CLAIMS

1. An 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 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 antibody that specifically binds to a C1q protein, 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 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.

3. The antibody of claim 2, wherein the antibody comprises a light chain HVR comprising 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 wherein the antibody comprises a heavy chain HVR comprising 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 any one of claims 1-3, 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 1-4, 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. A murine anti-human C1q monoclonal antibody M1 produced by a hybridoma cell line with ATCC Accession Number PTA-120399, or progeny thereof.

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

26. The antibody of any one of claims 1-23, which has been engineered to increase brain penetration.

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

28. The antibody of claim 27, wherein the first antigen is a C1q protein and the second antigen is an antigen facilitating transport across the blood-brain-barrier.

29. The antibody of claim 27 or 28, 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.

30. The antibody of any one of claims 1-23, which is of the IgG class.

31. The antibody of claim 30, which has an IgG_1, IgG_2, IgG_3, or IgG_4 isotype.

32. The antibody of any one of claims 1-23, which is an antibody fragment.

33. The antibody of claim 32, which is a Fab, $F(ab')_2$ or Fab' fragment.

34. The antibody of claim 32 or 33, wherein the antibody fragment specifically binds to and neutralizes a biological activity of C1q.

35. A polynucleotide comprising a nucleic acid sequence encoding the antibody of any one of claims 1-24.

36. A host cell comprising the nucleic acid sequence of claim 35.

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

38. A pharmaceutical composition comprising the antibody of any one of claims 1-24 and a pharmaceutically acceptable carrier.

39. The antibody of any one of claims 1-24 for use in therapy.

40. The use of the antibody of any one of claims 1-24 in the manufacture of a medicament for the treatment or prevention of a disease associated with complement activation, wherein the disease associated with complement activation is a neurodegenerative disorder, an inflammatory disease, autoimmune disease, or metabolic disorder.

41. The use of claim 40, wherein the disease associated with complement activation is a neurodegenerative disorder 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.

42. The use of claim 41, wherein the neurodegenerative disorder is associated with loss of synapses or loss nerve connections.

43. The use of claim 41 or 42, wherein the disease is a neurodegenerative disorder associated with synapse loss that is dependent on the complement receptor 3(CR3)/C3 or complement receptor CR1.

44. The use of any one of claims 41-43, wherein the disease is a neurodegenerative disorder associated with pathological activity-dependent synaptic pruning.

45. The use of any one of claims 41-44, wherein the disease is a neurodegenerative disorder associated with synapse phagocytosis by microglia.

46. The use of claim 40, wherein the disease is an inflammatory disease, autoimmune disease, or metabolic disorder selected from the group consisting of diabetes, obesity, rheumatoid arthritis (RA), acute respiratory distress syndrome (ARDS), remote tissue injury after ischemia and reperfusion, 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, cryoglobulinemia, 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, hyperacute rejection, hemodialysis, chronic occlusive pulmonary distress syndrome (COPD), asthma, and aspiration pneumonia.

47. The method of claim 40, 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.

48. A kit comprising an antibody of any one of claims 1-24, 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.

49. The kit of claim 48, wherein the disease associated with complement activation is a neurodegenerative disorder.

50. The kit of claim 49, wherein the neurodegenerative disorder is associated with loss of synapses or loss nerve connections.

51. The kit of claim 49 or 50, wherein the neurodegenerative disorder is associated with synapse loss that is dependent on the complement receptor 3(CR3)/C3 or complement receptor CR1.

52. The kit of any one of claims 49-51, wherein the neurodegenerative disorder is associated with pathological activity-dependent synaptic pruning.

53. The kit of any one of claims 49-52, wherein the neurodegenerative disorder is associated with synapse phagocytosis by microglia.

54. The kit of any one of claims 49-53, 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.

55. The kit of claim 48, wherein the disease associated with complement activation is an inflammatory disease, autoimmune disease, or metabolic disorder.

56. The kit of claim 55, 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, 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, cryoglobulinemia, 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, hyperacute rejection, hemodialysis, chronic occlusive pulmonary distress syndrome (COPD), asthma, and aspiration pneumonia.

57. The kit of claim 48, 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.

58. A diagnostic kit comprising an antibody of any one of claims 1-24.

59. 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 1-24, and
b) detecting antibody bound to synapses, thereby detecting synapses in the biological sample.

60. The method of claim 59, wherein the biological sample comprises a biopsy specimen, a tissue, or a cell.

61. The method of any one of claims 59-60, wherein the antibody is detected by immunofluorescence microscopy, immunocytochemistry, immunohistochemistry, ELISA, FACS analysis, or immunoprecipitation.