

Claims

1. An IgM, IgA, IgG/IgM, or IgG/IgA antibody comprising a modified J-chain, wherein the modified J-chain comprises an extraneous binding moiety introduced into a native sequence J-chain, wherein the IgG/IgM or IgG/IgA antibody is a hybrid antibody comprising an IgM or IgA tailpiece at the IgG heavy chain, conferring the ability to incorporate and form polymers with the modified J-chain.
2. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 1, wherein the native sequence J-chain is the native human J-chain sequence of SEQ ID NO: 1, or a functional fragment thereof.
3. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 2, wherein the native sequence J-chain is the native human J-chain sequence of SEQ ID NO: 1.
4. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 3, wherein the extraneous binding moiety is introduced into the native human J-chain sequence of SEQ ID NO: 1 by direct or indirect fusion.
5. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 4, wherein the binding moiety is introduced by indirect fusion through a peptide linker.
6. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 5, wherein the indirect fusion is through a peptide linker at or around the C- and/or N-terminus of the binding moiety.
7. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 6, wherein the extraneous binding moiety is introduced into the native human J-chain sequence of SEQ ID NO: 1 at or around the C-terminus.
8. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 7, wherein the extraneous binding moiety is introduced into the native human J-chain sequence of SEQ ID NO: 1 within about 10 residues from the C-terminus.

9. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 6, wherein the extraneous binding moiety is introduced into the native human J-chain sequence of SEQ ID NO: 1 at or around the N-terminus.

10. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 9, wherein the extraneous binding moiety is introduced into the native human J-chain sequence of SEQ ID NO: 1 within about 10 amino acid residues from the N-terminus.

11. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 5, wherein the extraneous binding moiety is introduced into the native human J-chain sequence in between cysteine residues 92 and 101 of SEQ ID NO: 1.

12. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 5, wherein the extraneous binding moiety is introduced into the native human J-chain sequence of SEQ ID NO: 1 at or near a glycosylation site.

13. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 5, wherein said peptide linker is about 10 to 20 amino acids long.

14. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 13, wherein said peptide linker is about 15 to 20 amino acids long.

15. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 14, wherein said peptide linker is 15 amino acids long.

16. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 3, wherein the extraneous binding moiety is introduced into the native human J-chain sequence of SEQ ID NO: 1 by chemical or chemo-enzymatic derivatization.

17. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 16, wherein the extraneous binding moiety is introduced into the native human J-chain sequence of SEQ ID NO: 1 by a chemical linker.

18. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 17, wherein the chemical linker is a cleavable or non-cleavable linker.

19. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 18, wherein the cleavable linker is a chemically labile linker or an enzyme-labile linker.

20. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 18, wherein the linker is selected from the group consisting of N-succinimidyl-3-(2-pyridyldithio) propionate (SPDP), succinimidyl-4-(N-maleimidomethyl) cyclohexane-1-carboxylate (SMCC), N-succinimidyl-4-(2-pyridylthio) pentanoate (SPP), iminothiolane (IT), bifunctional derivatives of imidoesters, active esters, aldehydes, bis-azido compounds, bis-diazonium derivatives, diisocyanates, and bis-active fluorine compounds.

21. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 16, modified by insertion of an enzyme recognition site, and by post-translationally attaching an extraneous binding moiety at the enzyme recognition site through a peptide or non-peptide linker.

22. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of any one of claims 1 to 21, wherein the extraneous binding moiety is selected from the group consisting of antibodies, antigen-binding fragments of antibodies, antibody-drug conjugates, antibody-like molecules, antigen-binding fragments of antibody-like molecules, soluble and membrane-bound proteins, ligands, receptors, virus-like particles, protein toxins, enzymes, and alternative scaffolds.

23. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 22, wherein the alternative scaffold is selected from the group consisting of darpins, fibronectin domains, adnectins, and knottins.

24. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 22, wherein the antigen-binding fragment is selected from the group consisting of F(ab')₂, F(ab)₂, Fab', Fab, Fv, scFv, and single domain antibody.

25. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 24, wherein the antigen-binding fragment is scFv.

26. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of any one of claims 1 to 21, wherein the extraneous binding moiety binds to an effector cell.

27. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 26, wherein the effector cell is selected from the group consisting of T-cells, natural killer (NK) cells, macrophages and neutrophils.
28. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 27, wherein the effector cell is a T-cell.
29. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 28, wherein the extraneous binding moiety binds to CD3 ϵ on the T-cell.
30. The antibody of claim 29, wherein the modified J-chain comprises the amino acid sequence SEQ ID NO: 50 (V15J).
31. The antibody of claim 29, wherein the modified J-chain comprises the amino acid sequence SEQ ID NO: 51 (J15V).
32. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 27, wherein the effector cell is an NK cell.
33. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 32, wherein the extraneous binding moiety binds a target selected from the group consisting of CD16, CD64 and NKG2D on the NK cell.
34. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 27, wherein the effector cell is a macrophage.
35. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 34, wherein the extraneous binding moiety binds to CD14 on the macrophage.
36. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 27, wherein the effector cell is a neutrophil.
37. The IgM, IgA, IgG/IgM, or IgG/IgA antibody of claim 36, wherein the extraneous binding moiety binds to CD16b or CD177 on the neutrophil.
38. The antibody of any one of claims 1 to 37, which is an IgM antibody.

39. The antibody of any one of claims 1 to 37, which is an IgA antibody.
40. The antibody of any one of claims 1 to 39, which is bispecific.
41. The antibody of any one of claims 1 to 39, which is multi-specific.
42. The antibody of any one of claims 1-41, wherein said antibody has binding specificity to one or more binding targets selected from the group consisting of: target cells, soluble binding targets, cell surface receptors, matrix proteins, and transporter receptors.
43. The antibody of any one of claims 1-41, wherein said antibody binds to a tumor cell.
44. The antibody of any one of claims 1-41, wherein said antibody binds to a tumor target associated antigen listed in FIG. 19.
45. The antibody of claim 44, wherein the J-chain is modified to bind any of the effector cell targets listed in FIG. 19.
46. The antibody of claim 43, wherein the tumor cell is a hematologic cancer cell or a solid tumor cell.
47. The antibody of claim 46, wherein the hematologic cancer cell is from a hematologic cancer selected from the group consisting of: leukemia, lymphoma, myeloma, and myelodysplastic syndrome.
48. The antibody of claim 47, wherein the leukemia is acute myeloid leukemia, acute lymphoblastic leukemia, chronic myelogenous leukemia, or chronic lymphocytic leukemia.
49. The antibody of claim 47, wherein the lymphoma is Hodgkin's lymphoma or non-Hodgkin's lymphoma.
50. The antibody of claim 46, wherein the antibody binds to one or more of CD11A, CD19, CD20, CD22, CD33, CD70, CD56, CD138.
51. The antibody of claim 50, wherein the modified J-chain binds to CD3ε.

52. The antibody of claim 51, wherein the antibody binds to CD20 and the modified J-chain binds CD3ε.

53. The antibody of claim 46, wherein the solid tumor cell is from an epithelial cancer.

54. The antibody of claim 53, wherein the epithelial cancer is a biliary, breast, cervical, colorectal, endometrial, esophageal, gastric, head and neck, lung, medullary thyroid, renal, ovarian, pancreatic, liver, prostate, or urinary bladder cancer.

55. The antibody of claim 46, wherein the solid tumor cell is a melanoma tumor cell.

56. The antibody of claim 46, wherein the solid tumor cell is a glioma tumor cell.

57. The antibody of claim 43, wherein the antibody binds to a carbohydrate-based target on the tumor cell.

58. The antibody of any one of claims 1-41, wherein the antibody binds to a viral antigen.

59. The antibody of claim 58, wherein the viral antigen is an HBV antigen or an HIV antigen.

60. The antibody of claim 59, wherein the viral antigen is PreS1.

61. The antibody of claim 59, wherein the viral antigen is GP120.

62. A composition comprising the antibody of any one of the previous claims.

63. The composition of claim 62, which is a pharmaceutical composition, additionally comprising a pharmaceutically acceptable carrier.

64. The composition of claim 62, which is a diagnostic composition.

65. Use of an antibody according to any one of claims 1-61 in the preparation of a medicament for the treatment of a cancer or viral disease.