Claims

1. An antibody or antigen binding fragment thereof having affinity against Aβ protofibrils, wherein the antibody or antigen binding fragment thereof has a variable light chain according to SEQ ID NO: 8, wherein
x_1 is selected from A, D, E and Q, or a functional analogue thereof;
x_2 is selected from R, T, K, A and G, or a functional analogue thereof;
x_3 is selected from R, S, C, G and N, or a functional analogue thereof;
y_1 is selected from V and A;
y_2 is selected from I and V;
y_3 is selected from S and Q;
y_4 is selected from E and D; and optionally
a variable heavy chain according to SEQ ID NO: 14, wherein
z_1 is selected from V and I;
z_2 is selected from R and Q; and
z_3 is selected from A, N and T.
with the exception for the combination x_1=A, x_2=R and x_3=R.

2. The antibody or antigen binding fragment according to claim 1, wherein
x_1 is selected from A, D, E and Q;
x_2 is selected from R, T, K, A and G;
x_3 is selected from R, S, C, G and N;
y_1 is selected from V and A;
y_2 is selected from I and V;
y_3 is selected from S and Q;
y_4 is selected from E and D; and
a variable heavy chain according to SEQ ID NO: 14, wherein
z_1 is selected from V and I;
z_2 is selected from R and Q; and
z_3 is selected from A, N and T;
with the exception for the combination x_1=A, x_2=R and x_3=R.

3. The antibody or antigen binding fragment according to claim 1 or 2, wherein the light chain a comprises a combination of mutations selected from:

x_1 and (y_1 and/or y_2);

x_1 and (y_1 and/or y_2) and x_2 and (y_3 and/or y_4);

x_1 and (y_1 and/or y_2) and x_2 and x_3 and (y_3 and/or y_4);

x_1 and (y_1 and/or y_2) and x_3 and (y_3 and/or y_4);

x_2 (y_3 and/or y_4);

x_2 and x_3 and (y_3 and/or y_4); and

x_3 and (y_3 and/or y_4);

with the exception for the combination x_1=A, x_2=R and x_3=R.

4. The antibody or antigen binding fragment according to any one of claims 1 to 3, wherein the variable light chain comprises one or more mutations, selected from:

x_1 is D and (y_1 and/or y_2);

x_1 is D and (y_1 and/or y_2), x_2 is T and (y_3 and/or y_4);

x_1 is D and (y_1 and/or y_2), x_2 is T, x_3 is S and (y_3 and/or y_4);

x_1 is D and (y_1 and/or y_2) and x_3 is S and (y_3 and/or y_4);

x_2 is T (y_3 and/or y_4);

x_2 is T and x_3 is S and (y_3 and/or y_4); and

x_3 is S and (y_3 and/or y_4);

wherein y_1 is V or A and y_2 is V or I, with exclusion of the combination y_1=V and y_2=I;

y_3 is S or Q and y_4 is E or D with exclusion of the combination y_3=S and Y_4=E.

5. The antibody or antigen binding fragment according to any one of claims 1 to 4, wherein

x_1 is D;

x_2 is T;

x_3 is R;

y_1 is selected from V and A;

y_2 is selected from V and I;

y_3 is selected from Q and S;

y_4 is selected from D and E;

z_1 is V;

z_2 is R; and

z_3 is selected from N, T and A;

with exclusion of the combination wherein y_1 is V, y_2 is I, y_3, is S, y_4 is E, z_1 is V, z_2 is R and z_3 is A.

6. An antibody or antigen binding fragment thereof, according to claim 1, comprising a variable light chain comprising an amino acid sequence as set out in SEQ ID NO: 12; and a variable heavy chain comprising an amino acid sequence as set out in SEQ ID NO: 16.

7. An antibody or antigen binding fragment thereof, according to claim 1, comprising a variable light chain comprising an amino acid sequence as set out in SEQ ID NO: 9; and a variable heavy chain comprising an amino acid sequence as set out in SEQ ID NO: 15.

8. An antibody or antigen binding fragment thereof, according to claim 1, comprising a variable light chain comprising an amino acid sequence as set out in SEQ ID NO: 10; and a variable heavy chain comprising an amino acid sequence as set out in SEQ ID NO: 15.

9. An antibody or antigen binding fragment thereof, according to claim 1, comprising a variable light chain comprising an amino acid sequence as set out in SEQ ID NO: 11; and a variable heavy chain comprising an amino acid sequence as set out in SEQ ID NO: 15.

10. An antibody or antigen binding fragment thereof, according to claim 1, comprising a variable light chain comprising an amino acid sequence as set out in SEQ ID NO: 12; and a variable heavy chain comprising an amino acid sequence as set out in SEQ ID NO: 15.

