CLAIMS

~~What is claimed is:~~

1. ~~A humanized antibody that specifically binds to a C1q protein, wherein the antibody comprises a heavy chain variable region and a human heavy chain constant region, wherein the heavy chain variable region comprises an Fab region and the heavy chain constant region comprises an Fc region, wherein the Fab region specifically binds to the C1q protein, and wherein the Fc region is incapable of binding the C1q protein.~~
2. ~~The antibody of claim 1, wherein the Fc region is incapable of inducing complement activity.~~
3. ~~The antibody of claim 1 or claim 2, wherein the Fc region is incapable of inducing antibody-dependent cellular cytotoxicity (ADCC).~~
4. ~~The antibody of any one of claims 1-3, wherein the human heavy chain constant region is a human IgG4 heavy chain constant region.~~
5. ~~The antibody of claim 4, wherein the human IgG4 heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 37, or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 37.~~
6. ~~The antibody of claim 4, wherein the human IgG4 heavy chain constant region comprises an Fc region, and wherein the Fc region comprises one or more modifications.~~
7. ~~The antibody of claim 6, wherein the Fc region comprises one or more amino acid substitutions.~~
8. ~~The antibody of claim 7, wherein the Fc region comprises an amino acid substitution at position 248 according to Kabat numbering convention.~~
9. ~~The antibody of claim 8, wherein the Fc region comprises a leucine to glutamate amino acid substitution at position 248 according to Kabat numbering convention.~~
10. ~~The antibody of claim 8 or claim 9, wherein the amino acid substitution at position 248 according to Kabat numbering convention inhibits the Fc region from interacting with an Fc receptor.~~
11. ~~The antibody of any one of claims 7-10, wherein the Fc region comprises an amino acid substitution at position 241 according to Kabat numbering convention.~~
12. ~~The antibody of claim 11, wherein the Fc region comprises a serine to proline amino acid substitution at position 241 according to Kabat numbering convention.~~

13. The antibody of claim 11 or claim 12, wherein the amino acid substitution at position 241 according to Kabat numbering convention prevents arm switching in the antibody.

14. The antibody of any one of claims 1-13, wherein the antibody comprises a heavy chain variable domain and a light chain variable domain, wherein the heavy chain variable domain comprises an amino acid sequence selected from SEQ ID NOs: 1-4, or an amino acid sequence with at least about 95% homology to the amino acid sequence selected from SEQ ID NOs: 1-4.

15. The antibody of any one of claims 1-14, wherein the light chain variable domain comprises an amino acid sequence selected from SEQ ID NOs: 5-8, or an amino acid sequence with at least about 90% homology to the amino acid sequence selected from SEQ ID NOs: 5-8.

16. A humanized anti-C1q antibody, or an antigen-binding fragment thereof, the antibody comprising a heavy chain variable domain and a light chain variable domain, wherein the heavy chain variable domain comprises an amino acid sequence selected from SEQ ID NOs: 1-4, or an amino acid sequence with at least about 90% homology to the amino acid sequence selected from SEQ ID NOs: 1-4.

17. A humanized anti-C1q antibody, or an antigen-binding fragment thereof, the antibody comprising a heavy chain variable domain and a light chain variable domain, wherein the light chain variable domain comprises an amino acid sequence selected from SEQ ID NOs: 5-8, or an amino acid sequence with at least about 90% homology to the amino acid sequence selected from SEQ ID NOs: 5-8.

18. A humanized anti-C1q antibody, or an antigen-binding fragment thereof, the antibody comprising:

    a) a heavy chain variable domain comprising an amino acid sequence selected from SEQ ID NOs: 1-4, or an amino acid sequence with at least about 90% homology to the amino acid sequence selected from SEQ ID NOs: 1-4; and/or

    b) a light chain variable domain comprising an amino acid sequence selected from SEQ ID NOs: 5-8, or an amino acid sequence with at least about 90% homology to the amino acid sequence selected from SEQ ID NOs: 5-8.

