

CLAIMS:

1. An isolated multispecific antibody comprising:
a first binding moiety that has binding specificity for CD3, comprising:
a first heavy chain polypeptide subunit comprising a heavy chain variable domain comprising a CDR1 sequence comprising a sequence of SEQ ID NO: 36, a CDR2 sequence comprising a sequence of SEQ ID NO: 37, and a CDR3 sequence comprising a sequence of SEQ ID NO: 38; and
a first light chain polypeptide subunit comprising a light chain variable domain comprising a CDR1 sequence comprising a sequence of SEQ ID NO: 39, a CDR2 sequence comprising a sequence of SEQ ID NO: 40, and a CDR3 sequence comprising a sequence of SEQ ID NO: 41;
a second binding moiety that has binding specificity for CD19, comprising:
a second heavy chain polypeptide subunit comprising a heavy chain variable domain;
wherein the first heavy chain polypeptide subunit further comprises a mutated human IgG4 constant region comprising mutations S228P, F234A, L235A, and T366W; and the second heavy chain polypeptide subunit comprises a mutated human IgG4 constant region comprising mutations S228P, F234A, L235A, T366S, L368A, and Y407V.
2. The isolated multispecific antibody of claim 1, wherein the mutated human IgG4 constant region of the second heavy chain polypeptide subunit lacks a CH1 domain.
3. The isolated multispecific antibody of claim 1 or 2, wherein the mutated human IgG4 constant region of the first heavy chain polypeptide subunit comprises a sequence of SEQ ID NO: 73 or 55, and the mutated human IgG4 constant region of the second heavy chain polypeptide subunit comprises a sequence of SEQ ID NO: 72 or 54.
4. The isolated multispecific antibody of any one of claims 1-3, wherein:
the heavy chain variable domain of the first binding moiety comprises a sequence having at least 95% identity to SEQ ID NO: 42; and

the light chain variable domain of the first binding moiety comprises a sequence having at least 95% identity to SEQ ID NO: 43.

5. The isolated multispecific antibody of claim 4, wherein:

the heavy chain variable domain of the first binding moiety comprises the sequence of SEQ ID NO: 42; and

the light chain variable domain of the first binding moiety comprises the sequence of SEQ ID NO: 43.

6. The isolated multispecific antibody of any one of claims 1-5, wherein the second binding moiety comprises a single heavy chain variable region, in a monovalent or bivalent configuration.

7. The isolated multispecific antibody of claim 6, wherein the first light chain polypeptide subunit of the first binding moiety comprises a light chain constant domain.

8. A pharmaceutical composition comprising a multispecific antibody according to any one of claims 1-7.

9. A polynucleotide encoding a multispecific antibody according to any one of claims 1-7.

10. A vector comprising a polynucleotide according to claim 9.

11. A cell comprising a vector according to claim 10.

12. A method of producing a multispecific antibody according to any one of claims 1-7, comprising growing a cell according to claim 11 under conditions permissive for expression of the multispecific antibody, and isolating the multispecific antibody from the cell.

13. The multispecific antibody of any one of claims 1-7, or the pharmaceutical composition of claim 8, for use in therapy in an individual in need.

14. Use of the multispecific antibody according to any one of claims 1-7, or the pharmaceutical composition comprising the multispecific antibody of claim 8 in the manufacture of medicament for treating a disease or condition or disorder characterized by expression of CD19, wherein the multispecific antibody or the pharmaceutical composition comprising the multispecific antibody is to be administered to an individual in need in an effective dose.
15. The use of claim 14, wherein the disorder is diffuse large B-cell lymphoma (DLBCL).
16. The method of claim 14, wherein the disorder is acute lymphoblastic leukemia (ALL).
17. The method of claim 14, wherein the disorder is non-Hodgkin's lymphoma (NHL).
18. The method of claim 14, wherein the disorder is systemic lupus erythematosus (SLE).
19. The method of claim 14, wherein the disorder is rheumatoid arthritis (RA).
20. The method of claim 14, wherein the disorder is multiple sclerosis (MS).
21. A kit for treating a disease or disorder in an individual in need, comprising a multispecific antibody of any one of claims 1-7, or the pharmaceutical composition of claim 8, and instructions for use.
22. The kit of claim 21, further comprising at least one additional reagent.
23. The kit of claim 22, wherein the at least one additional reagent comprises a chemotherapeutic drug.
24. A bispecific three-chain antibody like molecule that binds to human CD3 and human CD19, comprising:
 - (i) a first polypeptide subunit comprising the amino acid sequence of SEQ ID NO: 49;
 - (ii) a second polypeptide subunit comprising the amino acid sequence of SEQ ID NO: 56,

wherein the first and second polypeptide subunits together form a first binding moiety that binds to human CD3; and

(iii) a third polypeptide subunit that binds to human CD19, comprising the amino acid sequence of SEQ ID NO: 67.

