

Claims

1. A trispecific antibody or a trispecific binding fragment thereof, comprising:
a first antigen-binding arm that binds to an epitope on cluster of differentiation 79B protein (CD79b), a second antigen-binding arm that binds to an epitope on cluster of differentiation 3 (CD3), and a third antigen-binding arm that binds to an epitope on cluster of differentiation 20 (CD20),

(i) wherein the first antigen-binding arm comprises a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2, and a LCDR3 of:

- a) SEQ ID NOs: 1, 2, 3, 4, 5 and 6, respectively;
- b) SEQ ID NOs: 13, 8, 9, 10, 11 and 12, respectively;
- c) SEQ ID NOs: 7, 8, 9, 10, 11 and 12, respectively;
- d) SEQ ID NOs: 14, 15, 16, 17, 5 and 6, respectively;
- e) SEQ ID NOs: 18, 8, 19, 20, 21 and 12, respectively;
- f) SEQ ID NOs: 22, 23, 24, 25, 5 and 6, respectively;
- g) SEQ ID NOs: 22, 26, 27, 28, 5 and 29, respectively; or
- h) SEQ ID NOs: 30, 31, 32, 33, 5 and 6, respectively.

(ii) wherein the second antigen-binding arm comprises a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3 of:

- a) SEQ ID NOs: 76, 77, 78, 79, 80 and 81, respectively;
- b) SEQ ID NOs: 76, 77, 75, 79, 80 and 81, respectively;
- c) SEQ ID NOs: 76, 77, 82, 79, 80 and 81, respectively; or
- d) SEQ ID NOs: 83, 84, 85, 86, 87 and 88, respectively.. and

(iii) wherein the third antigen-binding arm comprises a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2 and a LCDR3 of:

- a) SEQ ID NOs: 115, 116, 117, 118, 119 and 120, respectively;
- b) SEQ ID NOs: 121, 122, 123, 124, 119 and 125, respectively;
- c) SEQ ID NOs: 115, 116, 95, 96, 119 and 125, respectively; or
- d) SEQ ID NOs: 121, 116, 123, 124, 119 and 125, respectively.

2. The trispecific antibody or trispecific binding fragment of claim 1, wherein the first antigen-binding arm that binds CD79b comprises:

- a) the VH1 of SEQ ID NO: 35 and the VL1 of SEQ ID NO: 37;
- b) the VH1 of SEQ ID NO: 39 and the VL1 of SEQ ID NO: 41;
- c) the VH1 of SEQ ID NO: 43 and the VL1 of SEQ ID NO: 41;
- d) the VH1 of SEQ ID NO: 45 and the VL1 of SEQ ID NO: 47;
- e) the VH1 of SEQ ID NO: 49 and the VL1 of SEQ ID NO: 51;
- f) the VH1 of SEQ ID NO: 39 and the VL1 of SEQ ID NO: 53;
- g) the VH1 of SEQ ID NO: 55 and the VL1 of SEQ ID NO: 57;
- h) the VH1 of SEQ ID NO: 59 and the VL1 of SEQ ID NO: 61;
- i) the VH1 of SEQ ID NO: 63 and the VL1 of SEQ ID NO: 65;
- j) the VH1 of SEQ ID NO: 67 and the VL1 of SEQ ID NO: 69; or
- k) the VH1 of SEQ ID NO: 71 and the VL1 of SEQ ID NO: 73;

wherein the second antigen-binding arm that binds CD3 comprises:

- a) the VH2 of SEQ ID NO: 97 and the VL2 of SEQ ID NO: 99;
- b) the VH2 of SEQ ID NO: 101 and the VL2 of SEQ ID NO: 99;
- c) the VH2 of SEQ ID NO: 103 and the VL2 of SEQ ID NO: 99;
- d) the VH2 of SEQ ID NO: 105 and the VL2 of SEQ ID NO: 99; or
- e) the VH2 of SEQ ID NO: 107 and the VL2 of SEQ ID NO: 109; and

wherein the third antigen-binding arm that binds CD20 comprises:

- a) the VH3 of SEQ ID NO: 126 and the VL3 of SEQ ID NO: 128;
- b) the VH3 of SEQ ID NO: 130 and the VL3 of SEQ ID NO: 132;
- c) the VH3 of SEQ ID NO: 134 and the VL3 of SEQ ID NO: 136; or
the VH3 of SEQ ID NO: 138 and the VL3 of SEQ ID NO: 140.

