Claims

1. An isolated antibody that selectively binds to the C-terminal part of beta-amyloid, comprising

(i) a variable light chain fragment (V_L) sequence having at least 80% identity to SEQ ID. No. 7; and

(ii) a variable heavy chain fragment (V_H) sequence having at least 80% identity to SEQ ID. No. 17.

2. The antibody of claim 1, being an immunoglobulin, a single chain antibody (scFv), a Fab fragment, a F(ab')2 fragment, a Fd fragment or a Fv fragment.

3. The antibody of any one of the preceding claims, comprising the variable light chain as set forth in SEQ ID: No. 7 and the variable heavy chain as set forth in SEQ ID: No. 17.

4. The antibody of claim 3, being a scFv and having the sequence as set forth in Seq. ID. No. 24.

5. The antibody of any one of the preceding claims, preventing oligomerisation of beta-amyloid.

6. The antibody of any one of the preceding claims, demonstrating the characteristics of:

(i) Binding to both beta-amyloid$_{40}$ and beta-amyloid$_{42}$ with a high and substantially identical affinity;

(ii) Displaying a high affinity for oligomeric and monomeric forms of beta-amyloid;

(iii) Not substantially recognizing amyloid precursor protein (APP) *in vivo*; and

(iv) Having a solubility of at least 5 mg/ml, preferably at least 10 mg/ml, and more preferably

at least 20 mg/ml as measured according to the method of Atha and Ingham.

7. The antibody of claim 6, further demonstrating the characteristic of:

(v) Binding beta-amyloid plaques.

8. The antibody of any one of the preceding claims, being chemically modified.

9. The antibody of any one of the preceding claims, being linked to a therapeutic agent.

10. The antibody of any one of the preceding claims, being linked to a label, in particular to ^{64}Cu.

11. The antibody of any one of the preceding claims for use in diagnosis or screening of a subject

(i) for amyloidosis,

(ii) for Alzheimer's disease or

(iii) for determining a subject's risk for developing amyloidosis or Alzheimer's disease.

12. The antibody of claim 11, wherein the diagnosis is done by PET imaging.

13. A nucleic acid sequence encoding the antibody of anyone of claims 1 to 7.

14. A vector comprising the sequence of claim 13.

15. A host cell comprising the sequence of claim 13 or the vector of claim 14.

16. A method of producing the antibody of any oen of claims 1 to 7, comprising the steps of

(i) Culturing the host cell of claim 15 under conditions that allow for the synthesis of the antibody;

(ii) Recovering the antibody from the culture.

17. A pharmaceutical composition for treating, preventing and/or delaying the progression of a neurological disorder, in particular Alzheimer's Disease and/or passive immunization against Alzheimer's disease comprising the antibody of anyone of claims 1 to 10.

18. The pharmaceutical composition of claim 17, being suitable for intranasal, subcutaneous, intrathecal, intracranial or intravenous administration.

19. A test kit comprising the antibody of any one of claims 1 to 10.

20. A method of diagnosis comprising the steps of

(i) Labelling the antibody of anyone of claims 1 to 10;

(ii) Administering an effective dose of said antibody intranasally or systemically to a subject; and

(iii) Detecting the concentration and/or presence of the labelled antibody in body parts of the subject.

21. The method of claim 20, wherein the antibody is labelled with a positron emitting isotope.

22. The method of any one of claims 20 to 21, wherein the antibody is labelled with ^{64}Cu.

23. The method of any one of claims 20 to 22, wherein the subject undergoes PET imaging in step (iii).

24. The antibody of any one claims 1 to 10 for use in the treatment of a neurological disorder, in particular Alzheimer's Disease and/or passive immunization against Alzheimer's disease.

CLAIMS:

1. An isolated antibody that selectively binds to the C-terminal part of beta-amyloid, the antibody comprising a variable light chain fragment (VL) sequence comprising the variable light chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID Nos. 1, 2 and 3, respectively, and a variable heavy chain fragment (VH) sequence comprising the variable heavy chain CDR1, CDR2 and CDR3 sequences set forth in SEQ ID Nos. 4, 5 and 6, respectively, wherein:

a) position 1 of the light chain is an aspartate residue;

b) position 43 of the light chain is a proline residue;

c) position 46 of the light chain is an alanine residue;

d) position 61 of the light chain is an arginine residue;

e) position 104 of the light chain is a leucine residue;

f) position 105 of the light chain is a glutamate residue; and

g) position 106 of the light chain is a valine residue, according to Kabat numbering.

