In one embodiment the antibody is a humanized antibody and comprises in the heavy chain variable domain the HVRs of SEQ ID NO: 21, 22 and 17 and in the light chain variable domain the HVRs of SEQ ID NO: 23 to 25, wherein in each HVR 0 to 3 amino acid residues have been changed.

In one embodiment the antibody is a humanized antibody and the heavy chain variable domain is derived from a heavy chain variable domain of SEQ ID NO: 26 and the light chain variable domain is derived from a light chain variable domain of SEQ ID NO: 27.

The disclosure relates to an antibody that binds to the same epitope or an overlapping epitope as an antibody comprising in the heavy chain the HVRs of SEQ ID NO: 15 to 17 and in the light chain the HVRs of SEQ ID NO: 18 to 20.

The disclosure relates to an antibody that binds to the same or an overlapping epitope as an antibody comprising a heavy chain variable domain of SEQ ID NO: 26 and a light chain variable domain of SEQ ID NO: 27.

One aspect as reported herein is an antibody comprising in the heavy chain the HVRs of SEQ ID NO: 15 to 17 and in the light chain the HVRs of SEQ ID NO: 18 to 20, whereby (a) HVR-H1 comprises the amino acid sequence of SEQ ID NO: 15; (b) HVR-H2 comprises the amino acid sequence of SEQ ID NO: 16; (c) HVR-H3 comprises the amino acid sequence of SEQ ID NO: 17; (d) HVR-L1 comprises the amino acid sequence of SEQ ID NO: 18; (e) HVR-L2 comprises the amino acid sequence of SEQ ID NO: 19; and (f) HVR-L3 comprises the amino acid sequence of SEQ ID NO: 20.

One aspect as reported herein is an antibody comprising in the heavy chain the HVRs of SEQ ID NO: 21, 22 and 17 and in the light chain the HVRs of SEQ ID NO: 23 to 25, whereby (a) HVR-H1 comprises the amino acid sequence of SEQ ID NO: 21; (b) HVR-H2 comprises the amino acid sequence of SEQ ID NO: 22; (c) HVR-H3 comprises the amino acid sequence of SEQ ID NO: 17; (d) HVR-L1 comprises the amino acid sequence of SEQ ID NO: 23; (e) HVR-L2 comprises the amino acid sequence of SEQ ID NO: 24; and (f) HVR-L3 comprises the amino acid sequence of SEQ ID NO: 25.

The disclosure relates to a variant antibody that has been obtained from an antibody comprising a heavy chain variable domain of SEQ ID NO: 26 and a light chain variable domain of SEQ ID NO: 27.

One aspect as reported herein is an antibody that has been obtained from an antibody comprising a heavy chain variable domain of SEQ ID NO: 26 comprising (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 15; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 16; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 17; and a light chain variable domain of SEQ ID NO: 27 comprising (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 18; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 19; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 20.

In one embodiment the variant antibody is a humanized antibody that has been obtained by humanizing an antibody comprising a heavy chain variable domain of SEQ ID NO: 26 and a light chain variable domain of SEQ ID NO: 27.

One aspect as reported herein is a humanized antibody that specifically binds to human alpha-synuclein and comprising in the heavy chain variable domain the HVRs of SEQ ID NO: 15 to 17 and in the light chain variable domain the HVRs of SEQ ID NO: 18 to 20, whereby (a) HVR-H1 comprises the amino acid sequence of SEQ ID NO: 15; (b) HVR-H2 comprises the amino acid sequence of SEQ ID NO: 16; (c) HVR-H3 comprises the amino acid sequence of SEQ ID NO: 17; (d) HVR-L1 comprises the amino acid sequence of SEQ ID NO: 18; (e) HVR-L2 comprises the amino acid sequence of SEQ ID NO: 19; and (f) HVR-L3 comprises the amino acid sequence of SEQ ID NO: 20,wherein in each HVR 0 to 3 amino acid residues have been changed.

