

CLAIMS

1. A dimerized polypeptide comprising a Titin-T chain and an Obscurin-O chain, wherein,
i) the Titin-T chain is a variant of SEQ ID NO: 32, wherein the variant has amino acid residue substitutions at one or more positions selected from the group consisting of positions 60S and 64T as compared to SEQ ID NO: 32, and
ii) the Obscurin-O chain is a variant of SEQ ID NO: 33, wherein the variant has amino acid residue substitutions at one or more positions selected from the group consisting of positions 13S, 32F, 48V, 66C, 82H, and 93C as compared to SEQ ID NO: 33.

2. The dimerized polypeptide according to claim 1, wherein the variant of SEQ ID NO: 32 has amino acid residue substitutions of 60S and 64T, and the variant of SEQ ID NO: 33 has amino acid residue substitutions selected from any one of a) to c):

- a) 32F and 48V;
- b) 13S, 32F, 48V, and 82H; and
- c) 13S, 32F, 48V, 66C, 82H, and 93C.

3. The dimerized polypeptide according to claim 1 or 2, wherein the variant of SEQ ID NO: 32 further has amino acid residue substitutions at one or more positions selected from the group consisting of positions 3, 8, 11, 13, 20, 22, 25, 26, 39, 40, 42, 45, 47, 49, 56, 58, 66, 70, 75, 77, 79, 81, 82, 83, and 84 as compared to SEQ ID NO: 32;

preferably, the variant of SEQ ID NO: 32 further comprises one or more amino acid residue substitutions selected from the group consisting of 3W, 8C, 11I, 13L, 20C, 22M/22C, 25S, 26C, 39T, 40S, 42K, 45S, 47E, 49G, 56S, 58E, 66S/66K, 70R, 75V, 77S, 79T, 81R, 82M, 83D, and 84L, as compared to SEQ ID NO: 32;

more preferably, the variant of SEQ ID NO: 32 further comprises amino acid residue substitutions selected from any one of a) to l) as compared to SEQ ID NO: 32:

- a) 8C, 25S, and 39T;
- b) 20C, 25S, and 39T;
- c) 25S, 26C, and 39T;
- d) 22C, 25S, and 39T;
- e) 8C, 25S, 39T, 66S, and 77S;
- f) 8C, 25S, 39T, 66K, 70R, 79T, and 81R;
- g) 3W, 8C, 11I, 13L, 22M, 25S, 39T, and 82M;
- h) 8C, 11I, 25S, 39T, 66K, 79T, and 81R;
- i) 8C, 25S, 39T, 40S, 42K, 45S, 47E, 49G, 56S, 58E, 75V, 83D, and 84L;
- j) 8C, 25S, 39T, 47E, 49G, 56S, 58E, and 75V;
- k) 8C, 25S, 39T, 56S, 58E, and 75V; and
- l) 8C, 25S, 39T, 56S, 58E, 66S, and 77S;

most preferably, the variant of SEQ ID NO: 32 has amino acid residue substitutions selected from any one of A) to C) as compared to SEQ ID NO: 32:

- A) 8C, 11I, 25S, 39T, 60S, 64T, 66K, 79T, and 81R;

B) 8C, 11I, 20C, 25S, 39T, 60S, 64T, 66K, 79T, and 81R; and
C) 8C, 11I, 25S, 26C, 39T, 60S, 64T, 66K, 79T, and 81R.