19. A humanized anti-C1q antibody, or an antigen-binding fragment thereof, the antibody comprising:

a) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 1, or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 1; and

b) a light chain variable domain comprising an amino acid sequence selected from SEQ ID NOs: 5-8, or an amino acid sequence with at least about 90% homology to the amino acid sequence selected from SEQ ID NOs: 5-8.

20. A humanized anti-C1q antibody, or an antigen-binding fragment thereof, the antibody comprising:

a) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 2, or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 2; and

b) a light chain variable domain comprising an amino acid sequence selected from SEQ ID NOs: 5-8, or an amino acid sequence with at least about 90% homology to the amino acid sequence selected from SEQ ID NOs: 5-8.

21. A humanized anti-C1q antibody, or an antigen-binding fragment thereof, the antibody comprising:

a) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 3, or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 3; and

b) a light chain variable domain comprising an amino acid sequence selected from SEQ ID NOs: 5-8, or an amino acid sequence with at least about 90% homology to the amino acid sequence selected from SEQ ID NOs: 5-8.

22. A humanized anti-C1q antibody, or an antigen-binding fragment thereof, the antibody comprising:

a) a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 4, or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 4; and

b) a light chain variable domain comprising an amino acid sequence selected from SEQ ID NOs: 5-8, or an amino acid sequence with at least about 90% homology to the amino acid sequence selected from SEQ ID NOs: 5-8.

~~23. A humanized anti-C1q antibody, or an antigen-binding fragment thereof, the antibody comprising:~~

~~a) a heavy chain variable domain comprising an amino acid sequence selected from SEQ ID NOs: 1-4, or an amino acid sequence with at least about 90% homology to the amino acid sequence selected from SEQ ID NOs: 1-4; and~~

~~b) a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 5, or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 5.~~

~~24. A humanized anti-C1q antibody, or an antigen-binding fragment thereof, the antibody comprising:~~

~~a) a heavy chain variable domain comprising an amino acid sequence selected from SEQ ID NOs: 1-4, or an amino acid sequence with at least about 90% homology to the amino acid sequence selected from SEQ ID NOs: 1-4; and~~

~~b) a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 6, or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 6.~~

~~25. A humanized anti-C1q antibody, or an antigen-binding fragment thereof, the antibody comprising:~~

~~a) a heavy chain variable domain comprising an amino acid sequence selected from SEQ ID NOs: 1-4, or an amino acid sequence with at least about 90% homology to the amino acid sequence selected from SEQ ID NOs: 1-4; and~~

~~b) a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 7, or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 7.~~

~~26. A humanized anti-C1q antibody, or an antigen-binding fragment thereof, the antibody comprising:~~

~~a) a heavy chain variable domain comprising an amino acid sequence selected from SEQ ID NOs: 1-4, or an amino acid sequence with at least about 90% homology to the amino acid sequence selected from SEQ ID NOs: 1-4; and~~

~~b) a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 8, or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 8.~~

27. The antibody or antigen-binding fragment of any one of claims 1-26, wherein the antibody binds specifically to both human C1q and mouse C1q.

28. The antibody or antigen-binding fragment of any one of claims 1-26, wherein the antibody binds specifically to rat C1q.

29. The antibody or antigen-binding fragment of any one of claims 1-26, wherein the antibody binds specifically to human C1q, mouse C1q, and rat C1q.

30. The antibody or antigen-binding fragment of any one of claims 1-26, wherein the antibody or antigen-binding fragment thereof binds essentially the same C1q epitope as the antibody M1 produced by the hybridoma cell line with ATCC Accession Number PTA-120399 or anti-C1q binding fragments thereof.

31. The antibody or antigen-binding fragment of any one of claims 1-26, wherein the antibody or antigen-binding fragment thereof inhibits the binding of the monoclonal antibody M1 produced by a hybridoma cell line with ATCC Accession Number PTA-120399 to human C1q or to mouse C1q.

