CLAIMS

What is claimed is:

1. An isolated anti-C1q antibody comprising a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises the HVR-L1, HVR-L2, and HVR-L3 of the monoclonal antibody M1 produced by a hybridoma cell line with ATCC Accession Number PTA-120399 or progeny thereof; and/or wherein the heavy chain variable domain comprises the HVR-H1, HVR-H2, and HVR-H3 of the monoclonal antibody M1 produced by a hybridoma cell line with ATCC Accession Number PTA-120399 or progeny thereof.

2. An isolated antibody that specifically binds to a C1q protein, wherein the antibody comprises a light chain HVR selected from the group consisting of HVR-L1 comprising the amino acid sequence of SEQ ID NO:5, HVR-L2 comprising the amino acid sequence of SEQ ID NO:6, and HVR-L3 comprising the amino acid sequence of SEQ ID NO:7; and/or wherein the antibody comprises a heavy chain HVR selected from the group consisting of HVR-H1 comprising the amino acid sequence of SEQ ID NO:9, HVR-H2 comprising the amino acid sequence of SEQ ID NO:10, and HVR-H3 comprising the amino acid sequence of SEQ ID NO:11.

3. The antibody of claim 2, wherein the antibody comprises HVR-L1 comprising the amino acid sequence of SEQ ID NO:5, HVR-L2 comprising the amino acid sequence of SEQ ID NO:6, and HVR-L3 comprising the amino acid sequence of SEQ ID NO:7; and/or wherein the antibody comprises HVR-H1 comprising the amino acid sequence of SEQ ID NO:9, HVR-H2 comprising the amino acid sequence of SEQ ID NO:10, and HVR-H3 comprising the amino acid sequence of SEQ ID NO:11.

4. The antibody of claim 2 or 3, further comprising a light chain variable domain comprising the amino acid sequence of SEQ ID NO:4.

5. The antibody of any one of claims 2-4, further comprising a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:8.

6. The antibody of any one of claims 1-5, which binds specifically to both human C1q and mouse C1q.

7. The antibody of any one of claims 1-5, which binds specifically to rat C1q.

8. The antibody of any one of claims 1-5, which binds specifically to human C1q, mouse C1q, and rat C1q.

9. The antibody of any one of claims 1-8, which has dissociation constant (K_D) for human C1q and mouse C1q that ranges from less than about 30 nM to less than about 100 pM.

10. The antibody of any one of claims 1-8, which has dissociation constant (K_D) for human C1q and mouse C1q of less than about 30 nM.

11. The antibody of any one of claims 1-8, which has dissociation constant (K_D) for human C1q and mouse C1q of less than about 20 nM.

12. The antibody of any one of claims 1-8, which has dissociation constant (K_D) for human C1q and mouse C1q of less than about 10 nM.

13. The antibody of any one of claims 1-8, which has dissociation constant (K_D) for human C1q and mouse C1q of less than about 5 nM.

14. The antibody of any one of claims 1-8, which has dissociation constant (K_D) for human C1q and mouse C1q of less than about 1 nM.

15. The antibody of any one of claims 1-8, which has dissociation constant (K_D) for human C1q and mouse C1q of less than about 100 pM.

16. The antibody of any one of claims 1-15, which specifically binds to and neutralizes a biological activity of C1q.

17. The antibody of claim 16, wherein said 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.

18. The antibody of claim 16 or 17, wherein said 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.

19. The antibody of claim 18, wherein CH50 hemolysis comprises human, mouse, and/or rat CH50 hemolysis.

20. The antibody of claim 18 or 19, which is capable of neutralizing at least 50%, at least 80%, or at least 90% of CH50 hemolysis.

21. The antibody of any one of claims 18-20, which is capable of neutralizing at least 50% of CH50 hemolysis at a dose of less than 200 ng/ml, less than 100 ng/ml, less than 50 ng/ml, or less than 20 ng/ml.