3. The trispecific antibody or trispecific binding fragment of claim 1, wherein the first antigen-binding arm that binds CD79b comprises the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 of SEQ ID NOs: 1, 2, 3, 4, 5 and 6, respectively;

the second antigen-binding arm that binds CD3 comprises the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 of SEQ ID NOs: 83, 84, 85, 86, 87 and 88, respectively; and

the third antigen-binding arm that binds CD20 comprises the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 of SEQ ID NOs: 121, 122, 123, 124, 119 and 125, respectively.

4. The trispecific antibody or trispecific binding fragment of any one of claims 1-3, 14 and 15, wherein the first antigen-binding arm that binds CD79b comprises the VH1 of SEQ ID NO: 35 and the VL1 of SEQ ID NO: 37;

the second antigen-binding arm that binds CD3 comprises the VH2 of SEQ ID NO: 107 and the VL2 of SEQ ID NO: 109; and

the third antigen-binding arm that binds CD20 comprises the VH3 of SEQ ID NO: 130 and the VL3 of SEQ ID NO: 132.

5. The trispecific antibody or trispecific binding fragment of claim 1, wherein the first antigen-binding arm that binds CD79b comprises the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 of SEQ ID NOs: 1, 2, 3, 4, 5 and 6, respectively;

the second antigen-binding arm that binds CD3 comprises the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 of SEQ ID NOs: 76, 77, 75, 79, 80 and 81, respectively; and

the third antigen-binding arm that binds CD20 comprises the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 of SEQ ID NOs: 121, 122, 123, 124, 119 and 125, respectively.

6. The trispecific antibody or trispecific binding fragment of any one of claims 1, 2 and 5, wherein the first antigen-binding arm that binds CD79b comprises the VH1 of SEQ ID NO: 35 and the VL1 of SEQ ID NO: 37;

the second antigen-binding arm that binds CD3 comprises the VH2 of SEQ ID NO: 97 and the VL2 of SEQ ID NO: 99; and

the third antigen-binding arm that binds CD20 comprises the VH3 of SEQ ID NO: 130 and the VL3 of SEQ ID NO: 132.

7. The trispecific antibody or trispecific binding fragment of claims 1-6, wherein
- a) the first antigen-binding arm comprises a heavy chain 1 (HC1) comprising the amino acid sequence of SEQ ID NO: 172, and a light chain (LC) comprising the amino acid sequence of SEQ ID NO: 174, and the polypeptide comprising the second antigen-binding arm and the third antigen-binding arm comprises the amino acid sequence of SEQ ID NO: 142;
 - b) the first antigen-binding arm comprises an HC1 comprising the amino acid sequence of SEQ ID NO: 176, the LC comprising the amino acid sequence of SEQ ID NO: 178, and the polypeptide comprising the second antigen-binding arm and the third antigen-binding arm comprises the amino acid sequence of SEQ ID NO: 142;
 - c) the first antigen-binding arm comprises an HC1 comprising the amino acid sequence of SEQ ID NO: 180, the LC comprising the amino acid sequence of SEQ ID NO: 182, and the polypeptide comprising the second antigen-binding arm and the third antigen-binding arm comprises the amino acid sequence of SEQ ID NO: 142
 - d) the first antigen-binding arm comprises an HC1 comprising the amino acid sequence of SEQ ID NO: 172, the LC comprising the amino acid sequence of SEQ ID NO: 174, and the polypeptide comprising the second antigen-binding arm and the third antigen-binding arm comprises the amino acid sequence of SEQ ID NO: 144;
 - e) the first antigen-binding arm comprises an HC1 comprising the amino acid sequence of SEQ ID NO: 176, the LC comprising the amino acid sequence of SEQ ID NO: 178, and the polypeptide comprising the second antigen-binding arm and the third antigen-binding arm comprises the amino acid sequence of SEQ ID NO: 144;
 - f) the first antigen-binding arm comprises an HC1 comprising the amino acid sequence of SEQ ID NO: 180, the LC comprising the amino acid sequence of SEQ ID NO: 182, and the polypeptide comprising the second antigen-binding arm and the third antigen-binding arm comprises the amino acid sequence of SEQ ID NO: 144;
 - g) the first antigen-binding arm comprises an HC1 comprising the amino acid sequence of SEQ ID NO: 180, the LC comprising the amino acid sequence of SEQ ID NO: 182, and the polypeptide comprising the second antigen-binding arm and the third antigen-binding arm comprises the amino acid sequence of SEQ ID NO: 148;