32. The antibody or antigen-binding fragment of any one of claims 1-31, wherein the antibody is of the IgG class.

33. The antibody or antigen-binding fragment of claim 32, wherein the antibody has an IgG1, IgG2, IgG3, or IgG4 isotype.

34. The antibody or antigen-binding fragment of claim 32, wherein the antibody has an IgG_4 isotype.

35. The antibody or antigen-binding fragment of claim 34, wherein the antibody comprises a human IgG4 constant region.

36. The antibody or antigen-binding fragment of claim 35, wherein the human IgG4 heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 37, or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 37.

37. The antibody or antigen-binding fragment of claim 35, wherein the human IgG4 constant region comprises an Fc region.

38. The antibody or antigen-binding fragment of claim 37, wherein the Fc region is incapable of binding the C1q protein.

39. The antibody or antigen-binding fragment of claim 37 or claim 38, wherein the Fc region is incapable of inducing complement activity.

40. The antibody or antigen-binding fragment of any one of claims 37-39, wherein the Fc region is incapable of inducing antibody-dependent cellular cytotoxicity (ADCC).

41. The antibody or antigen-binding fragment of any one of claims 37-40, wherein the Fc region comprises one or more modifications.

42. The antibody or antigen-binding fragment of claim 41, wherein the Fc region comprises one or more amino acid substitutions.

43. The antibody or antigen-binding fragment of claim 42, wherein the Fc region comprises an amino acid substitution at position 248 according to Kabat numbering convention.

44. The antibody or antigen-binding fragment of claim 43, wherein the Fc region comprises a leucine to glutamate amino acid substitution at position 248 according to Kabat numbering convention.

45. The antibody or antigen-binding fragment of claim 43 or claim 44, wherein the amino acid substitution at position 248 according to Kabat numbering convention inhibits the Fc region from interacting with an Fc receptor.

46. The antibody or antigen-binding fragment of any one of claims 42-45, wherein the Fc region comprises an amino acid substitution at position 241 according to Kabat numbering convention.

47. The antibody or antigen-binding fragment of claim 46, wherein the Fc region comprises a serine to proline amino acid substitution at position 241 according to Kabat numbering convention.

48. The antibody or antigen-binding fragment of claim 46 or claim47, wherein the amino acid substitution at position 241 according to Kabat numbering convention prevents arm switching in the antibody.

49. The antibody or antigen-binding fragment of any one of claims 1-34, wherein the antibody is a bispecific antibody.

50. The antibody or antigen-binding fragment of any one of claims 1-34, wherein the antibody has been engineered to increase brain penetration.

51. The antibody or antigen-binding fragment of any one of claims 1-34, wherein the antibody is a bispecific antibody recognizing a first antigen and a second antigen.

52. The antibody of claim 51, wherein the first antigen is a C1q protein and the second antigen is an antigen facilitating transport across the blood-brain-barrier.

53. The antibody of claim 51 or claim 52, wherein the second antigen is selected from transferrin receptor (TR), insulin receptor (HIR), insulin-like growth factor receptor (IGFR), low-density lipoprotein receptor related proteins 1 and 2 (LPR-1 and 2), diphtheria toxin receptor, CRM197, a llama single domain antibody, TMEM 30(A), a protein transduction domain, TAT, Syn-B, penetratin, a poly-arginine peptide, an angiopep peptide, and ANG1005.

54. The antibody or antigen-binding fragment of any one of claims 1-53, wherein the antigen-binding fragment is a Fab, $F(ab')_2$ or Fab' fragment.

55. The antibody or antigen-binding fragment of claim 54, wherein the antibody fragment has better brain penetration as compared to its corresponding full-length antibody.

56. The antibody or antigen-binding fragment of claim 54 or claim 55, wherein the antibody fragment has a shorter half-life as compared to its corresponding full-length antibody.