One aspect as reported herein is a humanized antibody that specifically binds to human alpha-synuclein and comprising in the heavy chain variable domain the HVRs of SEQ ID NO: 21, 22 and 17 and in the light chain variable domain the HVRs of SEQ ID NO: 23 to 25, whereby (a) HVR-H1 comprises the amino acid sequence of SEQ ID NO: 21; (b) HVR-H2 comprises the amino acid sequence of SEQ ID NO: 22; (c) HVR-H3 comprises the amino acid sequence of SEQ ID NO: 17; (d) HVR-L1 comprises the amino acid sequence of SEQ ID NO: 23; (e) HVR-L2 comprises the amino acid sequence of SEQ ID NO: 24; and (f) HVR-L3 comprises the amino acid sequence of SEQ ID NO: 25, wherein in each HVR 0 to 3 amino acid residues have been changed.

One aspect as reported herein is a humanized antibody that specifically binds to human alpha-synuclein and wherein the heavy chain variable domain is derived from a heavy chain variable domain of SEQ ID NO: 26 comprising (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 15; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 16; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 17; and the light chain variable domain is derived from a light chain variable domain of SEQ ID NO: 27 comprising (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 18; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 19; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 20.

In one embodiment of the disclosure the antibody is conjugated to a blood-brain-barrier shuttle module.

In one embodiment the blood-brain-barrier shuttle module is an antibody or antibody fragment that specifically binds to LRP1, LRP8, human transferrin receptor or human insulin-like growth factor receptor.

In one embodiment of the disclosurethe antibody is a monoclonal antibody.

In one embodiment of the disclosurethe antibody is a humanized antibody or a chimeric antibody.

In one embodiment of the disclosurethe antibody is

a) a full length antibody of the human subclass IgG1, or
b) a full length antibody of the human subclass IgG4, or
c) a full length antibody of the human subclass IgG1 with the mutations L234A, L235A and P329G,

d) a full length antibody of the human subclass IgG4 with the mutations S228P, L235E and P329G,

e) a full length antibody of the human subclass IgG1 with the mutations L234A, L235A and P329G in both heavy chains and the mutations T366W and S354C in one heavy chain and the mutations T366S, L368A, Y407V and Y349C in the respective other heavy chain, or

f) a full length antibody of the human subclass IgG4 with the mutations S228P, L235E and P329G in both heavy chains and the mutations T366W and S354C in one heavy chain and the mutations T366S, L368A, Y407V and Y349C in the respective other heavy chain.

Patent Claims

1. An antibody comprising in the heavy chain the HVRs of SEQ ID NO: 15 to 17 and in the light chain the HVRs of SEQ ID NO: 18 to 20, whereby
(a) HVR-H1 comprises the amino acid sequence of SEQ ID NO: 15;
(b) HVR-H2 comprises the amino acid sequence of SEQ ID NO: 16;
(c) HVR-H3 comprises the amino acid sequence of SEQ ID NO: 17;
(d) HVR-L1 comprises the amino acid sequence of SEQ ID NO: 18;
(e) HVR-L2 comprises the amino acid sequence of SEQ ID NO: 19; and
(f) HVR-L3 comprises the amino acid sequence of SEQ ID NO: 20.

2. An antibody comprising in the heavy chain the HVRs of SEQ ID NO: 21, 22 and 17 and in the light chain the HVRs of SEQ ID NO: 23 to 25, whereby
(a) HVR-H1 comprises the amino acid sequence of SEQ ID NO: 21;
(b) HVR-H2 comprises the amino acid sequence of SEQ ID NO: 22;
(c) HVR-H3 comprises the amino acid sequence of SEQ ID NO: 17;
(d) HVR-L1 comprises the amino acid sequence of SEQ ID NO: 23;
(e) HVR-L2 comprises the amino acid sequence of SEQ ID NO: 24; and
(f) HVR-L3 comprises the amino acid sequence of SEQ ID NO: 25.

3. An antibody that has been obtained from an antibody comprising a heavy chain variable domain of SEQ ID NO: 26 comprising (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 15; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 16; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 17; and a light chain variable domain of SEQ ID NO: 27 comprising (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 18; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 19; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 20.

