

CLAIMS

What is claimed is:

1. A humanized antibody that binds specifically to human complement factor Bb protein and comprises a heavy chain variable region (V_H) comprising the amino acid sequence of SEQ ID NO: 19 and a light chain variable region (V_L) comprising the amino acid sequence of SEQ ID NO: 27.

2. A humanized antibody that binds specifically to human complement factor Bb protein and comprises a heavy chain variable region (V_H) comprising the amino acid sequence of SEQ ID NO: 17 and a light chain variable region (V_L) comprising the amino acid sequence of SEQ ID NO: 26.

3. The humanized antibody of claim 1 or claim 2, wherein the humanized antibody binds specifically to the human complement factor Bb protein with an affinity of 10^{-6} to 10^{-9} M.

4. The humanized antibody of any one of claims 1-3, wherein the humanized antibody inhibits a complement pathway activity.

5. The humanized antibody of claim 4, wherein the complement activity is selected from the group consisting of: AP-mediated terminal membrane attack complex (MAC) deposition, AP-mediated hemolysis, C3 fragment deposition on red blood cells or other cell types, C3b/Bb-mediated cleavage of C3, and C3bBb3b-mediated cleavage of C5.

6. The humanized antibody of any one of claims 1-5, wherein the humanized antibody is a bispecific antibody or a multispecific antibody.

7. The humanized antibody of any one of claims 1-6, wherein the humanized antibody is selected from the group consisting of an Ig monomer, a Fab fragment, a $F(ab')_2$ fragment, a scFv, a scAb, and a Fv.

8. The humanized antibody of any one of claims 1-6, wherein the humanized antibody comprises a heavy chain constant region of the isotype IgG1, IgG2, IgG3, or IgG4.

9. The humanized antibody of claim 8, wherein the humanized antibody comprises an IgG4 constant region or a variant thereof.

10. The humanized antibody of claim 9, wherein the heavy chain constant region comprises an amino acid sequence that is at least 90% identical to any one of SEQ ID NOs: 28-30.

11. The humanized antibody of any one of claims 1 and 3-10, wherein the humanized antibody comprises a heavy chain comprising the amino acid sequence of any one of SEQ ID NOs: 32-34 and a light chain comprising the amino acid sequence of SEQ ID NO: 35.

12. The humanized antibody of any one of claims 2-10, wherein the humanized antibody comprises a heavy chain comprising the amino acid sequence of any one of SEQ ID NOs: 36-38 and a light chain comprising the amino acid sequence of SEQ ID NO: 39.

13. A conjugate comprising the humanized antibody of any one of claims 1-12.

14. A pharmaceutical composition comprising the humanized antibody of any one of claims 1-12 or the conjugate of claim 13.

15. The pharmaceutical composition of claim 14, further comprising a pharmaceutically acceptable excipient.

16. A device comprising the humanized antibody of any one of claims 1-12, the conjugate of claim 13, or the pharmaceutical composition of claim 14 or claim 15.

17. The device of claim 16, wherein the device is an injectable device.

18. The device of claim 17, wherein the injectable device is a syringe, a pen, or an electronic injection device (e-Device).

19. ~~A method of treating a subject having a complement-mediated disease or disorder, the method comprising: administering to the subject~~ Use of an effective amount of the humanized antibody of any one of claims 1-~~13~~12, the conjugate of claim ~~14~~13, or the pharmaceutical composition of claim ~~15-14~~ or ~~16-15~~ in the manufacture of a medicament for treating to treat the a complement-mediated disease or disorder in a subject.

20. The ~~method-use~~ of claim 19, wherein the complement-mediated disease is selected from the group consisting of: IgA nephropathy (Berger's disease), atypical hemolytic uremic syndrome (aHUS), paroxysmal nocturnal hemoglobinuria (PNH), idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP), lupus nephritis, ANCA vasculitis, membranous nephropathy, C3 glomerulonephritis (C3GN), focal segmental glomerulosclerosis (FSGS), multiple sclerosis, macular degeneration, age-related macular degeneration (AMD), rheumatoid arthritis, antiphospholipid antibody syndrome, asthma, ischemia-reperfusion injury, Type II membranoproliferative GN, spontaneous fetal loss, Pauci-immune vasculitis, epidermolysis bullosa, recurrent fetal loss, and traumatic brain injury.

21. ~~A method of inhibiting a complement pathway activity in a subject, the method comprising administering to the subject~~ Use of an effective amount of the humanized antibody of any one of claims 1-~~13~~12, the conjugate of claim ~~14~~13, or the pharmaceutical composition of claim ~~15-14~~ or ~~16-15~~ in the manufacture of a medicament for inhibiting a complement pathway activity in a subject ~~to inhibit the complement activity~~.

22. The ~~method-use~~ of claim 21, wherein the subject has a complement-mediated disease or disorder.

23. The ~~method-use~~ of claim 22, wherein the complement-mediated disease is selected from the group consisting of: IgA nephropathy (Berger's disease), atypical hemolytic uremic syndrome (aHUS), paroxysmal nocturnal hemoglobinuria (PNH), idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP), lupus nephritis, ANCA vasculitis, membranous nephropathy, C3 glomerulonephritis (C3GN), focal segmental glomerulosclerosis (FSGS), multiple sclerosis, macular degeneration, age-related macular degeneration (AMD), rheumatoid arthritis, antiphospholipid antibody syndrome, asthma, ischemia-reperfusion injury, Type II membranoproliferative GN, spontaneous fetal

loss, Pauci-immune vasculitis, epidermolysis bullosa, recurrent fetal loss, and traumatic brain injury.

24. The ~~method-use~~ of any one of claims 21-23, wherein the complement activity is selected from the group consisting of: AP-mediated terminal membrane attack complex (MAC) deposition, AP-mediated hemolysis, C3 fragment deposition on red blood cells or other cell types, C3b/Bb-mediated cleavage of C3, and C3bBb3b-mediated cleavage of C5.

25. The ~~method-use~~ of any one of claims 19-24, ~~wherein further comprising administering to the subject~~ a therapeutic agent is to be administered to the subject.

26. The ~~method-use~~ of any one of claims 19-25, wherein the humanized antibody, the conjugate, the pharmaceutical composition, or the administering ~~is~~ therapeutic agent is to be administered intravenously, subcutaneously, or intramuscularly.

27. A nucleic acid or nucleic acid set encoding or collectively encoding the humanized antibody of any one of claims 1-12.

28. A vector or vector set comprising the nucleic acid or nucleic acid set of claim 27.

29. A cell expressing the humanized antibody of any one of claims 1-3, the nucleic acid or nucleic acid set of claim 27, or the vector or vector set of claim 28.

30. The cell of claim 29, wherein the cell is a mammalian cell.

31. The cell of claim 30, wherein the mammalian cell is selected from the group consisting of: human embryonic kidney (HEK) cells, Chinese hamster ovary (CHO) cells, NS0 myeloma cells, SP2 cells, COS cells, and mammary epithelial cells.

32. A method of producing the humanized antibody, comprising culturing the cell of any one of claims 29-31 to produce the humanized antibody.

33. The method of claim 32, further comprising isolating the humanized antibody.