22. The antibody of any one of claims 1-21, which is a murine antibody.

23. The antibody of any one of claims 1-21, which is a humanized or chimeric antibody.

24. An isolated murine anti-human C1q monoclonal antibody M1 produced by a hybridoma cell line with ATCC Accession Number PTA-120399, or progeny thereof.

25. An isolated anti-C1q antibody which 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.

26. An isolated anti-C1q antibody, which binds to a C1q protein and binds to one or more amino acids of the C1q protein within amino acid residues selected from the group consisting of:

i. amino acid residues 196-226 of SEQ ID NO:1 (SEQ ID NO:16), or amino acid residues of a C1q protein chain A (C1qA) corresponding to amino acid residues 196-226 (GLFQVVSGGMVLQLQQGDQVWVEKDPKKGHI) of SEQ ID NO:1 (SEQ ID NO:16);

ii. amino acid residues 196-221 of SEQ ID NO:1 (SEQ ID NO:17), or amino acid residues of a C1qA corresponding to amino acid residues 196-221 (GLFQVVSGGMVLQLQQGDQVWVEKDP) of SEQ ID. NO:1 (SEQ ID NO:17);

iii. amino acid residues 202-221 of SEQ ID NO:1 (SEQ ID NO:18), or amino acid residues of a C1qA corresponding to amino acid residues 202-221 (SGGMVLQLQQGDQVWVEKDP) of SEQ ID NO:1 (SEQ ID NO:18);

iv. amino acid residues 202-219 of SEQ ID NO:1 (SEQ ID NO:19), or amino acid residues of a C1qA corresponding to amino acid residues 202-219 SGGMVLQLQQGDQVWVEK of SEQ ID NO:1 (SEQ ID NO:19); and

v. amino acid residues Lys 219 and/or Ser 202 of SEQ ID NO:1, or amino acid residues of a C1qA corresponding Lys 219 and/or Ser 202 of SEQ ID NO:1.

27. The antibody of claim 26, which further binds to one or more amino acids of the C1q protein within amino acid residues selected from the group consisting of:

(a) amino acid residues 218-240 of SEQ ID NO:3 (SEQ ID NO:20) or amino acid residues of a C1q protein chain C (C1qC) corresponding to amino acid residues 218-240 (WLAVNDYYDMVGI QGSDSVFSGF) of SEQ ID NO:3 (SEQ ID NO:20);

(b) amino acid residues 225-240 of SEQ ID NO:3 (SEQ ID NO:21) or amino acid residues of a C1qC corresponding to amino acid residues 225-240 (YDMVGI QGSDSVFSGF) of SEQ ID NO:3 (SEQ ID NO:21);

(c) amino acid residues 225-232 of SEQ ID NO:3 (SEQ ID NO:22) or amino acid residues of a C1qC corresponding to amino acid residues 225-232 (YDMVGIQG) of SEQ ID NO:3 (SEQ ID NO:22);

(d) amino acid residue Tyr 225 of SEQ ID NO:3 or an amino acid residue of a C1qC corresponding to amino acid residue Tyr 225 of SEQ ID NO:3;

(e) amino acid residues 174-196 of SEQ ID NO:3 (SEQ ID NO:23) or amino acid residues of a C1qC corresponding to amino acid residues 174-196 (HTANLCVLLYRSGVKVVTFCGHT) of SEQ ID NO:3 (SEQ ID NO:23);

(f) amino acid residues 184-192 of SEQ ID NO:3 (SEQ ID NO:24) or amino acid residues of a C1qC corresponding to amino acid residues 184-192 (RSGVKVVTF) of SEQ ID NO:3 (SEQ ID NO:24);

(g) amino acid residues 185-187 of SEQ ID NO:3 or amino acid residues of a C1qC corresponding to amino acid residues 185-187 (SGV) of SEQ ID NO:3; and

(h) amino acid residue Ser 185 of SEQ ID NO:3 or an amino acid residue of a C1qC corresponding to amino acid residue Ser 185 of SEQ ID NO:3.

