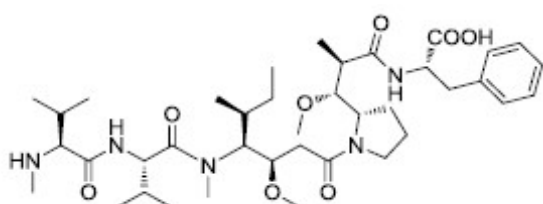


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D is selected from the group consisting of cytotoxic agents, therapeutic antibodies, radioisotopes, oligonucleotides and analogs thereof, biologically active peptides, protein toxins and enzymes; preferably, D is a molecule with anti-tumor biological activity;



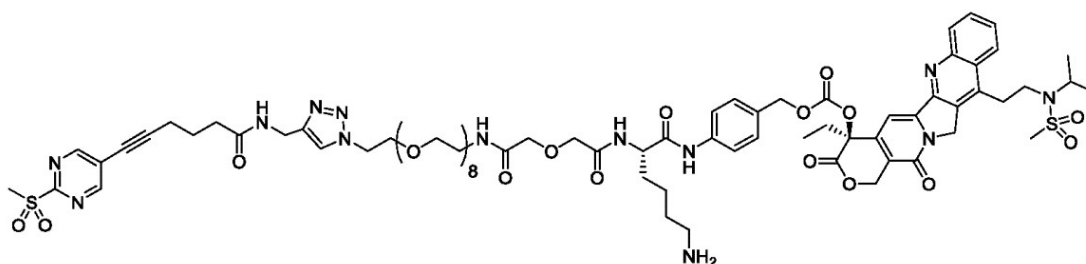
further preferably, D is



or

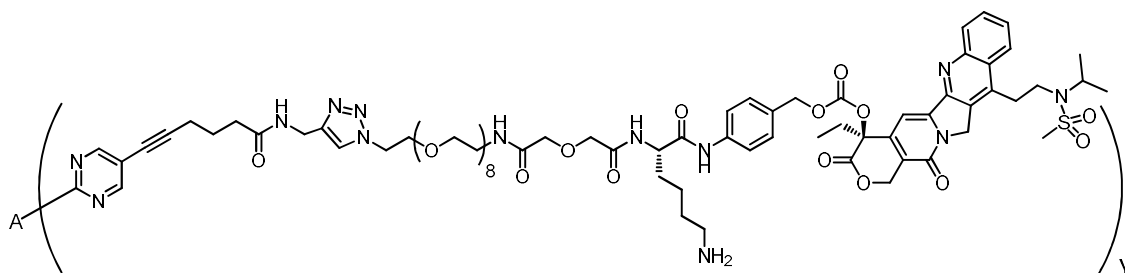
γ is an integer of 1 to 10.

16. The antibody-drug conjugate according to claim 15, wherein the (L-D) moiety has the structure of Formula (1), which is connected by forming a thioether bond with a sulfhydryl group of A,



Formula (1),

the antibody-drug conjugate has the structure of Formula (2):



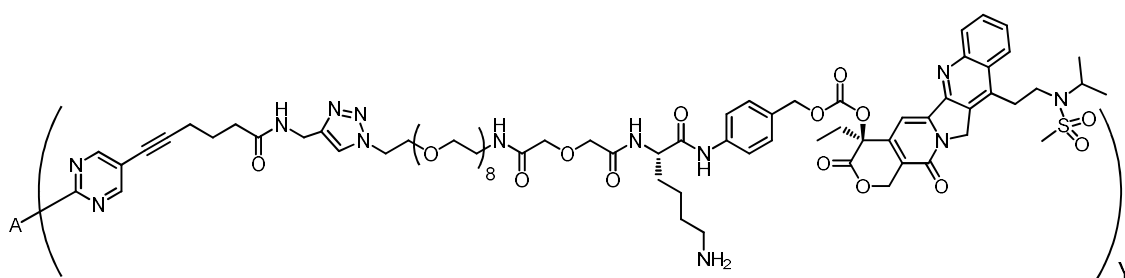
Formula (2),

wherein γ is an integer from 1 to 10, and A represents the antibody or antigen-binding fragment thereof according to any one of claims 1 to 11.

