Claims

1. A humanized antibody that specifically binds complement component Cl s, wherein the

antibody comprises:

a) a VH region comprising the amino acid sequence:

(Q/E)VQL(V/Q)QSGAE(V/L)KKPGASVK(LN)SC(T/A)ASGFNIKDDYIHWV(K/R)QAP GQGLEWI

GRIDPADGHTKYAPKFQVK(V/A)TITADTST(S/N)TAY(L/M)(E/Q)LSSL(R/T)SEDTAV YYCARY GYGREVFDYWGQGTTVTVSS (SEQ ID NO:26); and

b) a VL region comprising the amino acid sequence:

DIVLTQSPDSLAVSLGERATISCKASQSVDYDGDSYMNWYQQK(T/P)GQPPK(I/L) LIYDASNLES

GIPARFSGSGSGTDFTLTISSLE(E/P)EDFA(I/V)YYCQQSNEDPWTFGGGTKVEIK (SEQ ID NO:27).

2. The humanized antibody of claim 1, wherein the antibody is selected from the group consisting of:

a) an antibody comprising a VH region comprising the amino acid sequence set forth in SEQ ID NO:14 and a VL region comprising the amino acid sequence set forth in SEQ ID NO:22;

b) an antibody comprising a VH region comprising the amino acid sequence set forth in SEQ ID NO:10 and a VL region comprising the amino acid sequence set forth in SEQ ID NO:20;

c) an antibody comprising a VH region comprising the amino acid sequence set forth in SEQ ID NO:10 and a VL region comprising the amino acid sequence set forth in SEQ ID NO:22;

d) an antibody comprising a VH region comprising the amino acid sequence set forth in SEQ ID NO:10 and a VL region comprising the amino acid sequence set forth in SEQ ID NO:24;

e) an antibody comprising a VH region comprising the amino acid sequence set forth in SEQ ID NO:12 and a VL region comprising the amino acid sequence set forth in SEQ ID NO:20;

f) an antibody comprising a VH region comprising the amino acid sequence set forth in SEQ ID NO:12 and a VL region comprising the amino acid sequence set forth in SEQ ID NO:22;

g) an antibody comprising a VH region comprising the amino acid sequence set forth in SEQ ID NO:12 and a VL region comprising the amino acid sequence set forth in SEQ ID NO:24;

h) an antibody comprising a VH region comprising the amino acid sequence set forth in SEQ ID NO:14 and a VL region comprising the amino acid sequence set forth in SEQ ID NO:20;

i) an antibody comprising a VH region comprising the amino acid sequence set forth in SEQ ID NO:14 and a VL region comprising the amino acid sequence set forth in SEQ ID NO:24;

j) an antibody comprising a VH region comprising the amino acid sequence set forth in SEQ ID NO:16 and a VL region comprising the amino acid sequence set forth in SEQ ID NO:20;

k) an antibody comprising a VH region comprising the amino acid sequence set forth in SEQ ID NO:16 and a VL region comprising the amino acid sequence set forth in SEQ ID NO:22;

l) an antibody comprising a VH region comprising the amino acid sequence set

forth in SEQ ID NO:16 and a VL region comprising the amino acid sequence set forth in SEQ ID NO:24;

m) an antibody comprising a VH region comprising the amino acid sequence set forth in SEQ ID NO:18 and a VL region comprising the amino acid sequence set forth in SEQ ID NO:20;

n) an antibody comprising a VH region comprising the amino acid sequence set forth in SEQ ID NO:18 and a VL region comprising the amino acid sequence set forth in SEQ ID NO:22; and

o) an antibody comprising a VH region comprising the amino acid sequence set forth in SEQ ID NO:18 and a VL region comprising the amino acid sequence set forth in SEQ ID NO:24.

3. The humanized antibody of claim 1, wherein the humanized antibody is a Fab fragment, a $F(ab')_2$ fragment, a scFv, and a Fv.

4. The humanized antibody of claim 1, wherein the humanized antibody comprises a heavy chain constant region of the isotype IgGl, IgG2, IgG3, or IgG4.

5. A composition comprising:

a) the humanized antibody of any one of claim 1; and

b) a pharmaceutically acceptable excipient.

6. The composition of claim 5, wherein the composition comprises one or more of a

tonicity agent, a suspending agent, an emulsifying agent, a stabilizer, a preservative, a lyoprotectant, a surfactant, and a sugar.

