

CLAIMS

What is claimed is:

1. A multispecific antibody comprising:
 - a) a first antigen-binding fragment that specifically binds CD3, wherein the first antigen-binding fragment is fused to a first masking moiety (MM1) via a first cleavable moiety (CM1) comprising a first cleavage site, wherein the first antigen-binding fragment comprises a first immunoglobulin light chain variable domain (VL1) and a first immunoglobulin heavy chain variable domain (VH1) of an anti-CD3 antibody, wherein the MM1 is fused to the N-terminus of the VL1 via the CM1, wherein the MM1 inhibits binding of the multispecific antibody to CD3 when the CM1 is not cleaved, and wherein the MM1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 35, 417, and 597-599 and the CM1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 77, 127-129, 418, 420, 431 and 477-490, and 516-555; and
 - b) a second antigen-binding fragment that specifically binds a target antigen; wherein the MM1 competes with CD3 to specifically bind the CD3-binding moiety; and wherein
 - i. the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and
the VL1 comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;
 - ii. the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 392, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL1 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;
iii. the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 392, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL1 comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 401;
iv. the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL1 comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;
v. the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL1 comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 401;
vi. the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and

the VL1 comprises

- a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
- a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
- a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;

vii. the VH1 comprises

- a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
- a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
- a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and

the VL1 comprises

- a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 398,
- a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 399, and
- a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;

viii. the VH1 comprises

- a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
- a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 394, and
- a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and

the VL1 comprises

- a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
- a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
- a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;

ix. the VH1 comprises

- a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
- a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and
- a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and

the VL1 comprises

- a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
- a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
- a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;

x. the VH1 comprises

- a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
- a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 394, and

a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL1 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;

xi. the VH1 comprises

a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and
the VL1 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;

xii. the VH1 comprises

a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and
the VL1 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;

xiii. the VH1 comprises

a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and
the VL1 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381; or

xiv. the VH1 comprises

a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,

a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and
the VL1 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381.

2. The multispecific antibody of claim 1, wherein the first antigen-binding fragment is a scFv comprising, from N-terminus to C-terminus, VL1, a linker, and VH1.

3. The multispecific antibody of claim 2, wherein the multispecific antibody comprises a first polypeptide, a second polypeptide, and a third polypeptide, wherein:

(i) the first polypeptide comprises a structure represented by the formula:

VH2-CH1-hinge-CH2-first CH3 (1a);

(ii) the second polypeptide comprises a structure represented by the formula:

MM1-CM1-VL1-VH1-hinge-CH2-second CH3 (1b); and

(iii) the third polypeptide comprises a structure represented by the formula:

VL2-CL (1c);

wherein:

CL is an immunoglobulin light chain constant domain;

CH1 is an immunoglobulin heavy chain constant domain 1;

CH2 is an immunoglobulin heavy chain constant domain 2;

first CH3 is a first immunoglobulin heavy chain constant domain 3;

second CH3 is a second immunoglobulin heavy chain constant domain 3;

hinge is an immunoglobulin hinge region connecting the CH1 and CH2 domains;

wherein the VL1 and the VH1 associate to form a scFv that specifically binds CD3; and

wherein the VL2 and the VH2 associate to form a Fv that specifically binds the target antigen.

4. The multispecific antibody of claim 1, wherein the second antigen-binding fragment comprises a second immunoglobulin light chain variable domain (VL2) and a second immunoglobulin heavy chain variable domain (VH2) of an antibody that specifically binds the target antigen.

5. The multispecific antibody of claim 4, wherein the second antigen-binding fragment is selected from the group consisting of a Fab, a Fv, a scFab and a scFv.

6. The multispecific antibody of claim 5, wherein the second antigen-binding fragment is fused to a second masking moiety (MM2) via a second cleavable moiety (CM2), wherein the CM2 comprises a second cleavage site, wherein the MM2 inhibits binding of the multispecific antibody to the target antigen when the CM2 is not cleaved, and wherein the multispecific antibody binds the target antigen via the second antigen-binding fragment when the CM2 is cleaved.