4. The dimerized polypeptide according to any one of claims 1 to 3, wherein the variant of SEQ ID NO: 33 further has amino acid residue substitutions at one or more positions selected from the group consisting of positions 2, 3, 7, 9, 11, 12, 13, 14, 17, 20, 22, 25, 30, 32, 34, 36, 41, 42, 44, 45, 53, 58, 62, 67, 69, 76, 88, 89, 92, 94, and 97 as compared to SEQ ID NO: 33;

preferably,

the variant of SEQ ID NO: 33 further has one or more amino acid residue substitutions selected from the group consisting of 2E, 3C, 7K/7R, 9C, 11L, 12S, 13Y, 14T, 17E, 20L, 22M/22S, 25S, 30D, 32P, 34E, 36T, 41K, 42L, 44I, 45T, 53L, 58V, 62E/62K/62H, 67Q/67T, 69S, 76S, 88C, 89L, 92E, 94G, and 97G as compared to SEQ ID NO: 33; more preferably, the variant of SEQ ID NO: 33 further has amino acid residue substitutions selected from any one of A)-R) as compared to SEQ ID NO: 33:

A) 88C;

B) 3C;

C) 9C;

D) 25S, 76S, and 88C;

E) 25S, 76S, and 3C;

F) 25S, 76S, and 9C;

G) 7K, 25S, 62K, 76S, and 88C;

H) 7K, 25S, 62H, 76S, and 88C;

I) 7R, 25S, 62K, 76S, and 88C;

J) 7R, 25S, 62H, 76S, and 88C;

K) 11L, 25S, 62K, 76S, and 88C;

L) 11L, 25S, 62H, 76S, and 88C;

M) 12S, 13Y, 14T, 22S, 25S, 62K, 76S, and 88C;

N) 2E, 11L, 17E, 25S, 30D, 32P, 34E, 36T, 44I, 45T, 58V, 62E, 67Q, 69S, 76S, 88C, and 97G;

O) 11L, 20L, 22M, 25S, 53L, 62K, 76S, and 88C;

P) 11L, 25S, 41K, 45T, 62K, 67Q, 69S, 76S, 88C, and 89L;

Q) 11L, 25S, 42L, 45T, 62K, 67T, 69S, 76S, 88C, 92E, and 94G; and

R) 11L, 12S, 13Y, 22S, 25S, 42L, 45T, 62K, 67Q, 69S, 76S, 88C, 92E, and 94G;

most preferably, the variant of SEQ ID NO: 33 has amino acid residue substitutions selected from any one of a) to j) as compared to SEQ ID NO: 33:

a) 25S, 32F, 41K, 45T, 48V, 62K, 67Q, 69S, 76S, 88C, and 89L;

b) 13S, 25S, 32F, 41K, 45T, 48V, 62K, 67Q, 69S, 76S, 82H, 88C, and 89L;

c) 3C, 13S, 25S, 32F, 41K, 45T, 48V, 62K, 67Q, 69S, 76S, 82H, 88C, and 89L;

d) 9C, 13S, 25S, 32F, 41K, 45T, 48V, 62K, 67Q, 69S, 76S, 82H, 88C, and 89L;

e) 13S, 32F, 41K, 45T, 48V, 62K, 67Q, 69S, 82H, 88C, and 89L;

- f) 3C, 13S, 32F, 41K, 45T, 48V, 62K, 67Q, 69S, 82H, 88C, and 89L;
- g) 9C, 13S, 32F, 41K, 45T, 48V, 62K, 67Q, 69S, 82H, 88C, and 89L;
- h) 13S, 25S, 32F, 41K, 45T, 48V, 62K, 66C, 67Q, 69S, 76S, 82H, 88C, 89L, and 93C;
- i) 3C, 13S, 25S, 32F, 41K, 45T, 48V, 62K, 66C, 67Q, 69S, 76S, 82H, 88C, 89L, and 93C;
and
- j) 9C, 13S, 25S, 32F, 41K, 45T, 48V, 62K, 66C, 67Q, 69S, 76S, 82H, 88C, 89L, and 93C.