7. A method of reducing the level of a complement component cleavage product in a human, the method comprising administering to the human the composition of

claim 5, in an amount effective to inhibit Cls and to reduce the level of the cleavage product.

8. The method of claim 7, wherein the administering is selected from the group consisting of intravenously administering, intramuscularly administering, intrathecally administering, and subcutaneously administering.

9. A method of inhibiting C1s-mediated cleavage of a complement component in a human, the method comprising administering to the human the composition of claim 5 in an amount effective to inhibit C1s-mediated cleavage of a complement component.

10. A method comprising administering to a human a composition comprising a humanized antibody that specifically binds complement component C1s, wherein the antibody comprises:

a) a VH region comprising the amino acid sequence: (Q/E)VQL(V/Q)QSGAE(V/L)KKPGASVK(L/V)SC(T/A)ASGFNIKDDYIHWV(K/R)QAPGQGLEWIGRIDPADGHTKYAPKFQVK(V/A)TITADTST(S/N)TAY(L/M)(E/Q)LSSL(R/T)SEDTAVYYCARYGYGREVFDYWGQGTTVTVSS (SEQ ID NO:26); and

b) a VL region comprising the amino acid sequence: DIVLTQSPDSLAVSLGERATISCKASQSVDYDGDSYMNWYQQK(T/P)GQPPK(I/L)LIYDASNLESGIPARFSGSGSGTDFTLTISSLE(E/P)EDFA(I/V)YYCQQSNEDPWTFGGGTKVEIK (SEQ ID NO:27).

11. The method of claim 9, wherein the human has Alzheimer's disease, amyotrophic lateral sclerosis, anaphylaxis, argyrophilic grain dementia, arthritis, asthma, atherosclerosis,

atypical hemolytic uremic syndrome, autoimmune diseases, Barraquer-Simons syndrome, Behçet's disease, British type amyloid angiopathy, bullous pemphigoid, Buerger's disease, C1q nephropathy, cancer, catastrophic antiphospholipid syndrome, cerebral amyloid angiopathy, cold agglutinin disease, corticobasal degeneration, Creutzfeldt-Jakob disease, Crohn's disease, cryoglobulinemic vasculitis, dementia pugilistica, dementia with Lewy Bodies (DLB), diffuse neurofibrillary tangles with calcification, Discoid lupus erythematosus, Down's syndrome, Evan's syndrome, focal segmental glomerulosclerosis, formal thought disorder, frontotemporal dementia (FTD), frontotemporal dementia with parkinsonism linked to chromosome 17, frontotemporal lobar degeneration, Gerstmann-Straussler-Scheinker disease, Guillain-Barré syndrome, Hallervorden-Spatz disease, hemolytic-uremic syndrome, hereditary angioedema, hypophosphastasis, idiopathic pneumonia syndrome, immune complex diseases, inclusion body myositis, infectious disease, inflammatory disease, ischemia/reperfusion injury, mild cognitive impairment, immunothrombocytopenic purpura (ITP), molybdenum cofactor deficiency (MoCD) type A, membranoproliferative glomerulonephritis (MPGN) I, membranoproliferative glomerulonephritis (MPGN) II (dense deposit disease), membranous nephritis, multi-infarct dementia, lupus, glomerulonephritis, Kawasaki disease, multifocal motor neuropathy, multiple sclerosis, multiple system atrophy, myasthenia gravis, myocardial infarction, myotonic dystrophy, neuromyelitis optica, Niemann-Pick disease type C, non-Guamanian motor neuron disease with neurofibrillary tangles, Parkinson's disease, Parkinson's disease with dementia, paroxysmal nocturnal hemoglobinuria, Pemphigus vulgaris, Pick's disease, postencephalitic parkinsonism, polymyositis, prion protein cerebral amyloid angiopathy, progressive, subcortical gliosis, progressive supranuclear palsy, psoriasis, sepsis, Shiga-toxin E coli (STEC)-HuS, spinal muscular atrophy, stroke, subacute sclerosing panencephalitis, Tangle only dementia, transplant rejection, vasculitis, Wegner's granulomatosis, sickle cell

disease, cryoglobulinemia, mixed cryoglobulinemia, essential mixed cryoglobulinemia, Type II mixed cryoglobulinemia, Type III mixed cryoglobulinemia, nephritis, drug-induced thrombocytopenia, lupus nephritis, Epidermolysis bullosa acquisita, delayed hemolytic transfusion reaction, hypocomplementemic urticarial vasculitis syndrome, pseudophakic bullous keratopathy, or platelet refractoriness.

