CLAIMS

1. An antibody Fab fragment that binds to C1q.

2. The antibody Fab fragment of claim 1, comprising a heavy chain variable domain and a light chain variable domain, wherein the heavy chain variable domain comprises SEQ ID NO: 1 and light chain variable domain comprises SEQ ID NO: 3.

3 An antibody Fab, wherein the antibody Fab fragment comprises the complementarity determining regions (CDRs) of the heavy and light chains, and wherein

the heavy chain CDR1 sequence comprises amino acid residues 26-35, the heavy chain CDR2 sequence comprises amino acid residues 50-66, and the heavy chain CDR3 sequence comprises amino acid residues 99-110 of SEQ ID NO: 1, and

the light chain CDR1 sequence comprises amino acid residues 24-34, the light chain CDR2 sequence comprises amino acid residues 50-56, and the light chain CDR3 sequence comprises amino acid residues 89-97 of SEQ ID NO: 3.

4. An antibody Fab fragment that binds to a protein in the complement cascade, wherein the heavy chain variable domain comprises an amino acid sequence selected from SEQ ID NOs: 5-8, or an amino acid sequence with at least 95% homology to the amino acid sequence from SEQ ID NOs: 5-8.

5. The antibody Fab fragment of claim 4, wherein the light chain variable domain comprises an amino acid sequence selected from SEQ ID NOs: 9-12, or an amino acid sequence with at least 90% homology to the amino acid sequence from SEQ ID NOs: 9-12.

6. An antibody Fab fragment that specifically binds to a C1q protein, the antibody Fab fragment comprising:

a) a heavy chain variable domain comprising an amino acid sequence selected from SEQ ID NOs: 5-8, or an amino acid sequence with at least 95% homology to the amino acid sequence from SEQ ID NOs: 5-8; and/or

b) a light chain variable domain comprises an amino acid sequence selected from SEQ ID NOs: 9-12, or an amino acid sequence with at least 90% homology to the amino acid sequence from SEQ ID NOs: 9-12.

7. The antibody Fab fragment of any preceding claim, wherein the antibody Fab fragment binds the same C1q epitope as the antibody M1 produced by the hybridoma cell line with ATCC Accession Number PTA-120399.

8. The antibody Fab fragment of claims 1-7, wherein the antibody Fab fragment inhibits the binding of the monoclonal antibody M1 produced by the hybridoma cell line with ATCC Accession Number PTA-120399 to human C1q or to mouse C1q.

9. The antibody Fab fragment of claims 1-7, wherein the antibody Fab fragment binds specifically to both human C1q and mouse C1q.

10. The antibody Fab fragment of claims 1-7, wherein the antibody Fab fragment binds to rat C1q, dog C1q, rhesus C1q, or cynomolgus monkey C1q, or combinations thereof.

11. The antibody Fab fragment of claims 1-7, wherein the antibody Fab fragment binds human C1q, mouse C1q and/or rat C1q, and at least one of the following: dog C1q, rhesus C1q, and cynomolgus monkey C1q.

12. The antibody Fab fragment of any preceding claim, wherein the antibody Fab fragment is of an IgG class.

13. The antibody Fab fragment of claim 12, wherein the IgG class is IgG1.

14. The antibody Fab fragment of any preceding claim, wherein the antibody Fab fragment has been engineered to increase brain penetration.

15. The antibody Fab fragment of any preceding claim, wherein the antibody Fab fragment has a dissociation constant (K_D) for human C1q that ranges from 10 pM to 20 pM, or 1 pM to less than 10 pM.

16. The antibody Fab fragment of any one of claims 1-15, wherein the antibody Fab fragment has dissociation constant (K_D) for mouse C1q that ranges from 1 pM to 200 pM.

17. The antibody Fab fragment of any one of claims 1-14, wherein the antibody Fab fragment specifically binds to and neutralizes a biological activity of C1q.

18. The antibody Fab fragment of claim 17, 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, (10) C1q binding to calreticulin, (11) C1q binding to apoptotic cells, or (12) C1q binding to components of a nerve cell membrane.

19. The antibody Fab fragment of claim 17 or 18, 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.

20. The antibody Fab fragment of claim 19, wherein CH50 hemolysis comprises human, mouse, rat, dog , rhesus, and/or cynomolgus monkey CH50 hemolysis.

21. The antibody Fab fragment of claim 19 or claim 20, wherein the antibody Fab fragment is capable of neutralizing from at least about 50%, to at least about 90% of CH50 hemolysis.

22. The antibody Fab fragment of claims 19-21, wherein the antibody Fab fragment 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.