57. The antibody or antigen-binding fragment of any one of claims 1-56, wherein the antibody has a dissociation constant (K_D) for human C1q that ranges from less than about 10 pM to less than about 5 pM.

58. The antibody or antigen-binding fragment of any one of claims 1-57, wherein the antibody has dissociation constant (K_D) for mouse C1q that ranges from less than about 125 nM to less than about 5 pM.

59. The antibody or antigen-binding fragment of any one of claims 1-58, wherein the antibody specifically binds to and neutralizes a biological activity of C1q.

60. The antibody of claim 59, wherein the biological activity is (1) C1q binding to an autoantibody, (2) C1q binding to C1r, (3) C1q binding to C1s, (4) C1q binding to phosphatidylserine, (5) C1q binding to pentraxin-3, (6) C1q binding to C-reactive protein (CRP), (7) C1q binding to globular C1q receptor (gC1qR), (8) C1q binding to complement receptor 1 (CR1), (9) C1q binding to beta-amyloid, or (10) C1q binding to calreticulin.

61. The antibody of claim 59 or claim 60, wherein the biological activity is (1) activation of the classical complement activation pathway, (2) activation of antibody and complement dependent cytotoxicity, (3) CH50 hemolysis, (4) synapse loss, (5) B-cell antibody production, (6) dendritic cell maturation, (7) T-cell proliferation, (8) cytokine production (9) microglia activation, (10) Arthus reaction, (11)

phagocytosis of synapses or nerve endings, or (12) activation of complement receptor 3 (CR3/C3) expressing cells.

62. The antibody of claim 61, wherein CH50 hemolysis comprises human, mouse, and/or rat CH50 hemolysis.

63. The antibody of claim 61 or claim 62, wherein the antibody is capable of neutralizing from at least about 50%, to at least about 90% of CH50 hemolysis.

64. The antibody of any one of claims 61-63, wherein the antibody is capable of neutralizing at least 50% of CH50 hemolysis at a dose of less than 150 ng, less than 100 ng, less than 50 ng, or less than 20 ng.

65. The antibody of any one of claims 61-64, wherein the antibody binds C1q with a binding stoichiometry that ranges from 20:1 to 1.0:1 or less than 1.0:1.

66. An isolated polynucleotide comprising a nucleic acid sequence encoding the antibody of any one of claims 1-65.

67. An isolated host cell comprising the nucleic acid sequence of claim 66.

68. A pharmaceutical composition comprising the antibody of any one of claims 1-65 and a pharmaceutically acceptable carrier.

69. A method of treating or preventing a disease associated with complement activation in an individual in need of such treatment, the method comprising the step of administering a therapeutically effective dose of the antibody of any one of claims 1-65.

70. The method of claim 69, wherein the disease associated with complement activation is a neurodegenerative disorder.

71. The method of claim 70, wherein the neurodegenerative disorder is associated with loss of synapses or loss nerve connections.

72. The method of claim 70 or claim 71, wherein the neurodegenerative disorder is associated with synapse loss that is dependent on the complement receptor 3(CR3)/C3 or complement receptor CR1.

73. The method of any one of claims 70-72, wherein the neurodegenerative disorder is associated with pathological activity-dependent synaptic pruning.

74. The method of any one of claims 70-73, wherein the neurodegenerative disorder is associated with synapse phagocytosis by microglia.

75. The method of any one of claims 70-74, wherein the neurodegenerative disorder is selected from Alzheimer's disease, amyotrophic lateral sclerosis, multiple sclerosis,

glaucoma, myotonic dystrophy, Guillain-Barre´ syndrome (GBS), Myastenia Gravis, Bullous Pemphigoid, spinal muscular atrophy, Down syndrome, Parkinson's disease, and Huntington's disease.

76. The method of claim 69, wherein the disease associated with complement activation is an inflammatory disease, autoimmune disease, or metabolic disorder.

