All patents and publications referred to herein are hereby incorporated in their entirety by reference.

SUMMARY OF THE INVENTION

The present invention includes an isolated antibody that binds with greater specificity to an amyloid beta (Aβ) protein globulomer than to an amyloid beta protein monomer. Thus, preferential binding is observed. The antibody may be, for example, a monoclonal antibody such as 8F5 or 8C5. The ratio of binding specificity to the globulomer versus the monomer is at least 1.4. In particular, the ratio is preferably at least about 1.4 to at least about 16.9. (A ratio of 1.0-17.5 including the endpoints) is also considered to fall within the scope of the present invention as well as decimal percentages thereof. For example, 1.1, 1.2, 1.3, …, 2.0, 2.1, 2.2…,17.1, 17.2, 17.3, 17.4, 17.5 as well as all full integers in between and percentages thereof are considered to fall within the scope of the present invention.) The amyloid beta protein monomer may be, for example, Aβ(1-42) monomer or Aβ(1-40) monomer.

The present invention provides a monoclonal antibody or fragment thereof that binds to amyloid beta globulomer comprising:

a) a light chain variable region complementarity determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO:8;

b) a light chain variable region CDR 2 comprising the amino acid sequence of SEQ ID NO:9; and

c) a light chain variable region CDR 3 comprising the amino acid sequence of SEQ ID NO:10; and

d) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:3.

The present invention provides a humanized monoclonal antibody or fragment thereof that binds to amyloid beta globulomer comprising:

a) a light chain variable region complementarity determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO:8;

b) a light chain variable region CDR 2 comprising the amino acid sequence of SEQ ID NO:9; and

c) a light chain variable region CDR 3 comprising the amino acid sequence of SEQ ID NO:10; and

d) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:3.

The present invention provides a monoclonal antibody or fragment thereof that binds to amyloid beta globulomer comprising:

a) a heavy chain variable region complementarity determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO:5;

b) a heavy chain variable region CDR 2 comprising the amino acid sequence of SEQ ID NO:6;

c) a heavy chain variable region CDR 3 comprising the amino acid sequence of SEQID NO:7; and

d) a light chain variable region comprising the amino acid sequence of SEQ ID NO 4.

The present invention provides a humanized monoclonal antibody or fragment thereof that binds to amyloid beta globulomer comprising:

a) a heavy chain variable region complementarity determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO:5;

b) a heavy chain variable region CDR 2 comprising the amino acid sequence of SEQ ID NO:6;

c) a heavy chain variable region CDR 3 comprising the amino acid sequence of SEQ ID NO:7; and

d) a light chain variable region comprising the amino acid sequence of SEQ ID NO 4.

The present invention provides a monoclonal antibody or fragment thereof that binds to amyloid beta globulomer comprising a heavy chain variable region and light chain variable region, wherein the heavy chain variable region comprises a sequence having at least 96% identity to SEQ ID NO:3, and the light chain variable region comprises a sequence having at least 96% identity to SEQ ID NO:4.

The present invention provides a humanized monoclonal antibody or fragment thereof that binds to amyloid beta globulomer comprising a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises a sequence having at least 96% identity to SEQ ID NO:3, and the light chain variable region comprises a sequence having at least 96% identity to SEQ ID NO:4.

The present invention provides a monoclonal antibody or fragment thereof that binds to amyloid beta globulomer comprising a heavy chain variable region and a light chain variable region wherein:

the light chain variable region of the monoclonal antibody comprises the amino acid sequence of RSSQSLVYSNGDTYLH (SEQ ID NO: 8); the amino acid sequence of KVSNRFS (SEQ ID NO: 9); and the amino acid sequence of SQSTHVPWT (SEQ ID NO: 10); and

the heavy chain variable region of the monoclonal antibody comprises the amino acid sequence of GFTFSSYGMS; the amino acid sequence of SINSNGGSTYYPDSVKG (SEQ ID NO: 6); and the amino acid sequence of GDY.

The present invention provides a humanized monoclonal antibody or fragment thereof that binds to amyloid beta globulomer comprising a light chain variable region and a heavy chain variable region wherein:

the light chain variable region of the monoclonal antibody comprises the amino acid sequence of RSSQSLVYSNGDTYLH (SEQ ID NO: 8); the amino acid sequence of KVSNRFS (SEQ ID NO: 9); and the amino acid sequence of SQSTHVPWT (SEQ ID NO:10); and

the heavy chain variable region of the monoclonal antibody comprises the amino acid sequence of GFTFSSYGMS; the amino acid sequence of SINSNGGSTYYPDSVKG (SEQ ID NO: 6); and the amino acid sequence of GDY.

