

CLAIMS:

1. An isolated multispecific antibody comprising:
a first heavy chain polypeptide subunit comprising a mutated human IgG4 constant region comprising mutations S228P, F234A, L235A, and T366W; and
a second heavy chain polypeptide subunit comprising 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 first heavy chain polypeptide subunit or the mutated human IgG4 constant region of 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, further comprising a first binding moiety that has binding specificity for CD3, 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 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.
5. The isolated multispecific antibody of claim 4, wherein:
the CDR1, CDR2 and CDR3 sequences in the heavy chain variable domain of the first binding moiety are present in a human VH framework; and
the CDR1, CDR2 and CDR3 sequences in the light chain variable domain of the first binding moiety are present in a human Vkappa framework.
6. The isolated multispecific antibody of claim 5, 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.

7. The isolated multispecific antibody of claim 6, 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.
8. The isolated multispecific antibody of any one of claims 1-7, further comprising a second binding moiety having binding specificity to a protein other than CD3.
9. The isolated multispecific antibody of claim 8, wherein the second binding moiety comprises a single heavy chain variable region, in a monovalent or bivalent configuration.
10. The isolated multispecific antibody of claim 9, wherein the first binding moiety comprises a light chain polypeptide subunit and a heavy chain polypeptide subunit, and wherein the second binding moiety comprises a heavy chain polypeptide subunit.
11. The isolated multispecific antibody of claim 10, wherein the light chain polypeptide subunit of the first binding moiety comprises a light chain constant domain.
12. The isolated multispecific antibody of any one of claims 8-11, wherein the protein other than CD3 is a tumor-associated antigen (TAA) or a tumor-specific antigen (TSA).
13. The isolated multispecific antibody of claim 12, wherein the TAA is B-cell maturation antigen (BCMA).
14. The isolated multispecific antibody of claim 12, wherein the TAA is CD19.
15. The isolated multispecific antibody of claim 12, wherein the TAA is prostate specific membrane antigen (PSMA).

16. A pharmaceutical composition comprising a multispecific antibody according to any one of claims 1-15.
17. A polynucleotide encoding a multispecific antibody according to any one of claims 1-15.
18. A vector comprising a polynucleotide according to claim 17.
19. A cell comprising a vector according to claim 18.
20. A method of producing a multispecific antibody according to any one of claims 1-15, comprising growing a cell according to claim 19 under conditions permissive for expression of the multispecific antibody, and isolating the multispecific antibody from the cell.
21. A method of treatment, comprising administering to an individual in need an effective dose of the multispecific antibody of any one of claims 1-15, or the pharmaceutical composition of claim 16.
22. Use of a multispecific antibody of any one of claims 1-15 in the preparation of a medicament for the treatment of a disease or disorder in an individual in need.
23. The multispecific antibody of any one of claims 1-15, or the pharmaceutical composition of claim 16, for use in therapy in an individual in need.
24. A method for treating a disease or condition characterized by expression of BCMA, comprising administering to an individual in need an effective dose of the multispecific antibody according to claim 13, or a pharmaceutical composition comprising the multispecific antibody of claim 13.
25. The method of claim 24, wherein the disease is an autoimmune disease.
26. The method of claim 24, wherein the disease is a cancer.
27. The method of claim 26, wherein the cancer is a myeloma.
28. The method of claim 27, wherein the myeloma is multiple myeloma.