28. An isolated anti-C1q antibody, which binds to a C1q protein and binds to one or more amino acids of the C1q protein within amino acid residues selected from the group consisting of:

(a) amino acid residues 218-240 of SEQ ID NO:3 (SEQ ID NO:20) or amino acid residues of a C1qC corresponding to amino acid residues 218-240 (WLAVNDYYDMVGI QGSDSVFSGF) of SEQ ID NO:3 (SEQ ID NO:20);

(b) amino acid residues 225-240 of SEQ ID NO:3 (SEQ ID NO:21) or amino acid residues of a C1qC corresponding to amino acid residues 225-240 (YDMVGI QGSDSVFSGF) of SEQ ID NO:3 (SEQ ID NO:21);

(c) amino acid residues 225-232 of SEQ ID NO:3 (SEQ ID NO:22) or amino acid residues of a C1qC corresponding to amino acid residues 225-232 (YDMVGIQG) of SEQ ID NO:3 (SEQ ID NO:22);

(d) amino acid residue Tyr 225 of SEQ ID NO:3 or an amino acid residue of a C1qC corresponding to amino acid residue Tyr 225 of SEQ ID NO:3;

(e) amino acid residues 174-196 of SEQ ID NO:3 (SEQ ID NO:23) or amino acid residues of a C1qC corresponding to amino acid residues 174-196 (HTANLCVLLYRSGVKVVTFCGHT) of SEQ ID NO:3 (SEQ ID NO:23);

(f) amino acid residues 184-192 of SEQ ID NO:3 (SEQ ID NO:24) or amino acid residues of a C1qC corresponding to amino acid residues 184-192 (RSGVKVVTF) of SEQ ID NO:3 (SEQ ID NO:24);

(g) amino acid residues 185-187 of SEQ ID NO:3 or amino acid residues of a C1qC corresponding to amino acid residues 185-187 (SGV) of SEQ ID NO:3; and

(h) amino acid residue Ser 185 of SEQ ID NO:3 or an amino acid residue of a C1qC corresponding to amino acid residue Ser 185 of SEQ ID NO:3.

29. The antibody of claim 28, wherein the antibody binds to amino acid residue Lys 219 and Ser 202 of the human C1qA as shown in SEQ ID NO:1 or amino acids of a human C1qA corresponding to Lys 219 and Ser 202 as shown in SEQ ID NO:1, and amino acid residue Tyr 225 of the human C1qC as shown in SEQ ID NO:3 or an amino acid residue of a human C1qC corresponding to Tyr 225 as shown in SEQ ID NO:3.

30. The antibody of claim 28, wherein the antibody binds to amino acid residue Lys 219 of the human C1qA as shown in SEQ ID NO:1 or an amino acid residue of a human C1qA corresponding to Lys 219 as shown in SEQ ID NO:1, and amino acid residue Ser 185 of

the human C1qC as shown in SEQ ID NO:3 or an amino acid residue of a human C1qC corresponding to Ser 185 as shown in SEQ ID NO:3.

31. The antibody of any one of claims 25-30, wherein the antibody is a humanized antibody, a chimeric antibody, or a human antibody.

32. The antibody of any one of claims 25-31, which binds specifically to both human C1q and mouse C1q.

33. The antibody of any one of claims 25-31, which binds specifically to rat C1q.

34. The antibody of any one of claims 25-31, which binds specifically to human C1q, mouse C1q, and rat C1q.

35. The antibody of any one of claims 25-34, which has dissociation constant (K_D) for human C1q and mouse C1q that ranges from less than about 30 nM to less than about 100 pM.

36. The antibody of any one of claims 25-34, which has dissociation constant (K_D) for human C1q and mouse C1q of less than about 30 nM.

37. The antibody of any one of claims 25-34, which has dissociation constant (K_D) for human C1q and mouse C1q of less than about 20 nM.