The present invention provides a pharmaceutical composition for treating a neurodegenerative disorder comprising

the monoclonal antibody or fragment thereof as described herein.

The present invention provides the use of the monoclonal antibody or fragment thereof as described herein in the manufacture of a medicament for treating or preventing a neurodegenerative disorder.

The present invention provides the use of the monoclonal antibody or fragment thereof as described herein in the manufacture of a medicament for treating a neurodegenerative disorder.

The present invention provides a pharmaceutical composition for treating or preventing a neurodegenerative disorder comprising an isolated monoclonal antibody or fragment thereof that binds to amyloid beta globulomer, wherein the monoclonal antibody or fragment thereof comprises a heavy chain variable region comprising three complementarity determining

regions (CDRs) and a light chain variable region comprising three CDRs, wherein:

a) the heavy chain variable region is a heavy chain variable region encoded by SEQ ID NO:1 and the light chain variable region is a light chain variable region encoded by SEQ ID NO:2; or

b) the heavy chain variable region comprises SEQ ID NO:3 and the light chain variable region comprises SEQ ID NO:4.

The present invention provides a pharmaceutical composition for treating or preventing a neurodegenerative disorder comprising an isolated monoclonal antibody (8F5) produced by a hybridoma having American Type Culture Collection designation number PTA-7238.

The present invention provides the use of an isolated monoclonal antibody or fragment thereof that binds to amyloid beta globulomer for the manufacture of a medicament for treating or preventing a neurodegenerative disorder, wherein the monoclonal antibody or fragment thereof comprises a heavy chain variable region comprising three complementarity determining regions (CDRs) and a light chain variable region comprising three CDRs, wherein:

a) the heavy chain variable region is a heavy chain variable region encoded by SEQ ID NO:1 and the light chain variable region is a light chain variable region encoded by SEQ ID NO:2; or

b) the heavy chain variable region comprises SEQ ID NO:3 and the light chain variable region comprises SEQ ID NO:4.

Further, the present invention also encompasses a monoclonal antibody (referred to herein as "8F5") produced by a hybridoma having American Type Culture

Collection designation number PTA-7238 as well as the hybridoma that produces this monoclonal antibody (i.e., 8F5). Also, the present invention includes a monoclonal antibody (referred to herein as "8C5") produced by a hybridoma having American Type Culture Collection designation number PTA-7407 as well as the hybridoma that produces this monoclonal antibody (i.e., 8C5).

Additionally, the present invention includes a monoclonal antibody comprising a variable heavy chain encoded by SEQ ID NO:1. This antibody may be murine, human or humanized.

WHAT IS CLAIMED IS:

1. A monoclonal antibody or fragment thereof that binds to amyloid beta globulomer comprising:

a) a light chain variable region complementarity determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO:8;

b) a light chain variable region CDR 2 comprising the amino acid sequence of SEQ ID NO:9; and

c) a light chain variable region CDR 3 comprising the amino acid sequence of SEQ ID NO:10; and

d) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:3.

2. A humanized monoclonal antibody or fragment thereof that binds to amyloid beta globulomer comprising:

a) a light chain variable region complementarity determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO:8;

b) a light chain variable region CDR 2 comprising the amino acid sequence of SEQ ID NO:9; and

c) a light chain variable region CDR 3 comprising the amino acid sequence of SEQ ID NO:10; and

d) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:3.

3. A monoclonal antibody or fragment thereof that binds to amyloid beta globulomer comprising:

a) a heavy chain variable region complementarity determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO:5;

b) a heavy chain variable region CDR 2 comprising the amino acid sequence of SEQ ID NO:6;

c) a heavy chain variable region CDR 3 comprising the amino acid sequence of SEQID NO:7; and

d) a light chain variable region comprising the amino acid sequence of SEQ ID NO 4.

4. A humanized monoclonal antibody or fragment thereof that binds to amyloid beta globulomer comprising:

a) a heavy chain variable region complementarity determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO:5;

b) a heavy chain variable region CDR 2 comprising the amino acid sequence of SEQ ID NO:6;

c) a heavy chain variable region CDR 3 comprising the amino acid sequence of SEQ ID NO:7; and

d) a light chain variable region comprising the amino acid sequence of SEQ ID NO 4.

5. A monoclonal antibody or fragment thereof that binds to amyloid beta globulomer comprising a heavy chain variable region and light chain variable region, wherein the heavy chain variable region comprises a sequence having at least 96% identity to SEQ ID NO:3, and the light chain variable region comprises a sequence having at least 96% identity to SEQ ID NO:4.