7. The multispecific antibody of claim 6, wherein the MM2 is fused to the N-terminus of the VL2 via the CM2.

8. The multispecific antibody of claim 7, wherein the multispecific antibody comprises a first polypeptide, a second polypeptide, and a third polypeptide, wherein:

(i) the first polypeptide comprises a structure represented by the formula:

VH2-CH1-hinge-CH2-first CH3 (2a);

(ii) the second polypeptide comprises a structure represented by the formula:

MM1-VL1-VH1-hinge-CH2-second CH3 (2b); and

(iii) the third polypeptide comprises a structure represented by the formula:

MM2-CM2-VL2-CL (2c);

wherein:

CL is an immunoglobulin light chain constant domain;

CH1 is an immunoglobulin heavy chain constant domain 1;

CH2 is an immunoglobulin heavy chain constant domain 2;

first CH3 is a first immunoglobulin heavy chain constant domain 3;

second CH3 is a second immunoglobulin heavy chain constant domain 3;

hinge is an immunoglobulin hinge region connecting the CH1 and CH2 domains;

wherein the VL1 and the VH1 associate to form a scFv that specifically binds CD3; and

wherein the VL2 and the VH2 associate to form a Fv that specifically binds the target antigen.

9. The multispecific antibody of claim 1, wherein the CD3 is human CD3.

10. The multispecific antibody of claim 1, wherein the VH1 comprises

a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,

- a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 392, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL1 comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400.
11. The multispecific antibody of claim 1, wherein the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 394, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL1 comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381.
12. The multispecific antibody of claim 1, wherein the first antigen-binding fragment comprises a VH1 and a VL1, and wherein:
- a) the VH1 comprises the amino acid sequence according to Formula (VII):
EVQLVESGGGLVX₁PGGSLRLSCAASGFTFX₂X₃YAIX₄WVRQAPGKGLEWVX₅RI
RSKYNNYATYYAX₆SVKX₇RFTISRDX₈SKNTLYLQX₉NSLRAEDTAVYYCX₁₀RH
GNX₁₁GX₁₂SYVSWFAYWGQGTLLTVSS (SEQ ID NO: 388), wherein X₁ is K or Q,
X₂ is N or S, X₃ is S or T, X₄ is H or N, X₅ is G or S, X₆ is D or E, X₇ is D or G, X₈ is D
or N, X₉ is I or L, X₁₀ is A or V, X₁₁ is F or Y, X₁₂ is N or T; and
 - b) the VL1 comprises the amino acid sequence according to Formula (VIII):
X₁AVVTQEPSLTVSPGGTVTLTCX₂SSTGAVTTSNYX₃NWX₄QQKPGQAPRGLIGG
TX₅X₆RAPGX₇PARFSGSLLGGKAALTLGAQPEDEAEYYCALWYSX₈X₉WVFGG
GTKLTVL (SEQ ID NO: 389), wherein X₁ is E or Q, X₂ is A, G, P, or R, X₃ is A or P,
X₄ is F or V, X₅ is K or N, X₆ is F or K, X₇ is A, I, T, or V, X₈ is A, D, N, or T, and X₉ is
H or L.
13. The multispecific antibody of claim 12, wherein:
- a) the VH1 comprises the amino acid sequence of SEQ ID NO: 402, and the VL1 comprises
the amino acid sequence of SEQ ID NO: 403;

- b) the VH1 comprises the amino acid sequence of SEQ ID NO: 402, and the VL1 comprises the amino acid sequence of SEQ ID NO: 404;
 - c) the VH1 comprises the amino acid sequence of SEQ ID NO: 405, and the VL1 comprises the amino acid sequence of SEQ ID NO: 406;
 - d) the VH1 comprises the amino acid sequence of SEQ ID NO: 407, and the VL1 comprises the amino acid sequence of SEQ ID NO: 404;
 - e) the VH1 comprises the amino acid sequence of SEQ ID NO: 407, and the VL1 comprises the amino acid sequence of SEQ ID NO: 403;
 - f) the VH1 comprises the amino acid sequence of SEQ ID NO: 407, and the VL1 comprises the amino acid sequence of SEQ ID NO: 408;
 - g) the VH1 comprises the amino acid sequence of SEQ ID NO: 409, and the VL1 comprises the amino acid sequence of SEQ ID NO: 408;
 - h) the VH1 comprises the amino acid sequence of SEQ ID NO: 410, and the VL1 comprises the amino acid sequence of SEQ ID NO: 411;
 - i) the VH1 comprises the amino acid sequence of SEQ ID NO: 412, and the VL1 comprises the amino acid sequence of SEQ ID NO: 413;
 - j) the VH1 comprises the amino acid sequence of SEQ ID NO: 410, and the VL1 comprises the amino acid sequence of SEQ ID NO: 413;
 - k) the VH1 comprises the amino acid sequence of SEQ ID NO: 414, and the VL1 comprises the amino acid sequence of SEQ ID NO: 403;
 - l) the VH1 comprises the amino acid sequence of SEQ ID NO: 415, and the VL1 comprises the amino acid sequence of SEQ ID NO: 413;
 - m) the VH1 comprises the amino acid sequence of SEQ ID NO: 416, and the VL1 comprises the amino acid sequence of SEQ ID NO: 413; or
 - n) the VH1 comprises the amino acid sequence of SEQ ID NO: 416, and the VL1 comprises the amino acid sequence of SEQ ID NO: 411.
14. The multispecific antibody of claim 13, wherein the VH1 comprises the amino acid sequence of SEQ ID NO: 402, and the VL1 comprises the amino acid sequence of SEQ ID NO: 403.