17. The antibody-drug conjugate according to claim 13, wherein the therapeutic agent is a radioisotope;

preferably, the radioisotope is selected from the group consisting of ^{212}Bi , ^{213}Bi , ^{131}I , ^{125}I , ^{111}In , ^{177}Lu , ^{186}Re , ^{188}Re , ^{153}Sm , ^{90}Y .

18. An antibody-drug conjugate, which is:

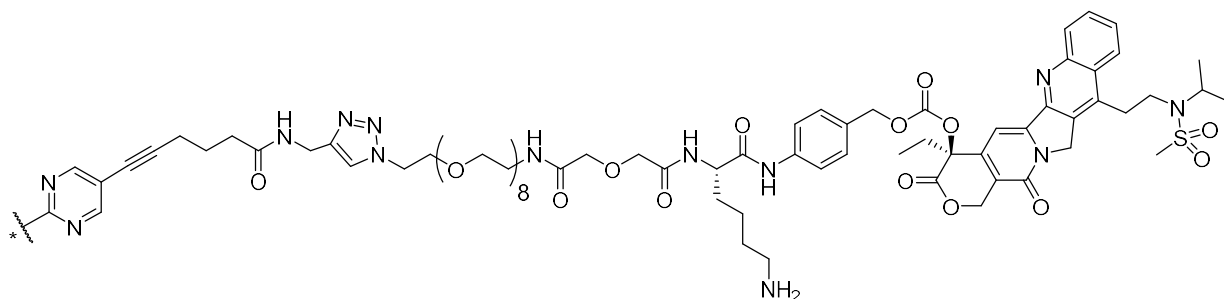


Formula (2),

wherein A is an anti-human Nectin-4 humanized monoclonal antibody comprising a VH sequence as set forth in SEQ ID NO: 57, and a VL sequence as set forth in SEQ ID NO: 58, wherein the anti-human Nectin-4 humanized monoclonal antibody is linked to the rest of the conjugate via one or more thiol group(s), and γ is an integer from 1 to 10.

19. The antibody-drug conjugate of claim 18, wherein γ is an integer from 6 to 8.

20. The antibody-drug conjugate of claim 18 or 19, wherein each light chain of the anti-human Nectin-4 humanized monoclonal antibody is conjugated to 0 to 1, and each heavy chain of the anti-human Nectin-4 humanized monoclonal antibody is conjugated to 0 to 4, of the following structure:



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wherein * is the point of attachment to a thiol group of the anti-human Nectin-4 humanized monoclonal antibody.

~~18~~21. A composition, comprising the antibody-~~drug~~ conjugate according to any one of claims 13 to ~~17~~20, wherein the molar ratio (DAR value) of therapeutic agent to the antibody or antigen-binding fragment thereof in the composition is a decimal or integer between 1 and 10 (e.g., ~~a decimal or integer between 1 and 8, such as 1.0, 1.5, 2.0, 2.5, 3.0, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.79, 3.8, 3.9, 4.0, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 6.95, 7.0, 7.03, 7.1, 7.12, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8, 7.9 or 8.0~~).

22. A pharmaceutical composition, comprising one or more of the antibody-drug conjugate of any one of claims 18 to 20, and one or more pharmaceutical excipients.

23. The pharmaceutical composition of claim 22, which has a drug-to-antibody ratio (“DAR”) of from about 7.0 to about 8.0.

24. The pharmaceutical composition of claim 23, which has a DAR of about 7.71.

25. A pharmaceutical composition for use in therapy, the pharmaceutical composition comprising the antibody-drug conjugate of any one of claims 18 to 20.

26. The pharmaceutical composition of any one of claims 22 to 24 for use in therapy.

27~~19~~. A chimeric antigen receptor (CAR), comprising the antibody or antigen-binding fragment thereof according to any one of claims 1 to 11, a transmembrane domain, and one or more intracellular T cell signaling domains.