4. A humanized antibody that specifically binds to human alpha-synuclein and comprising in the heavy chain variable domain the HVRs of SEQ ID NO: 15 to 17 and in the light chain variable domain the HVRs of SEQ ID NO: 18 to 20, whereby
(a) HVR-H1 comprises the amino acid sequence of SEQ ID NO: 15;
(b) HVR-H2 comprises the amino acid sequence of SEQ ID NO: 16;
(c) HVR-H3 comprises the amino acid sequence of SEQ ID NO: 17;
(d) HVR-L1 comprises the amino acid sequence of SEQ ID NO: 18;

(e) HVR-L2 comprises the amino acid sequence of SEQ ID NO: 19; and

(f) HVR-L3 comprises the amino acid sequence of SEQ ID NO: 20,

wherein in each HVR 0 to 3 amino acid residues have been changed.

5. A humanized antibody that specifically binds to human alpha-synuclein and comprising in the heavy chain variable domain the HVRs of SEQ ID NO: 21, 22 and 17 and in the light chain variable domain the HVRs of SEQ ID NO: 23 to 25, whereby

(a) HVR-H1 comprises the amino acid sequence of SEQ ID NO: 21;

(b) HVR-H2 comprises the amino acid sequence of SEQ ID NO: 22;

(c) HVR-H3 comprises the amino acid sequence of SEQ ID NO: 17;

(d) HVR-L1 comprises the amino acid sequence of SEQ ID NO: 23;

(e) HVR-L2 comprises the amino acid sequence of SEQ ID NO: 24; and

(f) HVR-L3 comprises the amino acid sequence of SEQ ID NO: 25,

wherein in each HVR 0 to 3 amino acid residues have been changed.

6. A humanized antibody that specifically binds to human alpha-synuclein and wherein the heavy chain variable domain is derived from a heavy chain variable domain of SEQ ID NO: 26 comprising (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 15; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 16; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 17; and the light chain variable domain is derived from a light chain variable domain of SEQ ID NO: 27 comprising (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 18; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 19; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 20.

7. The antibody according to any one of claims 1 to 6, wherein the antibody is conjugated to a blood-brain-barrier shuttle module.

8. The antibody according to claim 7, wherein the blood-brain-barrier shuttle module is an antibody or antibody fragment that specifically binds to LRP1, LRP8, human transferrin receptor or human insulin-like growth factor receptor.

9. The antibody according to any one of claims 1 to 8, wherein the antibody is
   a) a full length antibody of the human subclass IgG1, or
   b) a full length antibody of the human subclass IgG4, or
   c) a full length antibody of the human subclass IgG1 with the mutations L234A, L235A and P329G,
   d) a full length antibody of the human subclass IgG4 with the mutations S228P, L235E and P329G,
   e) a full length antibody of the human subclass IgG1 with the mutations L234A, L235A and P329G in both heavy chains and the mutations T366W and S354C in one heavy chain and the mutations T366S, L368A, Y407V and Y349C in the respective other heavy chain, or
   f) a full length antibody of the human subclass IgG4 with the mutations S228P, L235E and P329G in both heavy chains and the mutations T366W and S354C in one heavy chain and the mutations T366S, L368A, Y407V and Y349C in the respective other heavy chain.

10. The antibody according to any one of claims 1 to 9, wherein the antibody
   i) inhibits alpha-synuclein induced cytotoxicity in human neurons and glia cells, and/or
   ii) inhibits cell-to-cell transmission of oligomeric human alpha-synuclein between neurons and glia cells, and/or
   iii) reduces alpha-synuclein-induced caspase activity in human neuronal cells, and/or
   iv) specifically binds to alpha-synuclein that has a free N-terminal methionine residue and does not specifically bind to alpha-synuclein that has a modified N-terminal methionine residue.

11. A pharmaceutical formulation comprising the antibody according to any one of claims 1 to 10 and a pharmaceutically acceptable carrier.

12. The antibody according to any one of claims 1 to 10 for use as a medicament.

13. The antibody according to any one of claims 1 to 10 for use in treating synucleinopathy.

14. The antibody according to any one of claims 1 to 10 for use in treating Parkinson's disease.

15. Use of the antibody according to any one of claims 1 to 10 in the manufacture of a medicament for treatment of Parkinson's disease.

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