6. A humanized monoclonal antibody or fragment thereof that binds to amyloid beta globulomer comprising a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises a sequence having at least 96% identity to SEQ ID NO:3, and the light chain variable region comprises a sequence having at least 96% identity to SEQ ID NO:4.

7. A monoclonal antibody or fragment thereof that binds to amyloid beta globulomer comprising a heavy chain variable region and a light chain variable region wherein:

the light chain variable region of the monoclonal antibody comprises the amino acid sequence of RSSQSLVYSNGDTYLH (SEQ ID NO: 8); the amino acid sequence of KVSNRFS (SEQ ID NO: 9); and the amino acid sequence of SQSTHVPWT (SEQ ID NO: 10); and

the heavy chain variable region of the monoclonal antibody comprises the amino acid sequence of GFTFSSYGMS; the amino acid sequence of SINSNGGSTYYPDSVKG (SEQ ID NO: 6); and the amino acid sequence of GDY.

8. The monoclonal antibody of claim 7, wherein all framework regions correspond to those of a human immunoglobulin consensus sequence.

9. A humanized monoclonal antibody or fragment thereof that binds to amyloid beta globulomer comprising a light chain variable region and a heavy chain variable region wherein:

the light chain variable region of the monoclonal antibody comprises the amino acid sequence of RSSQSLVYSNGDTYLH (SEQ ID NO: 8); the amino acid sequence of KVSNRFS (SEQ ID NO: 9); and the amino acid sequence of SQSTHVPWT (SEQ ID NO:10); and

the heavy chain variable region of the monoclonal antibody comprises the amino acid sequence of GFTFSSYGMS; the amino acid sequence of SINSNGGSTYYPDSVKG (SEQ ID NO: 6); and the amino acid sequence of GDY.

10. The monoclonal antibody or fragment thereof of any one of claims 1-9, wherein the monoclonal antibody binds with greater specificity to an amyloid beta protein globulomer than to an amyloid beta protein monomer.

11. A pharmaceutical composition for treating or preventing a neurodegenerative disorder comprising the monoclonal antibody or fragment thereof of any one of claims 1-10.

12. A pharmaceutical composition for treating a neurodegenerative disorder comprising

the monoclonal antibody or fragment thereof of any one of claims 1-10.

13. The pharmaceutical composition of claim 11 or 12, wherein the neurodegenerative disorder is Alzheimer's disease.

14. Use of the monoclonal antibody or fragment thereof of any one of claims 1-10 in the manufacture of a medicament for treating or preventing a neurodegenerative disorder.

15. Use of the monoclonal antibody or fragment thereof of any one of claims 1-10 in the manufacture of a medicament for treating a neurodegenerative disorder.

16. The use of claim 14 or 15, wherein the neurodegenerative disorder is Alzheimer's disease.

17. A pharmaceutical composition for treating or preventing a neurodegenerative disorder comprising an isolated monoclonal antibody or fragment thereof that binds to amyloid beta globulomer, wherein the monoclonal antibody or fragment thereof comprises a heavy chain variable region comprising three complementarity determining regions (CDRs) and a light chain variable region comprising three CDRs, wherein:

a) the heavy chain variable region is a heavy chain variable region encoded by SEQ ID NO:1 and the light chain variable region is a light chain variable region encoded by SEQ ID NO:2; or

b) the heavy chain variable region comprises SEQ ID NO:3 and the light chain variable region comprises SEQ ID NO:4.

18. A pharmaceutical composition for treating or preventing a neurodegenerative disorder comprising an isolated monoclonal antibody (8F5) produced by a hybridoma having American Type Culture Collection designation number PTA-7238.

19. The pharmaceutical composition of claim 17 or 18, wherein the monoclonal antibody or fragment thereof binds with greater specificity to an amyloid beta protein globulomer than to an amyloid beta protein monomer.

20. The pharmaceutical composition of any one of claims 17-19, wherein the neurodegenerative disorder is Alzheimer's disease.

21. Use of an isolated monoclonal antibody or fragment thereof that binds to amyloid beta globulomer for the manufacture of a medicament for treating or preventing a neurodegenerative disorder, wherein the monoclonal antibody or fragment thereof comprises a heavy chain variable region comprising three complementarity determining regions (CDRs) and a light chain variable region comprising three CDRs, wherein:

a) the heavy chain variable region is a heavy chain variable region encoded by SEQ ID NO:1 and the light chain variable region is a light chain variable region encoded by SEQ ID NO:2; or

b) the heavy chain variable region comprises SEQ ID NO:3 and the light chain variable region comprises SEQ ID NO:4.