

ANTI-CD19 ANTIBODIES AND METHODS OF MAKING AND USING THEREOF**CLAIMS**

What is claimed is:

1. A peptide having a binding specificity to human CD19, comprising an amino acid sequence having at least 98% of sequence identity to SEQ ID NO. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 91, or 93.
2. A scFv peptide, comprising the peptide of Claim 1.
3. The scFv peptide of Claim 2, having a binding affinity to human CD19 with a K_D not greater than 10nM.
4. An antibody having a binding specificity to human CD19, wherein the antibody comprises the peptide of Claim 1.
5. The antibody of Claim 4, wherein the antibody is a multi-specific antibody.
6. The antibody of Claim 4, comprising a scFv, wherein the scFv comprises the peptide of Claim 1.
7. The antibody of Claim 4, comprising a Fab, wherein the Fab comprises the peptide of Claim 1.
8. A multi-specific antibody-like protein comprising the peptide of Claim 1, wherein the multi-specific antibody-like protein has a N-terminal and a C-terminal, comprising in tandem from the N-terminal to the C-terminal, a first binding domain (D1) at the N-terminal,
a second binding domain (D2) comprising a light chain moiety,
a Fc region,
a third binding domain (D3), and
a fourth binding domain (D4) at the C-terminal,
wherein the light chain moiety comprises a fifth binding domain (D5) covalently attached to the C-terminal, a sixth binding domain (D6) covalently attached to the N-terminal, or both, and
wherein the D1, D2, D3, D4, D5 and D6 each has a binding specificity to a tumor antigen, an immune signaling antigen, or a combination thereof.
9. The multi-specific antibody-like protein of Claim 8, wherein D1 comprises the peptide of Claim 1.
10. The multi-specific antibody-like protein of Claim 8, wherein D1 comprises a peptide having an amino acid sequence with 95% sequence identity to SEQ ID NO. 7 or 19.
11. The multi-specific antibody-like protein of Claim 8, wherein D2 comprises the peptide of Claim 1.
12. The multi-specific antibody-like protein of Claim 8, wherein D2 comprises a peptide having an amino acid sequence with 95% sequence identity to SEQ ID NO. 91 or 93.
13. The multi-specific antibody-like protein of Claim 8, wherein D6 comprises the peptide of Claim 1.
14. The multi-specific antibody-like protein of Claim 8, wherein D6 comprises a peptide having an amino acid sequence with 95% sequence identity to SEQ ID NO. 7 or 19.

15. A multi-specific monoclonal antibody, comprising the multi-specific antibody-like protein of Claim 8.
16. The multi-specific monoclonal antibody of Claim 15, having a binding affinity to human CD19 with a K_d not greater than 10nM.
17. The multi-specific monoclonal antibody of Claim 15, wherein the antibody is a humanized antibody.
18. The multi-specific monoclonal antibody of Claim 15, wherein the antibody is an IgG.
19. An isolated nucleic acid sequence, encoding an amino acid sequence of the multi-specific monoclonal antibody of Claim 15.
20. An expression vector comprising the isolated nucleic acid of Claim 19.
21. A host cell comprising the nucleic acid of Claim 19, wherein the host cell is a prokaryotic cell or a eukaryotic cell.
22. A method of producing an antibody comprising culturing the host cell of Claim 21 so that the antibody is produced.
23. An immune-conjugate, comprising the multi-specific monoclonal antibody of Claim 15 and a drug unit, wherein the drug unit is linked to the multi-specific monoclonal antibody through a linker, and wherein the linker comprises a covalent bond selected from an ester bond, an ether bond, an amine bond, an amide bond, a disulfide bond, an imide bond, a sulfone bond, a phosphate bond, a phosphorus ester bond, a peptide bond, a hydrazone bond or a combination thereof.
24. The immune-conjugate of Claim 23, wherein the drug unit comprises a cytotoxic agent, an immune regulatory reagent, an imaging agent or a combination thereof.
25. The immune-conjugate of Claim 24, wherein the cytotoxic agent is selected from a growth inhibitory agent or a chemotherapeutic agent from a class of tubulin binders, DNA intercalators, DNA alkylators, enzyme inhibitors, immune modulators, antimetabolite agents, radioactive isotopes, or a combination thereof.
26. The immune-conjugate of Claim 24, wherein the cytotoxic agent is selected from a calicheamicin, camptothecin, ozogamicin, monomethyl auristatin E, emtansine, a derivative or a combination thereof.
27. The immune-conjugate of Claim 24, wherein the immune regulatory reagents activate or suppress immune cells, T cell, NK cell, B cell, macrophage, or dendritic cell.
28. The immune-conjugate of Claim 24, wherein the imaging agent may be radionuclide, a fluorescent agent, a quantum dots, or a combination thereof.
29. A pharmaceutical composition, comprising the multi-specific monoclonal antibody of Claim 15 and a pharmaceutically acceptable carrier.
30. The pharmaceutical composition of Claim 29, further comprising a chemotherapeutic agent, a growth inhibitory agent, a cytotoxic agent from class of calicheamicin, an antimitotic agent, a toxin, a radioactive isotope, a therapeutic agent, or a combination thereof.

31. A pharmaceutical composition, comprising the immune-conjugate of Claim 24 and a pharmaceutically acceptable carrier.
32. A method of treating a subject with a cancer, comprising administering to the subject an effective amount of the multi-specific monoclonal antibody of Claim 15.
33. The method of Claim 32, further comprising co-administering an effective amount of a therapeutic agent, wherein the therapeutic agent comprises an antibody, a chemotherapy agent, an enzyme, or a combination thereof.
34. The method of Claim 33, wherein the subject is a human.
35. A solution comprising an effective concentration of the multi-specific monoclonal antibody of Claim 15, wherein the solution is blood plasma in a subject.