- h) the first antigen-binding arm comprises an HC1 comprising the amino acid sequence of SEQ ID NO: 180, the LC comprising the amino acid sequence of SEQ ID NO: 182, and the polypeptide comprising the second antigen-binding arm and the third antigen-binding arm comprises the amino acid sequence of SEQ ID NO: 150;
- i) the first antigen-binding arm comprises an HC1 comprising the amino acid sequence of SEQ ID NO: 180, the LC comprising the amino acid sequence of SEQ ID NO: 182, and the polypeptide comprising the second antigen-binding arm and the third antigen-binding arm comprises the amino acid sequence of SEQ ID NO: 152;
- j) the first antigen-binding arm comprises an HC1 comprising the amino acid sequence of SEQ ID NO: 180, the LC comprising the amino acid sequence of SEQ ID NO: 182, and the polypeptide comprising the second antigen-binding arm and the third antigen-binding arm comprises the amino acid sequence of SEQ ID NO: 154;
- k) the first antigen-binding arm comprises an HC1 comprising the amino acid sequence of SEQ ID NO: 180, the LC comprising the amino acid sequence of SEQ ID NO: 182, and the polypeptide comprising the second antigen-binding arm and the third antigen-binding arm comprises the amino acid sequence of SEQ ID NO: 156;
- l) the first antigen-binding arm comprises an HC1 comprising the amino acid sequence of SEQ ID NO: 180, the LC comprising the amino acid sequence of SEQ ID NO: 182, and the polypeptide comprising the second antigen-binding arm and the third antigen-binding arm comprises the amino acid sequence of SEQ ID NO: 158;
- m) the first antigen-binding arm comprises an HC1 comprising the amino acid sequence of SEQ ID NO: 180, the LC comprising the amino acid sequence of SEQ ID NO: 182, and the polypeptide comprising the second antigen-binding arm and the third antigen-binding arm comprises the amino acid sequence of SEQ ID NO: 160;
- n) the first antigen-binding arm comprises an HC1 comprising the amino acid sequence of SEQ ID NO: 180, the LC comprising the amino acid sequence of SEQ ID NO: 182, and the polypeptide comprising the second antigen-binding arm and the third antigen-binding arm comprises the amino acid sequence of SEQ ID NO: 162;
- o) the first antigen-binding arm comprises an HC1 comprising the amino acid sequence of SEQ ID NO: 191, the LC comprising the amino acid sequence of SEQ ID NO:

- 182, and the polypeptide comprising the second antigen-binding arm and the third antigen-binding arm comprises the amino acid sequence of SEQ ID NO: 166;
- p) the first antigen-binding arm comprises an HC1 comprising the amino acid sequence of SEQ ID NO: 172, the LC comprising the amino acid sequence of SEQ ID NO: 174, and the polypeptide comprising the second antigen-binding arm and the third antigen-binding arm comprises the amino acid sequence of SEQ ID NO: 168; or
- q) the first antigen-binding arm comprises an HC1 comprising the amino acid sequence of SEQ ID NO: 172, the LC comprising the amino acid sequence of SEQ ID NO: 174, and the polypeptide comprising the second antigen-binding arm and the third antigen-binding arm comprises the amino acid sequence of SEQ ID NO: 170.

8. The trispecific antibody or trispecific binding fragment of any one of claims 1-7, wherein the first antigen-binding arm comprises an HC1 comprising the amino acid sequence of SEQ ID NO: 172, and a LC comprising the amino acid sequence of SEQ ID NO: 174, and the polypeptide comprising the second antigen-binding arm and the third antigen-binding arm comprises the amino acid sequence of SEQ ID NO: 170.

9. A synthetic polynucleotide encoding the trispecific antibody or trispecific binding fragment of any one of claims 1 to 8.

10. Use of the trispecific antibody or trispecific binding fragment of any one of claims 1 to 8 in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein a therapeutically effective amount of the trispecific antibody or trispecific binding fragment is to be administered to the subject.

11. The method of claim 10 wherein the cancer is a diffuse large B-cell lymphoma (DLBCL), mantle cell lymphoma (MCL), marginal zone lymphoma (MZL), follicular lymphoma (FL), chronic lymphocytic leukemia (CLL), or Waldenström macroglobulinemia (WM).