5. The dimerized polypeptide according to any one of claims 1 to 4, wherein, the Titin-T chain is a variant of SEQ ID NO: 32 or 68, wherein the variant has one or more amino acid residue substitutions selected from the group consisting of 60S and 64T; and the Obscurin-O chain is a variant of SEQ ID NO: 33 or 80, wherein the variant has one or more amino acid residue substitutions selected from the group consisting of 13S, 32F, 48V, 66C, 82H, and 93C;

preferably, the Titin-T chain has at least 85% sequence identity to any one of amino acid sequences of SEQ ID NO: 129 to SEQ ID NO: 131, and the Obscurin-O chain has at least 85% sequence identity to any one of amino acid sequences of SEQ ID NO: 132 to SEQ ID NO: 141;

more preferably, the Titin-T chain has an amino acid sequence set forth in any one of SEQ ID NO: 129 to SEQ ID NO: 131, and the Obscurin-O chain has an amino acid sequence set forth in any one of SEQ ID NO: 132 to SEQ ID NO: 141.

6. An antigen-binding molecule comprising the dimerized polypeptide according to any one of claims 1 to 5.

7. The antigen-binding molecule of claim 6, comprising a first antigen-binding moiety, wherein the first antigen-binding moiety comprises a domain-engineered Fab, wherein the domain-engineered Fab comprises a heavy chain variable region VH1, a light chain variable region VL1, and the dimerized polypeptide, but does not comprise a light chain constant region CL or a heavy chain constant region CH1, wherein the VH1 and the VL1 are each linked to any one of the peptide chains of the dimerized polypeptide via a linker; preferably, the C-terminus of the VH1 is fused to the N-terminus of the Titin-T chain of the dimerized polypeptide according to any one of claims 1 to 6 via a linker, and the C-terminus of the VL1 is fused to the N-terminus of the Obscurin-O chain of the dimerized polypeptide according to any one of claims 1 to 6 via a linker; or

the C-terminus of VL1 is fused to the N-terminus of the Titin-T chain of the dimerized polypeptide according to any one of claims 1 to 6 via a linker, and the C-terminus of VH1 is fused to the N-terminus of the Obscurin-O chain of the dimerized polypeptide according to any one of claims 1 to 6 via a linker.

8. The antigen-binding molecule according to claim 6 or 7, comprising a first antigen-binding moiety, wherein the first antigen-binding moiety comprises:

a. a peptide chain of [VH1]-[linker 1]-[Titin-T chain] in order from the N-terminus to the C-terminus, and a peptide chain of [VL1]-[linker 2]-[Obscurin-O chain] in order from the N-terminus to the C-terminus; or

b. a peptide chain of [VH1]-[linker 1]-[Obscurin-O chain] in order from the N-terminus to the C-terminus, and a peptide chain of [VL1]-[linker 2]-[Titin-T chain] in order from the N-terminus to the C-terminus;

wherein the linker 1 and the linker 2 are identical or different;

the Titin-T chain and the Obscurin-O chain are as defined in any one of claims 1 to 6;

preferably,

A) the linker 1 and the linker 2 are both $(G_xS)_y$ linkers, wherein x is selected from the group consisting of integers from 1 to 5, and y is selected from the group consisting of integers from 0 to 6, or

B) the linker 1 is a C-terminal truncated sequence of CH1, and the linker 2 is a C-terminal truncated sequence of CL;

more preferably,

A) the linker 1 is set forth in SEQ ID NO: 173; the linker 2 is set forth in SEQ ID NO: 174; or

B) the linker 1 and the linker 2 are both set forth in SEQ ID NO: 175; or

C) the linker 1 and the linker 2 are both set forth in SEQ ID NO: 176.

9. The antigen-binding molecule according to any one of claims 6 to 8, further comprising an Fc region, wherein the Fc region comprises a first subunit Fc1 and a second subunit Fc2 capable of associating with each other;

preferably, the Fc region has one or more amino acid substitutions that reduce homodimerization; and the Fc region has one or more amino acid substitutions capable of reducing binding of the Fc region to an Fc receptor;

more preferably, the Fc1 has a protuberance structure according to the knob-and-hole technique, and the Fc2 has a pore structure according to the knob-and-hole technique; or the Fc2 has a protuberance structure according to the knob-and-hole technique, and the Fc1 has a pore structure according to the knob-and-hole technique;

most preferably, the Fc1 has a sequence set forth in SEQ ID NO: 177, and the Fc2 has a sequence set forth in SEQ ID NO: 178; or the Fc1 has a sequence set forth in SEQ ID NO: 178, and the Fc2 has a sequence set forth in SEQ ID NO: 177.