77. The method of claim 76, wherein the inflammatory disease, autoimmune disease, or metabolic disorder is selected from diabetes, obesity, rheumatoid arthritis (RA), acute respiratory distress syndrome (ARDS), remote tissue injury after ischemia and reperfusion, complement activation during cardiopulmonary bypass surgery, dermatomyositis, pemphigus, lupus nephritis and resultant glomerulonephritis and vasculitis, cardiopulmonary bypass, cardioplegia-induced coronary endothelial dysfunction, type II membranoproliferative glomerulonephritis, IgA nephropathy, acute renal failure, cryoglobulemia, antiphospholipid syndrome, Chronic open-angle glaucoma, acute closed-angle glaucoma, macular degenerative diseases, age-related macular degeneration (AMD), (AMD-wet), Geographic atrophy choroidal neovascularization (CNV), uveitis, diabetic retinopathy, ischemia-related retinopathy, endophthalmitis, intraocular neovascular disease, diabetic macular edema, pathological myopia, von Hippel-Lindau disease, histoplasmosis of the eye, Neuromyelitis Optica (NMO), Central Retinal Vein Occlusion (CRVO), corneal neovascularization, retinal neovascularization, Leber's hereditary optic neuropathy, optic neuritis, Behcet's retinopathy, ischemic optic neuropathy, retinal vasculitis, ANCA vasculitis, Purtscher retinopathy, Sjogren's dry eye disease, dry AMD, sarcoidosis, temporal arteritis, polyarteritis nodosa, multiple sclerosis, allo-transplantation, hyperacute rejection, hemodialysis, chronic occlusive pulmonary distress syndrome (COPD), asthma, and aspiration pneumonia.

78. The method of claim 69, wherein the disease associated with complement activation is an autoimmune disease selected from myasthenia gravis, Diabetes mellitus type 1, Hashimoto's thyroiditis, Addison's disease, Coeliac disease, Crohn's disease, pernicious anaemia, Pemphigus vulgaris, vitiligo, autoimmune hemolytic anemias, paraneoplastic syndromes, a vasculitis disease, hypocomplementemic urticarial vasculitis (HUV), polymyalgia rheumatica, temporal arteritis, and Wegener's granulomatosis.

79. A kit comprising an antibody of any one of claims 1-65, and a package insert comprising instructions for using the antibody to treat or prevent a disease associated with complement activation in an individual in need of such treatment.

80. The kit of claim 79, wherein the disease associated with complement activation is a neurodegenerative disorder.

81. The kit of claim 80, wherein the neurodegenerative disorder is associated with loss of synapses or loss nerve connections.

82. The kit of claim 80 or 81, wherein the neurodegenerative disorder is associated with synapse loss that is dependent on the complement receptor 3(CR3)/C3 or complement receptor CR1.

83. The kit of any one of claims 80-82, wherein the neurodegenerative disorder is associated with pathological activity-dependent synaptic pruning.

84. The kit of any one of claims 80-83, wherein the neurodegenerative disorder is associated with synapse phagocytosis by microglia.

85. The kit of any one of claims 80-84, wherein the neurodegenerative disorder is selected from Alzheimer's disease, amyotrophic lateral sclerosis, multiple sclerosis, glaucoma, myotonic dystrophy, Down syndrome, Parkinson's disease, and Huntington's disease.

86. The kit of claim 79, wherein the disease associated with complement activation is an inflammatory disease, autoimmune disease, or metabolic disorder.