25. The bispecific three-chain antibody like molecule of claim 24, wherein the first polypeptide subunit comprises a light chain.

26. the bispecific three-chain antibody like molecule of claim 24, wherein the second polypeptide subunit comprises a heavy chain.

27. The bispecific three-chain antibody like molecule of claim 24, wherein the third polypeptide subunit comprises a monovalent heavy chain.

28. The bispecific three-chain antibody like molecule of claim 27, wherein the monovalent heavy chain comprises a heavy chain-only variable region in a monovalent configuration.

29. The bispecific three-chain antibody like molecule of claim 27, wherein the monovalent heavy chain lacks a CH1 domain.

30. A bispecific three-chain antibody like molecule that binds to human CD3 and human CD19, comprising:

(i) a first polypeptide subunit comprising the amino acid sequence of SEQ ID NO: 49;

(ii) a second polypeptide subunit comprising the amino acid sequence of SEQ ID NO: 75, wherein the first and second polypeptide subunits together form a first binding moiety that binds to human CD3; and

(iii) a third polypeptide subunit that binds to human CD19, comprising the amino acid sequence of SEQ ID NO: 78.

31. The bispecific three-chain antibody like molecule of claim 30, wherein the first polypeptide subunit comprises a light chain.

32. The bispecific three-chain antibody like molecule of claim 30, wherein the second polypeptide subunit comprises a heavy chain.
33. The bispecific three-chain antibody like molecule of claim 30, wherein the third polypeptide subunit comprises a monovalent heavy chain.
34. The bispecific three-chain antibody like molecule of claim 33, wherein the monovalent heavy chain comprises a heavy chain-only variable region in a monovalent configuration.
35. The bispecific three-chain antibody like molecule of claim 33, wherein the monovalent heavy chain lacks a CH1 domain.
36. A human, monoclonal IgG4 bispecific antibody comprising:
(i) a first binding arm that binds to human CD3; and
(ii) a second binding arm that binds to human CD19,
wherein the first binding arm comprises a first heavy chain comprising the amino acid sequence of SEQ ID NO: 56 and a light chain comprising the amino acid sequence of SEQ ID NO: 49; and
wherein the second binding arm comprises a monovalent second heavy chain comprising the amino acid sequence of SEQ ID NO: 67.
37. The human, monoclonal IgG4 bispecific antibody of claim 36, wherein the second binding arm does not comprise a light chain.
38. The human, monoclonal IgG4 bispecific antibody of claim 36, wherein the monovalent second heavy chain comprises a heavy chain-only variable region in a monovalent configuration.
39. The human, monoclonal IgG4 bispecific antibody of claim 36, wherein the monovalent second heavy chain lacks a CH1 domain.

40. A human, monoclonal IgG4 bispecific antibody comprising:
- (i) a first binding arm that binds to human CD3; and
 - (ii) a second binding arm that binds to human CD19,
- wherein the first binding arm comprises a first heavy chain comprising the amino acid sequence of SEQ ID NO: 75 and a light chain comprising the amino acid sequence of SEQ ID NO: 49; and
- wherein the second binding arm comprises a monovalent second heavy chain comprising The amino acid sequence of SEQ ID NO: 78.
41. The human, monoclonal IgG4 bispecific antibody of claim 40, wherein the second binding arm does not comprise a light chain.
42. The human, monoclonal IgG4 bispecific antibody of claim 40, wherein the monovalent second heavy chain comprises a heavy chain-only variable region in a monovalent configuration.
43. The human, monoclonal IgG4 bispecific antibody of claim 40, wherein the monovalent second heavy chain lacks a CH1 domain.