2. The antibody of claim 1, wherein:

a) position 9 of the heavy chain is a proline residue;

b) position 28 of the heavy chain is a threonine residue;

c) position 71 of the heavy chain is a valine residue;

d) position 73 of the heavy chain is an arginine residue;

e) position 75 of the heavy chain is a serine residue;

f) position 76 of the heavy chain is a serine residue; and

g) position 78 of the heavy chain is an alanine residue, according to Kabat numbering.

3. The antibody of claim 1, comprising the variable heavy chain fragment (VH) sequence set forth in SEQ ID: No. 17.

4. The antibody of claim 1, comprising the variable light chain fragment (VL) sequence set forth in SEQ ID NO: 7.

5. The antibody of claim 1, further comprising the sequence set forth in SEQ ID NO: 25.

6. The antibody of claim 1, demonstrating the characteristics of:

(i) binding to both beta-amyloid$_{40}$ and beta-amyloid$_{42}$, with a high and substantially identical affinity;

(ii) displaying a high affinity for oligomeric and monomeric forms of beta-amyloid; and/or

(iii) having a solubility of at least 5 mg/ml.

7. The antibody of claim 6, further demonstrating at least one of the following characteristics:

(i) mediating the uptake of fibrillar beta-amyloid by microglia;

(ii) binding beta-amyloid plaques; and/or

(iii) removing beta-amyloid fibrils in the brain and/or inhibiting the formation of amyloid fibrils in the brain.

8. The antibody of claim 1, wherein the antibody inhibits oligomerization of beta-amyloid.

9. The antibody of claim 1, wherein the antibody is a full-length antibody.

10. The antibody of claim 1, being an antigen-binding fragment wherein the antigen-binding fragment is an Fv fragment, a single domain fragment, a single chain antibody (scFv), a Fab fragment or a F(ab')$_2$ fragment.

11. The antibody of claim 1, linked to a therapeutic agent.

12. The antibody of claim 1, being chemically modified.

13. The antibody of claim 1, linked to a label.

14. The antibody of claim 13, wherein the label comprises ^{64}Cu.

15. A diagnostic or scientific tool comprising the antibody of any one of claim 1, 12 or 13.

16. A test kit comprising the antibody of any one of claim 1, 12 or 13.

17. A diagnostic or scientific tool comprising the antibody of claim 12.

18. A diagnostic or scientific tool comprising the antibody of claim 13.

19. A test kit comprising the antibody of claim 12.

20. A test kit comprising the antibody of claim 13.

21. An isolated antibody that selectively binds to the C-terminal part of beta-amyloid, wherein the antibody comprises the variable light chain fragment (VL) sequence set forth in SEQ ID NO: 7 and the variable heavy chain fragment (VH) sequence set forth in SEQ ID NO: 17.

22. The antibody of claim 21, wherein the antibody is a full-length antibody.

23. The antibody of claim 21, being an antigen-binding fragment wherein the antigen-binding fragment is an Fv fragment, a single domain fragment, a single chain antibody (scFv), a Fab fragment or a $F(ab')_2$ fragment.

24. An isolated antibody that selectively binds to the C-terminal part of beta-amyloid, wherein the antibody comprises SEQ ID NO: 24.

25. The antibody of claim 21 or 24 being chemically modified.

26. A diagnostic or scientific tool comprising the antibody of claim 25.

27. A test kit comprising the antibody of claim 25.

28. The antibody of claim 21 or 24 linked to a therapeutic agent.

29. The antibody of claim 21 or 24 linked to a label.

30. The antibody of claim 29, wherein the label comprises ^{64}Cu.

31. A diagnostic or scientific tool comprising the antibody of claim 29.

32. A test kit comprising the antibody of claim 29.

33. The antibody of claim 21 or 24 demonstrating the characteristics of:

(i) binding to both beta-amyloid$_{40}$ and beta-amyloid$_{42}$, with a high and substantially identical affinity;

(ii) displaying a high affinity for oligomeric and monomeric forms of beta-amyloid; and/or

(iii) having a solubility of at least 5 mg/ml.

34. The antibody of claim 33, further demonstrating at least one of the following characteristics:

(i) mediating the uptake of fibrillar beta-amyloid by microglia;

(ii) binding beta-amyloid plaques; and/or

(iii) removing beta-amyloid fibrils in the brain and/or inhibiting the formation of amyloid fibrils in the brain.

35. A diagnostic or scientific tool comprising the antibody of claim 21 or 24.

36. A test kit comprising the antibody of claim 21 or 24.

37. The antibody of claim 21 or 24, wherein the antibody inhibits oligomerization of beta-amyloid.