29. A method for treating a disease or condition characterized by expression of PSMA, comprising administering to an individual in need an effective dose of the multispecific antibody according to claim 15, or a pharmaceutical composition comprising the multispecific antibody of claim 15.
30. The method of claim 29, wherein the disease is a cancer.
31. The method of claim 29, wherein the cancer is prostate cancer.
32. A method for treating a disease or condition characterized by expression of CD19, comprising administering to an individual in need an effective dose of the multispecific antibody according to claim 14, or a pharmaceutical composition comprising the multispecific antibody of claim 14.
33. The method of claim 32, wherein the disorder is diffuse large B-cell lymphoma (DLBCL).
34. The method of claim 32, wherein the disorder is acute lymphoblastic leukemia (ALL).
35. The method of claim 32, wherein the disorder is non-Hodgkin's lymphoma (NHL).
36. The method of claim 32, wherein the disorder is systemic lupus erythematosus (SLE).
37. The method of claim 32, wherein the disorder is rheumatoid arthritis (RA).
38. The method of claim 32, wherein the disorder is multiple sclerosis (MS).
39. A kit for treating a disease or disorder in an individual in need, comprising a multispecific antibody of any one of claims 1-15, or the pharmaceutical composition of claim 16, and instructions for use.
40. The kit of claim 39, further comprising at least one additional reagent.
41. The kit of claim 40, wherein the at least one additional reagent comprises a chemotherapeutic drug.
42. A bispecific three-chain antibody like molecule comprising:
a first polypeptide subunit comprising:

- a light chain variable domain (VL) comprising a sequence of SEQ ID NO: 43; and
 - a light chain constant domain (CL);
 - a second polypeptide subunit comprising:
 - a heavy chain variable domain (VH) comprising a sequence of SEQ ID NO: 42; and
 - a heavy chain constant domain (CH) comprising a sequence of SEQ ID NO: 72 or 73;
 - wherein the light chain variable domain and the heavy chain variable domain together form a first binding moiety that binds to CD3; and
 - a third polypeptide subunit comprising:
 - a heavy chain-only variable region, in a monovalent or bivalent configuration, that binds to a protein other than CD3; and
 - a heavy chain constant domain (CH) comprising a sequence of SEQ ID NO: 54 or 55.
43. The bispecific three-chain antibody like molecule of claim 42, wherein the third polypeptide subunit comprises a heavy chain-only variable region in a bivalent configuration that binds to BCMA.
44. The bispecific three-chain antibody like molecule of claim 43, comprising:
 - a first polypeptide subunit comprising a sequence of SEQ ID NO: 49;
 - a second polypeptide subunit comprising a sequence of SEQ ID NO: 56; and
 - a third polypeptide subunit comprising a sequence of SEQ ID NO: 58.
45. A pharmaceutical composition comprising the bispecific three-chain antibody like molecule of any one of claims 42-44.
46. A polynucleotide encoding a bispecific three-chain antibody like molecule according to any one of claims 42-44.
47. A vector comprising a polynucleotide according to claim 46.
48. A cell comprising a vector according to claim 47.
49. A method of producing a bispecific three-chain antibody like molecule according to any one of claims 42-44, comprising growing a cell according to claim 48 under conditions permissive for expression of the bispecific three-chain antibody like molecule, and isolating the bispecific three-chain antibody like molecule from the cell.

50. A method of treatment, comprising administering to an individual in need an effective dose of the bispecific three-chain antibody like molecule of any one of claims 42-44, or the pharmaceutical composition of claim 45.
51. Use of a bispecific three-chain antibody like molecule of any one of claims 42-44 in the preparation of a medicament for the treatment of a disease or disorder in an individual in need.
52. The bispecific three-chain antibody like molecule of any one of claims 42-44, or the pharmaceutical composition of claim 45, for use in therapy in an individual in need.
53. A method for treating a disease or condition characterized by expression of BCMA, comprising administering to an individual in need an effective dose of the bispecific three-chain antibody like molecule according to any one of claims 42-44, or the pharmaceutical composition of claim 45.
54. The method of claim 53, wherein the disease is an autoimmune disease.
55. The method of claim 53, wherein the disease is a cancer.
56. The method of claim 55, wherein the cancer is a myeloma.
57. The method of claim 56, wherein the myeloma is multiple myeloma.
58. A kit for treating a disease or disorder in an individual in need, comprising a bispecific three-chain antibody like molecule of any one of claims 42-44, or the pharmaceutical composition of claim 45, and instructions for use.
59. The kit of claim 58, further comprising at least one additional reagent.
60. The kit of claim 59, wherein the at least one additional reagent comprises a chemotherapeutic drug.