10. The antigen-binding molecule according to any one of claims 6 to 9, comprising the first antigen-binding moiety and a second antigen-binding moiety, wherein the second antigen-binding moiety comprises a heavy chain variable region VH2 and a light chain variable region VL2, and the first antigen-binding moiety and the second antigen-binding moiety bind to different antigens or different epitopes on the same antigen;

preferably, the second antigen-binding moiety comprises a Fab.

11. The antigen-binding molecule according to claim 10, comprising a first heavy chain, a first light chain, a second heavy chain, and a second light chain; wherein

a. the first heavy chain comprises [VH1]-[linker 1]-[Titin-T chain]-[linker 3]-[Fc1] in order from the N-terminus to the C-terminus,
the first light chain comprises [VL1]-[linker 2]-[Obscurin-O chain] in order from the N-terminus to the C-terminus,
the second heavy chain comprises [VH2]-[CH1]-[Fc2] in order from the N-terminus to the C-terminus, and
the second light chain comprises [VL2]-[CL] in order from the N-terminus to the C-terminus; or

b. the first heavy chain comprises [VH1]-[linker 1]-[Obscurin-O chain]-[linker 3]-[Fc1] in order from the N-terminus to the C-terminus,
the first light chain comprises [VL1]-[linker 2]-[Titin-T chain] in order from the N-terminus to the C-terminus,
the second heavy chain comprises [VH2]-[CH1]-[Fc2] in order from the N-terminus to the C-terminus, and
the second light chain comprises [VL2]-[CL] in order from the N-terminus to the C-terminus;

wherein the linker 1, the linker 2, and the linker 3 are identical or different;
preferably, the Fc1 and the Fc2 each independently have one or more amino acid substitutions that reduce homodimerization;
more preferably,

A) the linker 1, the linker 2, and the linker 3 are all $(G_xS)_y$, wherein x is selected from the group consisting of integers from 1 to 5, and y is selected from the group consisting of integers from 0 to 6, or

B) the linker 1 is a C-terminal truncated sequence of CH1, the linker 2 is a C-terminal truncated sequence of CL, and the linker 3 is $(G_xS)_y$, wherein x is selected from the group consisting of integers from 1 to 5, and y is selected from the group consisting of integers from 0 to 6;

most preferably,

A) the linker 1 is set forth in SEQ ID NO: 173; the linker 2 is set forth in SEQ ID NO: 174; linker 3 is a bond; or

B) the linker 1 and the linker 2 are both set forth in SEQ ID NO: 175; the linker 3 is a bond; or

C) the linker 1 and the linker 2 are both set forth in SEQ ID NO: 176; the linker 3 is a bond.

12. The antigen-binding molecule according to claim 11, wherein:

(I) the antigen-binding molecule is capable of binding to NGF and RANKL;
wherein the antigen-binding molecule comprises a first heavy chain, a first light chain, a second heavy chain, and a second light chain, wherein:

the first heavy chain comprises [VH1]-[linker 1]-[Obscurin-O chain]-[linker 3]-[Fc1] in order from the N-terminus to the C-terminus,
the first light chain comprises [VL1]-[linker 2]-[Titin-T chain] in order from the N-terminus to the C-terminus,
the second heavy chain comprises [VH2]-[CH1]-[Fc2] in order from the N-terminus to the C-terminus, and
the second light chain comprises [VL2]-[CL] in order from the N-terminus to the C-terminus;
wherein: the VH1 forms a first antigen-binding moiety binding to NGF with the VL1, and the VH2 forms a second antigen-binding moiety binding to RANKL with the VL2; or
the VH1 forms a first antigen-binding moiety binding to RANKL with the VL1, and the VH2 forms a second antigen-binding moiety binding to NGF with the VL2;
more preferably,
the VH1 has a sequence set forth in SEQ ID NO: 26, the VL1 has a sequence set forth in SEQ ID NO: 27, the VH2 has a sequence set forth in SEQ ID NO: 24, and the VL2 has a sequence set forth in SEQ ID NO: 25; or
the VH1 has a sequence set forth in SEQ ID NO: 24, the VL1 has a sequence set forth in SEQ ID NO: 25, the VH2 has a sequence set forth in SEQ ID NO: 26, and the VL2 has a sequence set forth in SEQ ID NO: 27;
and the Obscurin-O chain has a sequence set forth in any one of SEQ ID NOs: 132-141, and the Titin-T chain has a sequence set forth in any one of SEQ ID NOs: 129-131;
(II) the antigen-binding molecule is capable of binding to PDL1 and CTLA4;
wherein the antigen-binding molecule comprises a first heavy chain, a first light chain, a second heavy chain, and a second light chain, wherein:
the first heavy chain comprises [VH1]-[linker 1]-[Obscurin-O chain]-[linker 3]-[Fc1] in order from the N-terminus to the C-terminus,
the first light chain comprises [VL1]-[linker 2]-[Titin-T chain] in order from the N-terminus to the C-terminus,
the second heavy chain comprises [VH2]-[CH1]-[Fc2] in order from the N-terminus to the C-terminus, and
the second light chain comprises [VL2]-[CL] in order from the N-terminus to the C-terminus; wherein:
the VH1 forms a first antigen-binding moiety binding to PDL1 with the VL1, and the VH2 forms a second antigen-binding moiety binding to CTLA4 with the VL2; or
the VH1 forms a first antigen-binding moiety binding to CTLA4 with the VL1, and the VH2 forms a second antigen-binding moiety binding to PDL1 with the VL2;
more preferably,
the VH1 has a sequence set forth in SEQ ID NO: 156, the VL1 has a sequence set forth in SEQ ID NO: 155, the VH2 has a sequence set forth in SEQ ID NO: 169, and the VL2 has a sequence set forth in SEQ ID NO: 170; or
the VH1 has a sequence set forth in SEQ ID NO: 169, the VL1 has a sequence set forth

in SEQ ID NO: 170, the VH2 has a sequence set forth in SEQ ID NO: 156, and the VL2 has a sequence set forth in SEQ ID NO: 155;

and the Obscurin-O chain has a sequence set forth in any one of SEQ ID NOs: 132-141, and the Titin-T chain has a sequence set forth in any one of SEQ ID NOs: 129-131;

or

(III) the antigen-binding molecule is capable of binding to IL5 and TSLP;

wherein the antigen-binding molecule comprises a first heavy chain, a first light chain, a second heavy chain, and a second light chain, wherein:

the first heavy chain comprises [VH1]-[linker 1]-[Titin-T chain]-[linker 3]-[Fc1] in order from the N-terminus to the C-terminus;

the first light chain comprises [VL1]-[linker 2]-[Obscurin-O chain] in order from the N-terminus to the C-terminus;

the second heavy chain comprises [VH2]-[CH1]-[Fc2] in order from the N-terminus to the C-terminus; and

the second light chain comprises [VL2]-[CL] in order from the N-terminus to the C-terminus; wherein:

the VH1 forms a first antigen-binding moiety binding to IL5 with the VL1, and the VH2 forms a second antigen-binding moiety binding to TSLP with the VL2; or

the VH1 forms a first antigen-binding moiety binding to TSLP with the VL1, and the VH2 forms a second antigen-binding moiety binding to IL5 with the VL2;