23. The antibody Fab fragment of any one of claims 19-22, wherein the antibody Fab fragment binds C1q and inhibits biological function with a binding stoichiometry that ranges from less than 6:1 to 1:1, or less than 2:1 to 1:1.

24. The antibody Fab fragment of any preceding claim, wherein the antibody Fab fragment is humanized.

25. A host cell expressing the antibody Fab fragment of any preceding claim.

26. An isolated DNA sequence encoding the heavy and/or light chain regions of an antibody Fab fragment from any one of claims 1-24.

27. A cloning or expression vector comprising one or more DNA sequences of claim 26.

28. The host cell of claim 25 comprising one or more cloning or expression vectors of claim 26.

29. An isolated polynucleotide comprising a nucleic acid sequence encoding the antibody Fab fragment of any one of claims 1-24.

30. A process for producing the antibody Fab fragment of claims 1-24, comprising culturing the host cell of claim 30 and isolating the antibody Fab fragment.

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

32. A use of an antibody Fab fragment selected from any one of claims 1-24 in the manufacture of a medicament for inhibiting synapse loss in a patient suffering from adverse synapse loss.

33. The use of claim 32, wherein the patient has suffered synapse loss as a result of a neurodegenerative disorder, central nervous system disorder, or a peripheral nervous system disorder.

34. The use of claim 33, wherein the neurodegenerative disorder is Alzheimer's disease.

35. The use of claim 32, further comprising administration of neural progenitors, or a neurogenesis enhancer.

36. The use of claim 32, wherein the antibody Fab fragment binds to C1q and inhibits complement activation.

37. A use of the antibody Fab fragment selected from any one of claims 1-24 in the manufacture of a medicament for the treatment of a disease associated with complement activation in an individual in need thereof.

38. The use of claim 37, wherein the disease associated with complement activation is a neurodegenerative disorder.

39. The use of claim 38, wherein the neurodegenerative disorder is associated with loss of synapses or loss nerve connections.

40. The use of claim 38 or claim 39, wherein the neurodegenerative disorder is associated with synapse loss that is dependent on the complement receptor 3(CR3)/C3 or complement receptor CR1.

41. The use of any one of claims 38-40, wherein the neurodegenerative disorder is associated with pathological activity-dependent synaptic pruning.

42. The use of any one of claims 38-41, wherein the neurodegenerative disorder is associated with synapse phagocytosis by microglia.

43. The use of any one of claims 38-42, wherein the neurodegenerative disorder is selected from Alzheimer's disease, amyotrophic lateral sclerosis, multiple sclerosis, glaucoma, myotonic dystrophy, Guillain-Barre´ syndrome (GBS), Myasthenia Gravis, Bullous Pemphigoid, spinal muscular atrophy, Down syndrome, Parkinson's disease, or Huntington's disease.

44. The use of claim 38, wherein the disease associated with complement activation is an inflammatory disease, autoimmune disease, complement-associated eye disease or metabolic disorder.

45. The use of claim 44, wherein the inflammatory disease, autoimmune disease, complement-associated eye 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), 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, aspiration pneumonia, multiple sclerosis, Guillain-Barre syndrome, Myasthenia Gravis, Bullous Pemphigoid, or myositis.

46. The use of claim 38, 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, Wegener's granulomatosis, multiple sclerosis, Guillain-Barre syndrome, Myasthenia Gravis, Bullous Pemphigoid, or myositis.

47. A kit comprising an antibody Fab fragment of any one of claims 1-24, and a package insert comprising instructions for using the antibody Fab fragment to treat or prevent a disease associated with complement activation in an individual in need of such treatment.

48. A use of an antibody Fab fragment of any one of claims 1-24 in the preparation of a kit for determining a subject's risk of developing a disease associated with complement activation, wherein the antibody fragment is coupled to a detectable label; and wherein the risk of developing a disease associated with complement activation is characterized based on the comparison of the amount of C1q as compared to a reference.

49. The use of claim 48, wherein the detectable label comprises a nucleic acid, oligonucleotide, enzyme, radioactive isotope, biotin, or a fluorescent label.

50. The use of claim 49, wherein the detectable label is detected using an imaging agent for x-ray, CT, MRI, ultrasound, PET and SPECT.

51. The use of claim 49, where in the fluorescent label is selected from fluorescein, rhodamine, cyanine dyes or BODIPY.

52. A use of an anti-C1q antibody fragment in the manufacture of a medicament for reducing a subject's risk of developing a disease associated with complement activation, wherein the anti-C1q antibody fragment prevents or reduces the risk of developing a disease associated with complement activation, thereby preventing or reducing the risk of future diseases associated with complement activation.

53. The antibody Fab fragment of any one of claims 1-24, wherein the antibody Fab fragment has a shorter half-life as compared to its corresponding full-length antibody.