28~~20~~. An immune effector cell, expressing the CAR according to claim ~~19~~27 on surface; preferably, the immune effector cell is selected from the group consisting of cytotoxic T cells, natural killer cells and natural killer T cells.

29~~21~~. A nucleic acid molecule, encoding the antibody or antigen-binding fragment thereof according to any one of claims 1 to 11.

22~~30~~. An expression vector, comprising the nucleic acid molecule according to claim ~~21~~29.

23~~31~~. A host cell, comprising the nucleic acid molecule according to claim ~~21~~29 or the expression vector according to claim ~~24~~30;

preferably, the host cell is an eukaryotic cell; more preferably a mammalian cell; most preferably a Chinese hamster ovary cell; or

preferably, the host cell is a prokaryotic cell; more preferably, the host cell is *Escherichia coli*.

24~~32~~. A multispecific antibody, comprising the antibody or antigen-binding fragment thereof according to any one of claims 1 to 11 and at least one other antibody or antigen-binding fragment thereof or an antibody analog, so that the multispecific antibody is capable of binding

to Nectin-4 and at least one other antigen; preferably, the multispecific antibody is a bispecific or trispecific or tetraspecific antibody.

2533. A fusion protein, comprising the antibody or antigen-binding fragment thereof according to any one of claims 1 to 11, and an additional biologically active polypeptide;

preferably, the additional biologically active polypeptide is a polypeptide or protein having therapeutic activity, binding activity or enzymatic activity.

2634. A pharmaceutical composition, comprising the antibody or antigen-binding fragment thereof according to any one of claims 1 to 11, the antibody-drug conjugate according to any one of claims 13 to 1720, the composition according to ~~claim 18~~any one of claims 21 to 24, the immune effector cell according to claim 2028, the multispecific antibody according to claim 2432, or the fusion protein according to claim 2533, and a pharmaceutically acceptable carrier and/or excipient.

2735. Use of the antibody or antigen-binding fragment thereof according to any one of claims 1 to 11, the antibody-drug conjugate according to any one of claims 13 to 1720, the composition according to ~~claim 18~~any one of claims 21 to 24, the immune effector cell according to claim 2028, the multispecific antibody according to claim 2432, the fusion protein according to claim 2533 or the pharmaceutical composition according to claim 2634 in the manufacture of a medicament, ~~wherein the medicament is used for the treatment of~~ for treating a cancer; preferably, the cancer is selected from the group consisting of gastric cancer, liver cancer, liver cell carcinoma, bladder cancer, urothelial cancer, urethral cancer, renal pelvis cancer, ureteral cancer, lung cancer, non-small cell lung cancer, breast cancer, breast ductal cancer, triple-negative breast cancer, pancreatic cancer, ovarian cancer, head and neck cancer, colon cancer, rectal cancer and esophageal cancer.

2836. The pharmaceutical composition of claim 25 or 26 or the use according to claim 2735, wherein the pharmaceutical composition or the medicament is used in combination with one or more therapeutic agents selected from the group consisting of antineoplastic agents, chemotherapeutic agents, radioisotopes, immune checkpoint inhibitors.

~~29~~37. The pharmaceutical composition of claim 25 or 26 or the use according to claim ~~27~~35, wherein the pharmaceutical composition or the medicament is used in combination with one or more therapeutic regimens selected from the group consisting of surgery, radiotherapy, chemotherapy, targeted therapy, immunotherapy, hormone therapy, angiogenesis inhibition, and palliative care.

~~30~~38. A method of detecting the presence or determining the expression level of Nectin-4 in a sample, comprising:

(a) contacting the sample with the antibody or antigen-binding fragment thereof according to any one of claims 1 to 11, and

(b) detecting the formation or determining the amount of an immune complex of the antibody or antigen-binding fragment and Nectin-4 in the sample, so as to detect the presence or determine the expression level of Nectin-4 in the sample.