87. The kit of claim 86, wherein the inflammatory disease, autoimmune disease, or metabolic disorder is selected from diabetes, obesity, rheumatoid arthritis (RA), acute respiratory distress syndrome (ARDS), remote tissue injury after ischemia and reperfusion, complement activation during cardiopulmonary bypass surgery, dermatomyositis, pemphigus, lupus nephritis and resultant glomerulonephritis and vasculitis, cardiopulmonary bypass, cardioplegia-induced coronary endothelial dysfunction, type II membranoproliferative glomerulonephritis, IgA nephropathy, acute renal failure, cryoglobulemia, antiphospholipid syndrome, Chronic open-angle glaucoma, acute closed-angle glaucoma, macular degenerative diseases, age-related macular degeneration (AMD), (AMD-wet), Geographic atrophy choroidal neovascularization (CNV), uveitis, diabetic retinopathy, ischemia-related retinopathy, endophthalmitis, intraocular neovascular disease, diabetic macular edema, pathological myopia, von Hippel-Lindau disease, histoplasmosis of the eye,

Neuromyelitis Optica (NMO), Central Retinal Vein Occlusion (CRVO), corneal neovascularization, retinal neovascularization, Leber's hereditary optic neuropathy, optic neuritis, Behcet's retinopathy, ischemic optic neuropathy, retinal vasculitis, ANCA vasculitis, Purtscher retinopathy, Sjogren's dry eye disease, dry AMD, sarcoidosis, temporal arteritis, polyarteritis nodosa, multiple sclerosis, allo-transplantation, hyperacute rejection, hemodialysis, chronic occlusive pulmonary distress syndrome (COPD), asthma, and aspiration pneumonia.

88. The kit of claim 79, wherein the disease associated with complement activation is an autoimmune disease selected from myasthenia gravis, Diabetes mellitus type 1, Hashimoto's thyroiditis, Addison's disease, Coeliac disease, Crohn's disease, pernicious anaemia, Pemphigus vulgaris, vitiligo, autoimmune hemolytic anemias, paraneoplastic syndromes, a vasculitis disease, hypocomplementemic urticarial vasculitis (HUV), polymyalgia rheumatica, temporal arteritis, and Wegener's granulomatosis.

89. A diagnostic kit comprising an antibody of any one of claims 1-65.

90. A method of detecting synapses in an individual, the method comprising

a) administering an antibody of any one of claims 1-65 to the individual; and

b) detecting antibody bound to synapses, thereby detecting synapses in the individual.

91. The method of claim 90, wherein the antibody bound to synapses is detected using imaging techniques selected from positron emission tomography (PET), X-ray computed tomography, single-photon emission computed tomography (SPECT), computed tomography (CT), and computed axial tomography (CAT).

92. The method of claim 90 or claim 91, wherein the detection of antibody bound to synapses provides a quantitative measure of the number of synapses in the individual.

93. The method of any one of claims 90-92, wherein the individual has a neurodegenerative disease or autoimmune disease.

94. The method of any one of claims 90-93, wherein the number of synapses in the individual is measured repeatedly over a period of time and a loss of synapses in the individual is detected over time.

95. The method of claim 94, wherein the loss of synapses over time is a measure for the efficacy of a treatment for the neurodegenerative disease or autoimmune disease.

~~96. A method of detecting synapses in a biological sample, the method comprising~~

~~a) contacting the biological sample with an antibody of any one of claims 1-65; and~~

~~b) detecting antibody bound to synapses, thereby detecting synapses in the biological sample.~~

~~97. The method of claim 96, further comprising a step before step a) of obtaining the biological sample from an individual.~~

~~98. The method of claim 96 or claim 97, wherein the biological sample comprises a biopsy specimen, a tissue, or a cell.~~

~~99. The method of any one of claims 96-98, wherein the antibody is detected by immunofluorescence microscopy, immunocytochemistry, immunohistochemistry, ELISA, FACS analysis, immunoprecipitation, or micro-positron emission tomography.~~

1. A method for producing a humanized anti-C1q antibody or an antigen-binding fragment thereof, wherein the method comprises

(a) culturing a host cell comprising a nucleic acid sequence encoding the humanized anti-C1q antibody or antigen-binding fragment under conditions suitable for the expression of the humanized anti-C1q antibody or antigen-binding fragment, and