12. The method of claim 10, wherein the administering is selected from the group consisting of intravenously administering, intramuscularly administering, intrathecally administering, and subcutaneously administering.

13. A humanized antibody that specifically binds complement component C1s, wherein the antibody comprises a VH region comprising the amino acid sequence set forth in SEQ ID NO:14 and a VL region comprising the amino acid sequence set forth in SEQ ID NO:22.

14. The method of claim 10, wherein the human has cold agglutinin disease.

15. The method of claim 10, wherein the human has immunothrombocytopenic purpura (ITP).

16. The method of claim 10, wherein the human has bullous pemphigoid.

17. The method of claim 10, wherein the human has multifocal motor neuropathy.

18. The method of claim 10, wherein the human has an autoimmune disease.

19. The method of claim 10, wherein the human has antibody-mediated transplant rejection.

20. The method of claim 10, wherein the human has rheumatoid arthritis.

21. The humanized antibody of claim 13, wherein the antibody further comprises a heavy chain constant region of the isotype IgG4.

22. The humanized antibody of claim 13, wherein the humanized antibody is a Fab fragment, a F(ab')2 fragment, a scFv, or a Fv.

23. A composition comprising:

a) the humanized antibody of claim 13; and

b) a pharmaceutically acceptable excipient.

24. The composition of claim 23, wherein the composition comprises one or more of a tonicity agent, a suspending agent, an emulsifying agent, a stabilizer, a preservative, a lyoprotectant, a surfactant, and a sugar.

25. A method comprising administering to a human a humanized antibody that specifically binds complement component C1s, wherein the antibody comprises a VH region comprising the amino acid sequence set forth in SEQ ID NO:14 and a VL region comprising the amino acid sequence set forth in SEQ ID NO:22.

26. The method of claim 25, wherein the antibody further comprises a heavy chain

constant region of the isotype IgG4.

27. The method of claim 25, wherein the administering is selected from the group consisting of intravenously administering, intramuscularly administering, intrathecally administering, and subcutaneously administering.

28. The method of claim 25, wherein the human has cold agglutinin disease.

29. The method of claim 25, wherein the human has immunothrombocytopenic purpura (ITP).

30. The method of claim 25, wherein the human has bullous pemphigoid.

31. The method of claim 25, wherein the human has multifocal motor neuropathy.

32. The method of claim 25, wherein the human has an autoimmune disease.

33. The method of claim 25, wherein the human has antibody-mediated transplant rejection.

34. The method of claim 25, wherein the human has rheumatoid arthritis.

35. One or more nucleic acids encoding the humanized antibody of claim 1.

36. A vector comprising the one or more nucleic acids of claim 35.

37. An isolated host cell comprising the vector of claim 36.

38. The isolated host cell of claim 37, wherein the cell is a mammalian cell, an insect host cell, a yeast cell, or a prokaryotic cell.

39. The isolated host cell of claim 38, wherein the cell is a mammalian cell selected from HeLa cells, CHO cells, 293 cells, Vero cells, NIH 3T3 cells, Huh-7 cells, BHK cells, PC12 cells, COS cells, COS-7 cells, RAT1 cells, mouse L cells, HEK cells, and HLHepG2 cells.

40. A method of producing a humanized antibody that specifically binds complement component C1s, comprising culturing the isolated host cell of claim 37 so that the antibody is produced.

41. The method of claim 40, further comprising recovering the antibody.

42. One or more nucleic acids encoding the humanized antibody of claim 13.

43. A vector comprising the one or more nucleic acids of claim 42.

44. An isolated host cell comprising the vector of claim 43.

45. The isolated host cell of claim 44, wherein the cell is a mammalian cell, an insect host cell, a yeast cell, or a prokaryotic cell.

46. The isolated host cell of claim 45, wherein the cell is a mammalian cell selected from HeLa cells, CHO cells, 293 cells, Vero cells, NIH 3T3 cells, Huh-7 cells, BHK cells, PC12 cells, COS cells, COS-7 cells, RAT1 cells, mouse L cells, HEK cells, and HLHepG2 cells.

47. A method of producing a humanized antibody that specifically binds complement component C1s, comprising culturing the isolated host cell of claim 44 so that the antibody is produced.

48. The method of claim 47, further comprising recovering the antibody.