11. An antibody or antigen binding fragment thereof, according to claim 1, comprising a variable light chain comprising an amino acid sequence as set out in SEQ ID NO: 9; and a variable heavy chain comprising an amino acid sequence as set out in SEQ ID NO: 16.

12. An antibody or antigen binding fragment thereof, according to claim 1, comprising a variable light chain comprising an amino acid sequence as set out in SEQ ID NO: 10;

and a variable heavy chain comprising an amino acid sequence as set out in SEQ ID NO: 16.

13. An antibody or antigen binding fragment thereof, according to claim 1, comprising a variable light chain comprising an amino acid sequence as set out in SEQ ID NO: 11; and a variable heavy chain comprising an amino acid sequence as set out in SEQ ID NO: 16.

14. The antibody or antigen binding fragment according to any one of claims 1 to 13, wherein the antibody or the antigen binding fragment comprises an IgG heavy chain constant region.

15. An antibody according to any one of claims 1 to 14, for use in therapy.

16. An antibody according to any one of claims 1 to 14, for use in treatment and/or prophylaxis of Alzheimer's disease and other disorders associated with Aβ protein aggregation.

17. An antibody according to claim 16, for use, wherein such other disorders associated with Aβ protein aggregation are selected from traumatic brain injury (TBI), Lewy body dementia (LBD), Downs syndrome (DS), Amyotrophic lateral sclerosis (ALS), Frontotemporal dementia, tauopathies, systemic amyloidoses, atherosclerosis and Parkinson's disease dementia (PDD).

18. Use of an antibody according to any one of claims 1 to 14, in the manufacture of a medicament useful in the treatment and/or prophylaxis of Alzheimer's disease and other disorders associated with Aβ protein aggregation.

19. The use according to claim 18, wherein such other disorders associated with Aβ protein aggregation are selected from Traumatic brain injury (TBI), Lewy body dementia (LBD), Downs syndrome (DS), Amyotrophic lateral sclerosis (ALS), Frontotemporal dementia, tauopathies, systemic amyloidoses, atherosclerosis and Parkinson's disease dementia (PDD).

20. A method of reducing amount of Aβ protofibrils in a subject, comprising administering to said subject a therapeutically effective amount of the antibody or antigen binding fragment according to claims 1 to 14.

21. A method for treatment and/or prophylaxis of Alzheimer's disease in a subject having, or being at risk of developing said disease, comprising administering to said subject a therapeutically effective amount of the antibody or antigen binding fragment according to claims 1 to 14.

22. A method for treatment and/or prophylaxis of traumatic brain injury (TBI), Lewy body dementia (LBD), Down syndrome (DS), Amyotrophic lateral sclerosis (ALS), Frontotemporal dementia, tauopathies, systemic amyloidosis, atherosclerosis and Parkinson's disease dementia (PDD) in a subject having, or being at risk of developing said disease, comprising administering to said subject a therapeutically effective amount of the antibody or antigen binding fragment according to claims 1 to 14.

23. A method for measuring amount of Aβ protofibrils and/or aggregated Aβ protein in a person, comprising contacting the person's tissue or body fluid, *in vivo* or *in vitro*, with the antibody or antigen binding fragment according to claims 1 to 14 and measuring the amount of antibody or antigen binding fragment bound to said Aβ protofibrils and/or aggregated Aβ protein.

24. A method for diagnosis of Alzheimer's disease in persons having or at risk of developing the disease, comprising contacting the person's tissue or body fluid, *in vivo* or *in vitro*, with the antibody or antigen binding fragment according to claims 1 to 14, or a fragment thereof, and measuring the amount of said antibody bound to aggregated Aβ protein.

25. A method for diagnosis of traumatic brain injury (TBI), Lewy body dementia (LBD), Down syndrome (DS), Amyotrophic lateral sclerosis (ALS), Frontotemporal dementia, tauopathies, systemic amyloidosis, atherosclerosis and Parkinson's disease dementia (PDD)in persons having or at risk of developing any of said diseases, comprising contacting the person's tissue or body fluid, *in vivo* or *in vitro*, with the antibody or antigen binding fragment according to claims 1 to 14, or a fragment thereof, and measuring the amount of said antibody bound to aggregated Aβ protein.

26. A pharmaceutical composition comprising the antibody or antigen binding fragment according to any one of claims 1 to 14, together with pharmaceutically acceptable excipient and/or diluents.

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27. An antibody according to any one of claims 1 to 14, for veterinary use.