15. The multispecific antibody of claim 13, wherein the VH1 comprises the amino acid sequence of SEQ ID NO: 410, and the VL1 comprises the amino acid sequence of SEQ ID NO: 411.
16. The multispecific antibody of claim 1, wherein the MM1 comprises the amino acid sequence of SEQ ID NO: 417.
17. The multispecific antibody of claim 1, wherein the CM1 comprises the amino acid sequence of SEQ ID NO: 77.
18. The multispecific antibody of claim 1, wherein the CM1 comprises the amino acid sequence of SEQ ID NO: 418.
19. The multispecific antibody of claim 1, wherein the target antigen is HER2.
20. The multispecific antibody of claim 19, wherein the second antigen-binding fragment comprises a VH2 and a VL2 of an anti-HER2 antibody, and wherein:
- the VH2 comprises
 - a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 423,
 - a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 424, and
 - a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 71; and
 - the VL2 comprises
 - a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 72,
 - a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 73, and
 - a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 74.
21. The multispecific antibody of claim 20, wherein the VH2 comprises the amino acid sequence of SEQ ID NO: 75, and the VL2 comprises the amino acid sequence of SEQ ID NO: 76.
22. The multispecific antibody of claim 20, wherein:
- a) the MM2 comprises an amino acid sequence according to Formula (XI):
ESX₁X₂CX₃X₄DPFX₅CQX₆ (SEQ ID NO: 670), wherein X₁ is D or E, X₂ is A, F, V, or Y, X₃ is D or E, X₄ is A or L, X₅ is D or E, and X₆ is A, F, or Y;
 - b) the MM2 comprises an amino acid sequence according to Formula (XII):
X₁X₂X₃X₄X₅X₆CX₇X₈DPYECX₉X₁₀ (SEQ ID NO: 671), wherein X₁ is A, H, or S, X₂ is A, D, or S, X₃ is A, T, or V, X₄ is P, S, or T, X₅ is D or E, X₆ is A or V, X₇ is D or E, X₈ is A or L, X₉ is Q, S, or T, and X₁₀ is A, H, or V; or

- c) the MM2 comprises an amino acid sequence according to Formula (XIII):
YNSDDDCX₁SX₂YDPYTCYY (SEQ ID NO: 672), wherein X₁ is A, I, or V, and X₂ is H or R.
23. The multispecific antibody of claim 20, wherein the MM2 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 36, 419, 432-476 and 491-515.
24. The multispecific antibody of claim 23, wherein the MM2 comprises the amino acid sequence of SEQ ID NO: 419.
25. The multispecific antibody of claim 24, wherein the CM2 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 77, 127-129, 418, 420, 431, 477-490, and 516-555.
26. The multispecific antibody of claim 25, wherein the CM2 comprises the amino acid sequence of SEQ ID NO: 77 or 420.
27. The multispecific antibody of claim 26, comprising:
- a) a first polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 425,
a second polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 426, and
a third polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 112;
 - b) a first polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 427,
a second polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 428, and
a third polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 112;
 - c) a first polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 429,
a second polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 430, and
a third polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 115;