12. An antibody or an antigen-binding fragment thereof, that binds to an epitope on Cluster of Differentiation 79B protein (CD79b), comprising the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 of:

- a) SEQ ID NOs: 1, 2, 3, 4, 5 and 6, respectively;
- b) SEQ ID NOs: 13, 8, 9, 10, 11 and 12, respectively;
- c) SEQ ID NOs: 7, 8, 9, 10, 11 and 12, respectively;
- d) SEQ ID NOs: 14, 15, 16, 17, 5 and 6, respectively;
- e) SEQ ID NOs: 18, 8, 19, 20, 21 and 12, respectively;
- f) SEQ ID NOs: 22, 23, 24, 25, 5 and 6, respectively;
- g) SEQ ID NOs: 22, 26, 27, 28, 5 and 29, respectively; or
- h) SEQ ID NOs: 30, 31, 32, 33, 5 and 6, respectively.

13. The antibody or antigen-binding fragment of claim 12, comprising

- a) the VH of SEQ ID NO: 35 and the VL of SEQ ID NO: 37;
- b) the VH of SEQ ID NO: 39 and the VL of SEQ ID NO: 41;
- c) the VH of SEQ ID NO: 43 and the VL of SEQ ID NO: 41;
- d) the VH of SEQ ID NO: 45 and the VL of SEQ ID NO: 47;
- e) the VH of SEQ ID NO: 49 and the VL of SEQ ID NO: 51;
- f) the VH of SEQ ID NO: 39 and the VL of SEQ ID NO: 53;
- g) the VH of SEQ ID NO: 55 and the VL of SEQ ID NO: 57;
- h) the VH of SEQ ID NO: 59 and the VL of SEQ ID NO: 61;
- i) the VH of SEQ ID NO: 63 and the VL of SEQ ID NO: 65;
- j) the VH of SEQ ID NO: 67 and the VL of SEQ ID NO: 69; or
- k) the VH of SEQ ID NO: 71 and the VL of SEQ ID NO: 73.

14. A synthetic polynucleotide encoding the antibody or antigen-binding fragment of any one of claims 12 or 13.

15. A bispecific antibody, or a bispecific binding fragment thereof, comprising:

a first antigen-binding arm that binds to an epitope on cluster of differentiation 79B protein (CD79b), and a second antigen-binding arm binds to an epitope on cluster of differentiation 3 (CD3),

wherein the first antigen-binding arm comprises a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2, and a LCDR3 selected from:

- a) SEQ ID NOs: 1, 2, 3, 4, 5 and 6, respectively;
- b) SEQ ID NOs: 13, 8, 9, 10, 11 and 12, respectively;
- c) SEQ ID NOs: 7, 8, 9, 10, 11 and 12, respectively;
- d) SEQ ID NOs: 14, 15, 16, 17, 5 and 6, respectively;
- e) SEQ ID NOs: 18, 8, 19, 20, 21 and 12, respectively;
- f) SEQ ID NOs: 22, 23, 24, 25, 5 and 6, respectively;
- g) SEQ ID NOs: 22, 26, 27, 28, 5 and 29, respectively; or
- h) SEQ ID NOs: 30, 31, 32, 33, 5 and 6, respectively; and

wherein the second antigen-binding arm comprises a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2, and a LCDR3 selected from:

- a) SEQ ID NOs: 76, 77, 78, 79, 80 and 81, respectively;
- b) SEQ ID NOs: 76, 77, 75, 79, 80 and 81, respectively;
- c) SEQ ID NOs: 76, 77, 82, 79, 80 and 81, respectively; or
- d) SEQ ID NOs: 83, 84, 85, 86, 87 and 88, respectively.

16. The bispecific antibody or bispecific binding fragment of claim 15, wherein the first antigen-binding arm that binds CD79b comprises:

- a) the VH of SEQ ID NO: 35 and the VL of SEQ ID NO: 37;
- b) the VH of SEQ ID NO: 39 and the VL of SEQ ID NO: 41;
- c) the VH of SEQ ID NO: 43 and the VL of SEQ ID NO: 41;
- d) the VH of SEQ ID NO: 45 and the VL of SEQ ID NO: 47;
- e) the VH of SEQ ID NO: 49 and the VL of SEQ ID NO: 51;
- f) the VH of SEQ ID NO: 39 and the VL of SEQ ID NO: 53;
- g) the VH of SEQ ID NO: 55 and the VL of SEQ ID NO: 57;
- h) the VH of SEQ ID NO: 59 and the VL of SEQ ID NO: 61;
- i) the VH of SEQ ID NO: 63 and the VL of SEQ ID NO: 65;

- j) the VH of SEQ ID NO: 67 and the VL of SEQ ID NO: 69; or
 - k) the VH of SEQ ID NO: 71 and the VL of SEQ ID NO: 73; and
- wherein the second antigen-binding arm that binds CD3 comprises:
- a) the VH of SEQ ID NO: 97 and the VL of SEQ ID NO: 99;
 - b) the VH of SEQ ID NO: 101 and the VL of SEQ ID NO: 99;
 - c) the VH of SEQ ID NO: 103 and the VL of SEQ ID NO: 99;
 - d) the VH of SEQ ID NO: 105 and the VL of SEQ ID NO: 99; or
 - e) the VH of SEQ ID NO: 107 and the VL of SEQ ID NO: 109.