(b) optionally recovering the humanized anti-C1q antibody or antigen-binding fragment from the host cell or host cell culture medium,

wherein the humanized anti-C1q antibody or antigen-binding fragment comprises:

(i) a heavy chain variable domain, wherein the heavy chain variable domain comprises an amino acid sequence selected from SEQ ID NOs: 1-4, or an amino acid sequence with at least about 95% homology to the amino acid sequence selected from SEQ ID NOs: 1-4 and wherein the heavy chain variable domain comprises the hypervariable regions (HVRs) of SEQ ID NOs: 1-4; and

(ii) a light chain variable domain, wherein the light chain variable domain comprises an amino acid sequence selected from SEQ ID NOs: 5-8, or an amino acid sequence with at least about 95% homology to the amino acid sequence selected from SEQ ID NOs: 5-8 and wherein the light chain variable domain comprises the HVRs of SEQ ID NOs: 5-8.

2. The method of claim 1, comprising prior to (a)

(1) isolating and inserting a nucleic acid sequence encoding the humanized anti-C1q antibody or antigen-binding fragment into one or more vectors, and

(2) introducing the one or more vectors into the host cell.

3. The method of claim 1 or claim 2, wherein the host cell is a prokaryotic cell or a eukaryotic cell, optionally wherein the prokaryotic cell is a yeast cell or *E. coli* or the eukaryotic cell is a mammalian cell, optionally wherein the mammalian cell is a Chinese hamster ovary (CHO) cell.

4. A kit comprising a humanized anti-C1q antibody or an antigen-binding fragment thereof, wherein the humanized anti-C1q antibody or antigen-binding fragment comprises:

(i) a heavy chain variable domain, wherein the heavy chain variable domain comprises an amino acid sequence selected from SEQ ID NOs: 1-4, or an amino acid sequence with at least about 95% homology to the amino acid sequence selected from SEQ ID NOs: 1-4 and wherein the heavy chain variable domain comprises the hypervariable regions (HVRs) of SEQ ID NOs: 1-4; and

(ii) a light chain variable domain, wherein the light chain variable domain comprises an amino acid sequence selected from SEQ ID NOs: 5-8, or an amino acid sequence with at least about 95% homology to the amino acid sequence selected from SEQ ID NOs: 5-8 and wherein the light chain variable domain comprises the HVRs of SEQ ID NOs: 5-8.

5. A kit comprising a humanized anti-C1q antibody, or an antigen-binding fragment thereof produced by the method of any one of claims 1-3.

6. The kit of claim 4 or claim 5, further including instructions comprising a description of administration of the humanized anti-C1q antibody to treat or diagnose a disease associated with complement activation.

7. The kit of any one of claims 4-6, wherein the kit is in a packaging.

8. The method of any one of claims 1-3 or the kit of any one of claims 4-7, wherein the antibody or antigen-binding fragment comprises a human IgG4 heavy chain constant region.

9. The method or kit of any one of the preceding claims, wherein the human IgG4 heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 37.

10. The method or kit of claim 8, wherein the Fc region comprises an amino acid substitution at position 248 and/or position 241 according to Kabat numbering convention.

11. The method or kit of claim 10, wherein the amino acid substitution at position 248 is a leucine to glutamate amino acid substitution.

12. The method or kit of claim 10, wherein the amino acid substitution at position 241 is a serine to proline amino acid substitution.

13. The method of any one of claims 1-3 or the kit of any one of claims 4-7, wherein the antigen-binding fragment is a Fab, F(ab')2 or Fab' fragment.

14. A vector comprising a nucleic acid sequence that encodes a humanized anti-C1q antibody, wherein the anti-C1q antibody comprises:

a heavy chain variable domain comprising an amino acid sequence selected from SEQ ID NOs: 1-4 and a light chain variable domain comprising an amino acid sequence selected from SEQ ID NOs: 5-8.

15. The vector of claim 14, wherein the vector is an expression vector.