more preferably,

the VH1 has a sequence set forth in SEQ ID NO: 16, the VL1 has a sequence set forth in SEQ ID NO: 17, the VH2 has a sequence set forth in SEQ ID NO: 171, and the VL2 has a sequence set forth in SEQ ID NO: 172; or

the VH1 has a sequence set forth in SEQ ID NO: 171, the VL1 has a sequence set forth in SEQ ID NO: 172, the VH2 has a sequence set forth in SEQ ID NO: 16, and the VL2 has a sequence set forth in SEQ ID NO: 17;

and the Obscurin-O chain has a sequence set forth in any one of SEQ ID NOs: 132-141, and the Titin-T chain has a sequence set forth in any one of SEQ ID NOs: 129-131;

13. The antigen-binding molecule according to claim 12, wherein:

the Fc1 has a sequence set forth in SEQ ID NO: 177; the Fc2 has a sequence set forth in SEQ ID NO: 178; the CH1 has a sequence set forth in SEQ ID NO: 179; the CL has a sequence set forth in SEQ ID NO: 4; the linker 3 is a bond; the linker 1 and the linker 2 are selected from the group consisting of: a) linker 1 and linker 2 both set forth in SEQ ID NO: 175; and b) linker 1 set forth in SEQ ID NO: 173 and linker 2 set forth in SEQ ID NO: 174; or

the Fc1 has a sequence set forth in SEQ ID NO: 178; the Fc2 has a sequence set forth in SEQ ID NO: 177; the CH1 has a sequence set forth in SEQ ID NO: 179; the CL has a sequence set forth in SEQ ID NO: 4; the linker 3 is a bond; the linker 1 and the linker 2 are selected from the group consisting of: a) linker 1 and linker 2 both having sequences

set forth in SEQ ID NO: 175; and b) linker 1 having a sequence set forth in SEQ ID NO: 173 and linker 2 having a sequence set forth in SEQ ID NO: 174.

14. The antigen-binding molecule according to claim 10, comprising:

a. a first heavy chain comprising [VH1]-[linker 1]-[Titin-T chain]-[linker 3]-[VH2]-[CH1]-[Fc1] in order from the N-terminus to the C-terminus;

a second heavy chain comprising [VH1]-[linker 1]-[Titin-T chain]-[linker 3]-[VH2]-[CH1]-[Fc2] in order from the N-terminus to the C-terminus;

a first light chain comprising [VL1]-[linker 2]-[Obscurin-O chain] in order from the N-terminus to the C-terminus; and

a second light chain comprising [VL2]-[CL] in order from the N-terminus to the C-terminus; or

b. a first heavy chain comprising [VH1]-[linker 1]-[Obscurin-O chain]-[linker 3]-[VH2]-[CH1]-[Fc1] in order from the N-terminus to the C-terminus;

a second heavy chain comprising [VH1]-[linker 1]-[Obscurin-O chain]-[linker 3]-[VH2]-[CH1]-[Fc2] in order from the N-terminus to the C-terminus;

a first light chain comprising [VL1]-[linker 2]-[Titin-T chain] in order from the N-terminus to the C-terminus; and

a second light chain comprising [VL2]-[CL] in order from the N-terminus to the C-terminus;

wherein the linker 1, the linker 2, and the linker 3 are identical or different;

preferably, the Fc1 and the Fc2 are identical, or the Fc1 and the Fc2 each independently have one or more amino acid substitutions that reduce homodimerization;

more preferably,

A) the linker 1, the linker 2, and the linker 3 are all $(G_xS)_y$ linkers, wherein x is selected from the group consisting of integers from 1 to 5, and y is selected from the group consisting of integers from 0 to 6; preferably, all are set forth in SEQ ID NO: 175 or SEQ ID NO: 176, or

B) the linker 1 is a C-terminal truncated sequence of CH1, and preferably, the linker 1 is set forth in SEQ ID NO: 173; the linker 2 is a C-terminal truncated sequence of CL, and preferably, the linker 2 is set forth in SEQ ID NO: 174; the linker 3 is a $(G_xS)_y$ linker, wherein x is selected from the group consisting of integers from 1 to 5, and y is selected from the group consisting of integers from 0 to 6, and preferably, the linker 3 is set forth in SEQ ID NO: 175 or SEQ ID NO: 176;

most preferably,

the antigen-binding molecule is capable of binding to PDL1 and TIGIT.