17. The bispecific antibody or bispecific binding fragment of any one of claims 15-16, wherein the first antigen-binding arm comprises a heavy chain 1 (HC1) polypeptide and a light chain (LC) polypeptide and the second antigen-binding arm comprises a second antigen-binding arm polypeptide, and wherein,

- a) the HC1 comprises the amino acid sequence of SEQ ID NO: 172, the LC comprises the amino acid sequence of SEQ ID NO: 174, and the second antigen-binding arm polypeptide comprises the amino acid sequence of SEQ ID NO: 164;
- b) the HC1 comprises the amino acid sequence of SEQ ID NO: 176, the LC comprises the amino acid sequence of SEQ ID NO: 178, and the second antigen-binding arm polypeptide comprises the amino acid sequence of SEQ ID NO: 164;
- c) the HC1 comprises the amino acid sequence of SEQ ID NO: 180, the LC comprises the amino acid sequence of SEQ ID NO: 182, and the second antigen-binding arm polypeptide comprises the amino acid sequence of SEQ ID NO: 164;
- d) the HC1 comprises the amino acid sequence of SEQ ID NO: 172, the LC comprises the amino acid sequence of SEQ ID NO: 174, and the second antigen-binding arm polypeptide comprises the amino acid sequence of SEQ ID NO: 189;
- e) the HC1 comprises the amino acid sequence of SEQ ID NO: 176, the LC comprises the amino acid sequence of SEQ ID NO: 178, and the second antigen-binding arm polypeptide comprises the amino acid sequence of SEQ ID NO: 189; or
- f) the HC1 comprises the amino acid sequence of SEQ ID NO: 180, the LC comprises the amino acid sequence of SEQ ID NO: 182, and the second antigen-binding arm polypeptide comprises the amino acid sequence of SEQ ID NO: 189.

18. A synthetic polynucleotide encoding the bispecific antibody or bispecific binding fragment of any one of claims 15-17.

19. Use of the bispecific antibody or bispecific binding fragment of any one of claims 15-17 in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein a therapeutically effective amount of the bispecific antibody or bispecific binding fragment is to be administered to the subject.

20. The method of claim 19 wherein the cancer is a diffuse large B-cell lymphoma (DLBCL), mantle cell lymphoma (MCL), marginal zone lymphoma (MZL), follicular lymphoma (FL), chronic lymphocytic leukemia (CLL), or Waldenström macroglobulinemia (WM).

21. An antibody or an antigen-binding fragment thereof, that binds to an epitope on Cluster of Differentiation 3 protein (CD3), comprising the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 of:

- a) SEQ ID NOs: 76, 77, 78, 79, 80 and 81, respectively;
- b) SEQ ID NOs: 76, 77, 75, 79, 80 and 81, respectively;
- c) SEQ ID NOs: 76, 77, 82, 79, 80 and 81, respectively; or
- d) SEQ ID NOs: 83, 84, 85, 86, 87 and 88, respectively.

22. The antibody or an antigen-binding fragment thereof of claim 21, comprising:

- a) the VH of SEQ ID NO: 97 and the VL of SEQ ID NO: 99;
- b) the VH of SEQ ID NO: 101 and the VL of SEQ ID NO: 99;
- c) the VH of SEQ ID NO: 103 and the VL of SEQ ID NO: 99;
- d) the VH of SEQ ID NO: 105 and the VL of SEQ ID NO: 99; or
- e) the VH of SEQ ID NO: 107 and the VL of SEQ ID NO: 109.

23. A synthetic polynucleotide encoding the antibody or antigen-binding fragment of any one of claims 22 or 23.

24. The trispecific antibody or trispecific binding fragment of any one of claims 1 to 8 for use in treating cancer.

25. The bispecific antibody or bispecific binding fragment of any one of claims 15-17 for use in treating cancer.