38. The antibody of any one of claims 25-34, which has dissociation constant (K_D) for human C1q and mouse C1q of less than about 10 nM.

39. The antibody of any one of claims 25-34, which has dissociation constant (K_D) for human C1q and mouse C1q of less than about 5 nM.

40. The antibody of any one of claims 25-34, which has dissociation constant (K_D) for human C1q and mouse C1q of less than about 1 nM.

41. The antibody of any one of claims 25-34, which has dissociation constant (K_D) for human C1q and mouse C1q of less than about 100 pM.

42. The antibody of any one of claims 25-41, which specifically binds to and neutralizes a biological activity of C1q.

43. The antibody of claim 42, wherein said 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.

44. The antibody of claim 42 or 43, wherein said 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.

45. The antibody of claim 44, wherein CH50 hemolysis comprises human, mouse, and/or rat CH50 hemolysis.

46. The antibody of claim 44 or 45, which is capable of neutralizing at least 50%, at least 80%, or at least 90% of CH50 hemolysis.

47. The antibody of any one of claims 44-46, which is capable of neutralizing at least 50% of CH50 hemolysis at a dose of less than 200 ng/ml, less than 100 ng/ml, less than 50 ng/ml, or less than 20 ng/ml.

48. The antibody of any one of claims 1-23 and 25-47, which is a bispecific antibody.

49. The antibody of any one of claims 1-23 and 25-47, which has been engineered to increase brain penetration.

50. The antibody of any one of claims 1-23 and 25-47, which is a bispecific antibody recognizing a first antigen and a second antigen.

51. The antibody of claim 50, wherein the first antigen is a C1q protein and the second antigen is an antigen facilitating transport across the blood-brain-barrier.

52. The antibody of claim 50 or 51, wherein the second antigen is selected from the group consisting of 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.

53. The antibody of any one of claims 1-23 and 25-47, which is of the IgG class.

54. The antibody of claim 53 which has an IgG_1, IgG_2, IgG_3, or IgG_4 isotype.

55. The antibody of any one of claims 1-23 and 25-47, which is an antibody fragment.

56. The antibody of claim 55, which is a Fab, $F(ab')_2$ or Fab' fragment.

57. The antibody of claim 55 or 56, wherein the antibody fragment specifically binds to and neutralizes a biological activity of C1q.

58. The antibody of any one of claims 55-57, wherein the antibody fragment has better brain penetration as compared to its corresponding full-length antibody.

59. The antibody of any one of claims 55-58, wherein the antibody fragment has a shorter half-life as compared to its corresponding full-length antibody.

60. An isolated polynucleotide comprising a nucleic acid sequence encoding the antibody of any one of claims 1-59.

61. An isolated host cell comprising the nucleic acid sequence of claim 60.

62. A hybridoma cell with ATCC Accession Number PTA-120399, or progeny thereof.

63. A pharmaceutical composition comprising the antibody of any one of claims 1-59 and a pharmaceutically acceptable carrier.

64. 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 1-59.

65. The method of claim 64, wherein the disease associated with complement activation is a neurodegenerative disorder.

66. The method of claim 65, wherein the neurodegenerative disorder is associated with loss of synapses or loss nerve connections.

67. The method of claim 65 or 66, wherein the neurodegenerative disorder is associated with synapse loss that is dependent on the complement receptor 3(CR3)/C3 or complement receptor CR1.

68. The method of any one of claims 65-67, wherein the neurodegenerative disorder is associated with pathological activity-dependent synaptic pruning.

69. The method of any one of claims 65-68, wherein the neurodegenerative disorder is associated with synapse phagocytosis by microglia.

70. The method of any one of claims 65-69, wherein the neurodegenerative disorder is selected from the group consisting of Alzheimer's disease, amyotrophic lateral sclerosis, multiple sclerosis, glaucoma, myotonic dystrophy, Down syndrome, Parkinson's disease, and Huntington's disease.