- d) a first polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 83,
a second polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 84, and
a third polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 85;
- e) a first polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 683,
a second polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 684, and
a third polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 685;
- f) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 425,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 426, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 112;
- g) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 427,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 428, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 112;
- h) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 429,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 430, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 115;
- i) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 83,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 84, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 85;
- j) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 683,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 684, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 685;
- k) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 425 without the C-terminal lysine,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 426 without the C-terminal lysine, and

- a third polypeptide comprising the amino acid sequence of SEQ ID NO: 112;
 - l) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 427 without the C-terminal lysine,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 428 without the C-terminal lysine, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 112;
 - m) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 429 without the C-terminal lysine,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 430 without the C-terminal lysine, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 115;
 - n) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 83,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 84 without the C-terminal lysine, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 85 without the C-terminal lysine; or
 - o) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 683,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 684 without the C-terminal lysine, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 685 without the C-terminal lysine.
28. The multispecific antibody of claim 1, wherein the target antigen is CD20.
29. The multispecific antibody of claim 28, wherein the second antigen-binding fragment comprises a VH2 and a VL2 of an anti-CD20 antibody, and wherein:
- a) the VH2 comprises
 - a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 556,
 - a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 557, and
 - a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 558; and
 - the VL2 comprises
 - a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 559,
 - a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 560, and

- a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 561; or
 - b) the VH2 comprises
 - a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 86,
 - a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 557, and
 - a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 558; and
 - the VL2 comprises
 - a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 559,
 - a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 560, and
 - a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 561.
30. The multispecific antibody of claim 29, wherein the VH2 comprises the amino acid sequence of SEQ ID NO: 562, and the VL2 comprises the amino acid sequence of SEQ ID NO: 563.
31. The multispecific antibody of claim 29, comprising:
- a) a first polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 564,
a second polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 565, and
a third polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 567;
 - b) a first polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 564,
a second polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 565, and
a third polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 569;
 - c) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 564,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 565, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 567;
 - d) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 564,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 565, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 569;

- e) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 564,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 565 without
the C-terminal lysine, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 567 without the
C-terminal lysine;
 - f) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 564,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 565 without
the C-terminal lysine, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 569 without the
C-terminal lysine.
32. The multispecific antibody of claim 2, wherein the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 394, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL1 comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381.
33. The multispecific antibody of claim 32, wherein the ScFv comprises the amino acid
sequence of SEQ ID NO: 422.
34. The multispecific antibody of claim 32, wherein the MM1 comprises the amino acid
sequence of SEQ ID NO: 417.
35. The multispecific antibody of claim 33, wherein the MM1 comprises the amino acid
sequence of SEQ ID NO: 417.
36. The multispecific antibody of claim 34, wherein the CM1 comprises the amino acid
sequence of SEQ ID NO: 77.
37. The multispecific antibody of claim 35, wherein the CM1 comprises the amino acid
sequence of SEQ ID NO: 77.
38. The multispecific antibody of claim 34, wherein the CM1 comprises the amino acid
sequence of SEQ ID NO: 418.

39. The multispecific antibody of claim 35, wherein the CM1 comprises the amino acid sequence of SEQ ID NO: 418.
40. The multispecific antibody of claim 3, wherein the second polypeptide has the amino acid sequence of SEQ ID NO: 567.
41. The multispecific antibody of claim 40, wherein the first polypeptide has the amino acid sequence of SEQ ID NO: 565.
42. The multispecific antibody of claim 41, wherein the third polypeptide has the amino acid sequence of SEQ ID NO: 564.
43. The multispecific antibody of claim 8, wherein the second polypeptide has the amino acid sequence of SEQ ID NO: 85.
44. The multispecific antibody of claim 43, wherein the first polypeptide has the amino acid sequence of SEQ ID NO: 84.
45. The multispecific antibody of claim 44, wherein the third polypeptide has the amino acid sequence of SEQ ID NO: 83.
46. The multispecific antibody of claim 27, comprising:
a first polypeptide having an amino acid sequence of SEQ ID NO: 427,
a second polypeptide having an amino acid sequence of SEQ ID NO: 428, and
a third polypeptide having an amino acid sequence of SEQ ID NO: 112.
47. The multispecific antibody of any one of claim 31, comprising:
a first polypeptide having an amino acid sequence having an amino acid sequence of SEQ ID NO: 564,
a second polypeptide having an amino acid sequence of SEQ ID NO: 565, and
a third polypeptide having an amino acid sequence of SEQ ID NO: 567.