15. The antigen-binding molecule according to claim 14, comprising a first antigen-binding moiety capable of specifically binding to PDL1 and a second antigen-binding moiety capable of specifically binding to TIGIT, wherein the first antigen-binding moiety comprises a heavy chain variable region VH1 and a light chain variable region VL1, and

the second antigen-binding moiety comprises a heavy chain variable region VH2 and a light chain variable region VL2; wherein,
the VH1 comprises HCDR1, HCDR2, and HCDR3 set forth in SEQ ID NOs: 163, SEQ ID NO: 164, and SEQ ID NO: 165, respectively, and the VL1 comprises LCDR1, LCDR2, and LCDR3 set forth in SEQ ID NO: 166, SEQ ID NO: 167, and SEQ ID NO: 168, respectively; and
the VH2 comprises HCDR1, HCDR2, and HCDR3 set forth in SEQ ID NO: 157, SEQ ID NO: 158, and SEQ ID NO: 159, respectively, and the VL2 comprises LCDR1, LCDR2, and LCDR3 set forth in SEQ ID NO: 160, SEQ ID NO: 161, and SEQ ID NO: 162, respectively;
preferably,
the VH1 has a sequence set forth in SEQ ID NO: 156 or a sequence having at least 90% sequence identity to SEQ ID NO: 156, and the VL1 has a sequence set forth in SEQ ID NO: 155 or a sequence having at least 90% sequence identity to SEQ ID NO: 155; and
the VH2 has a sequence set forth in SEQ ID NO: 154 or a sequence having at least 90% sequence identity to SEQ ID NO: 154, and the VL2 has a sequence set forth in SEQ ID NO: 153 or a sequence having at least 90% sequence identity to SEQ ID NO: 153;
more preferably, the antigen-binding molecule has:
a heavy chain having a sequence set forth in SEQ ID NO: 148 or a sequence having at least 90% sequence identity to SEQ ID NO: 148;
a first light chain having a sequence set forth in SEQ ID NO: 146 or a sequence having at least 90% sequence identity to SEQ ID NO: 146; and
a second light chain having a sequence set forth in SEQ ID NO: 147 or a sequence having at least 90% sequence identity to SEQ ID NO: 147.

16. A domain-engineered antibody, being an antibody in which a heavy chain constant region CH1 and a light chain constant region CL are replaced with the dimerized polypeptide according to any one of claims 1 to 5, wherein
preferably, the heavy chain constant region CH1 is replaced with a Titin-T chain, and the light chain constant region CL is replaced with an Obscurin-O chain; or the light chain constant region CL is replaced with a Titin-T chain, and the heavy chain constant region CH1 is replaced with an Obscurin-O chain.

17. A pharmaceutical composition comprising the antigen-binding molecule according to any one of claims 6 to 15 or the domain-engineered antibody according to claim 16, and one or more pharmaceutically acceptable carriers, diluents, or excipients.

18. A nucleic acid molecule encoding the dimerized polypeptide according to any one of claims 1 to 5, the antigen-binding molecule according to any one of claims 6 to 15, or the domain-engineered antibody according to claim 16.

19. A host cell comprising the nucleic acid molecule according to claim 18.
20. Use of the antigen-binding molecule according to any one of claims 6 to 15, the domain-engineered antibody according to claim 16, or the pharmaceutical composition according to claim 17 in the preparation of a medicament for treating or preventing a disease.
21. A pharmaceutical composition comprising the antigen-binding molecule according to any one of claims 6 to 15 or the domain-engineered antibody according to claim 16 for use as a medicament.