71. The method of claim 64, wherein the disease associated with complement activation is an inflammatory disease, autoimmune disease, or metabolic disorder.

72. The method of claim 71, wherein the inflammatory disease, autoimmune disease, or metabolic disorder is selected from the group consisting of 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, macular degenerative diseases, age-related macular degeneration (AMD), 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, allo-transplantation, hyperacute rejection, hemodialysis, chronic occlusive pulmonary distress syndrome (COPD), asthma, and aspiration pneumonia.

73. The method of claim 64, wherein the disease associated with complement activation is an autoimmune disease selected from the group consisting of 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, polymyalgia rheumatica, temporal arteritis, and Wegener's granulomatosis.

74. A kit comprising an antibody of any one of claims 1-59, 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.

75. The kit of claim 74, wherein the disease associated with complement activation is a neurodegenerative disorder.

76. The kit of claim 75, wherein the neurodegenerative disorder is associated with loss of synapses or loss nerve connections.

77. The kit of claim 75 or 76, wherein the neurodegenerative disorder is associated with synapse loss that is dependent on the complement receptor 3(CR3)/C3 or complement receptor CR1.

78. The kit of any one of claims 75-77, wherein the neurodegenerative disorder is associated with pathological activity-dependent synaptic pruning.

79. The kit of any one of claims 75-78, wherein the neurodegenerative disorder is associated with synapse phagocytosis by microglia.

80. The kit of any one of claims 75-79, wherein the neurodegenerative disorder is selected from the group consisting of Alzheimer's disease, amyotrophic lateral sclerosis, multiple sclerosis, glaucoma, myotonic dystrophy, Down syndrome, Parkinson's disease, and Huntington's disease.

81. The kit of claim 74, wherein the disease associated with complement activation is an inflammatory disease, autoimmune disease, or metabolic disorder.

82. The kit of claim 81, wherein the inflammatory disease, autoimmune disease, or metabolic disorder is selected from the group consisting of 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, macular degenerative diseases, age-related macular degeneration (AMD), 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, allo-transplantation, hyperacute rejection, hemodialysis, chronic occlusive pulmonary distress syndrome (COPD), asthma, and aspiration pneumonia.

83. The kit of claim 74, wherein the disease associated with complement activation is an autoimmune disease selected from the group consisting of 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, polymyalgia rheumatica, temporal arteritis, and Wegener's granulomatosis.

84. A diagnostic kit comprising an antibody of any one of claims 1-59.

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

a) administering an antibody of any one of claims 1-59 to the individual, and

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

86. The method of claim 85, wherein the antibody bound to synapses is detected using imaging techniques selected from the group consisting of positron emission tomography (PET), X-ray computed tomography, single-photon emission computed tomography (SPECT), computed tomography (CT), and computed axial tomography (CAT).

87. The method of claim 85 or 86, wherein the detection of antibody bound to synapses provides a quantitative measure of the number of synapses in the individual.

88. The method of any one of claims 85-87, wherein the individual has a neurodegenerative disease or autoimmune disease.

89. The method of any one of claims 85-88, 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.

90. The method of claim 89, wherein the loss of synapses over time is a measure for the efficacy of a treatment for the neurodegenerative disease or autoimmune disease.

91. 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 1-59, and

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

92. The method of claim 91, further comprising a step before step a) of obtaining the biological sample from an individual.

93. The method of claim 91 or 92, wherein the biological sample comprises a biopsy specimen, a tissue, or a cell.

~~94. The method of any one of claims 91-93, wherein the antibody is detected by immunofluorescence microscopy, immunocytochemistry, immunohistochemistry, ELISA, FACS analysis, or immunoprecipitation.~~

1. A method for producing an anti-C1q antibody, comprising:

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

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

wherein the anti-C1q antibody comprises:

a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises the HVR-L1, HVR-L2, and HVR-L3 of the monoclonal antibody M1 produced by a hybridoma cell line with ATCC Accession Number PTA-120399 or progeny thereof; and wherein the heavy chain variable domain comprises the HVR-H1, HVR-H2, and HVR-H3 of the monoclonal antibody M1 produced by a hybridoma cell line with ATCC Accession Number PTA-120399 or progeny thereof.

2. A method for producing an anti-C1q antibody, comprising:

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

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

wherein the anti-C1q antibody comprises:

HVR-L1 comprising the amino acid sequence of SEQ ID NO:5, HVR-L2 comprising the amino acid sequence of SEQ ID NO:6, and HVR-L3 comprising the amino acid sequence of SEQ ID NO:7; and

HVR-H1 comprising the amino acid sequence of SEQ ID NO:9, HVR-H2 comprising the amino acid sequence of SEQ ID NO:10, and HVR-H3 comprising the amino acid sequence of SEQ ID NO:11.

3. The method of claim 1 or claim 2, wherein the antibody comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO:4.

4. The method of any one of claims 1-3, wherein the antibody comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:8.

5. The method of any one of claims 1-4, wherein the antibody binds specifically to both human C1q and mouse C1q; or rat C1q; or human C1q, mouse C1q, and rat C1q.

6. The method of any one of claims 1-5, wherein the antibody has dissociation constant (K_D) for human C1q and mouse C1q that ranges from less than about 30 nM to less than about 100 pM; or has dissociation constant (K_D) for human C1q and mouse C1q of less than about 30 nM; or has dissociation constant (KD) for human C1q and mouse C1q of less than about 20 nM; or has dissociation constant (KD) for human C1q and mouse C1q of less than about 10 nM; or has dissociation constant (KD) for human C1q and mouse C1q of less than about 5 nM; or has dissociation constant (KD) for human C1q and mouse C1q of less than about 1 nM; or has dissociation constant (KD) for human C1q and mouse C1q of less than about 100 pM.

7. The method of any one of claims 1-6, wherein the antibody specifically binds to and neutralizes a biological activity of C1q, wherein said 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; and/or
(11) activation of the classical complement activation pathway,
(12) activation of antibody and complement dependent cytotoxicity,
(13) CH50 hemolysis for example, human, mouse, and/or rat CH50 hemolysis,

(14) synapse loss,

(15) B-cell antibody production,

(16) dendritic cell maturation,

(17) T-cell proliferation,

(18) cytokine production,

(19) microglia activation,

(20) Arthus reaction,

(21) phagocytosis of synapses or nerve endings, or

(22) activation of complement receptor 3 (CR3/C3) expressing cells.

8. The method of claim 7, wherein the antibody is capable of neutralizing at least 50%, at least 80%, or at least 90% of CH50 hemolysis.

9. The method of claim 7 or claim 8, wherein the antibody is capable of neutralizing at least 50% of CH50 hemolysis at a dose of less than 200 ng/ml, less than 100 ng/ml, less than 50 ng/ml, or less than 20 ng/ml.

10. The method of any one of claims 1-9, wherein the antibody is a murine antibody or humanized or chimeric antibody.

11. The method of any one of claims 1-10, wherein the antibody is of the IgG class.

12. The method of claim 11, wherein the antibody has an IgG_1, IgG_2, IgG_3, or IgG_4 isotype.

13. The method of any one of claims 1-10, wherein the antibody is an antibody fragment.

14. The method of claim 13, wherein the antibody is a Fab, $F(ab')_2$ or Fab' fragment.

15. The method of claim 13 or claim 14, wherein the antibody fragment specifically binds to and neutralizes a biological activity of C1q.

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

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

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

17. The method of any one of claims 1-2 or 16, 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.

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

a heavy chain variable domain comprising an amino acid sequence of SEQ ID NO: 8 and a light chain variable domain comprising an amino acid sequence of SEQ ID NO: 4.

19. The vector of claim 18, wherein the vector is an expression vector.