CLAIMS

1. A human monoclonal anti-α-synuclein antibody.

2. The antibody of claim 1, which is capable of specifically binding α-synuclein in the native monomer form.

3 The antibody of claim 1 or 2, which is capable of binding α-synuclein in the oligomeric or aggregated form.

4. The antibody of any one claims 1 to 3, wherein the antibody specifically binds α-synuclein compared to β-synuclein or γ-synuclein.

5. The antibody of any one of claims 1 to 4, which recognizes an N-terminal$_{1-60}$ fragment or C-terminal$_{96-140}$ fragment of α-synuclein.

6. The antibody of any one of claims 1 to 4, which does not recognize a truncated form of α-synuclein.

7. The antibody of any one of claims 1 to 6 or an α-synuclein binding fragment thereof comprising in its variable region at least one complementarity determining region (CDR) as depicted in Fig. 1.

8. The antibody or binding fragment of claim 7 comprising an amino acid sequence of the V_H and/or V_L region as depicted in Fig 1.

9. An antibody or antigen-binding molecule which competes with an antibody of any one of claims 1 to 8 for specific binding to α-synuclein.

10. The antibody of claim 9, which is a chimeric murine-human or a murinized antibody.

11. The antibody of any one of claims 1 to 10, which is selected from the group consisting of a single chain Fv fragment (scFv), an F(ab') fragment, an F(ab) fragment, and an $F(ab')_2$ fragment.

12. A polynucleotide encoding at least the binding domain or variable region of an immunoglobulin chain of the antibody of any one of claims 1 to 11.

13. A vector comprising the polynucleotide of claim 12, optionally in combination with a polynucleotide of claim 12 that encodes the variable region of the other immunoglobulin chain of the antibody.

14. A host cell comprising a polynucleotide of claim 10 or a vector of claim 13.

15. A method for preparing an anti-α-synuclein antibody or immunoglobulin chain(s) thereof, said method comprising
    (a) culturing the cell of claim 14; and
    (b) isolating said antibody or immunoglobulin chain(s) thereof from the culture.

16. An antibody or immunoglobulin chain(s) thereof encoded by a polynucleotide of claim 12 or obtainable by the method of claim 15.

17. The antibody of any one of claims 1 to 11 or 16, which is detectably labeled.

18. The antibody of claim 17, wherein the detectable label is selected from the group consisting of an enzyme, a radioisotope, a fluorophore and a heavy metal.

19. The antibody of any one of claims 1 to 11 or 16 to 18, which is attached to a drug.

20. A composition comprising the antibody of any one of claims 1 to 11 or 16 to 19, the polynucleotide of claim 12, the vector of claim 13 or the cell of claim 14.

21. The composition of claim 20, which is a pharmaceutical composition and further comprises a pharmaceutically acceptable carrier.

22. The composition of claim 21, which is a vaccine.

23. The pharmaceutical composition of claim 21 or 22 further comprising an additional agent useful for treating a synucleinopathic disease.

24. The composition of claim 20, which is a diagnostic composition, and optionally comprises reagents conventionally used in immuno or nucleic acid based diagnostic methods.

25. Use of an antibody of any one of claims 1 to 11 or 16 to 19 or an α-synuclein binding molecule having substantially the same binding specificities of any one thereof, the polynucleotide of claim 12, the vector of claim 13 or the cell of claim 14 for the preparation of a pharmaceutical or diagnostic composition for prophylactic and therapeutic treatment of a synucleinopathic disease, monitoring the progression of a synucleinopathic disease or a response to a synucleinopathic disease treatment in a subject.

26. A method of diagnosing a synucleinopathic disease in a subject, the method comprising:

(a) assessing a level of α-synuclein in a sample from the subject to be diagnosed with an antibody of any one of claims 1 to 11 or 16 to 19, an α-synuclein binding fragment thereof or an α-synuclein binding molecule having substantially the same binding specificities of any one thereof; and

(b) comparing the level of the α-synuclein to a reference standard that indicates the level of the α-synuclein in one or more control subjects,

wherein a difference or similarity between the level of the α-synuclein and the reference standard indicates that the subject has Parkinson's disease.

27. The use of claim 25 or the method of claim 26, wherein the synucleinopathic disease is selected from the group consisting of Parkinson's disease (PD), Parkinon's disease dementia (PDD), dementia with Lewy bodies (DLB), the Lewy body variant of Alzheimer's disease (LBVAD), multiple systems atrophy (MSA), pure autonomic

failure (PAF), neurodegeneration with brain iron accumulation type-1 (NBIA-I), Alzheimer's disease, Pick disease, juvenile-onset generalized neuroaxonal dystrophy (Hallervorden-Spatz disease), amyotrophic lateral sclerosis, traumatic brain injury and Down syndrome.

28. A kit for the diagnosis of a synucleinopathic disease, said kit comprising an antibody of any one of claims 1 to 11 or 16 to 19 or an α-synuclein binding molecule having substantially the same binding specificities of any one thereof, the polynucleotide of claim 12, the vector of claim 13 or the cell of claim 14, optionally with reagents and/or instructions for use.

29. Use of an α-synuclein binding molecule comprising at least one CDR of an antibody of any one of claims 1 to 11 or 16 to 19 for the preparation of a composition for in vivo detection of or targeting a therapeutic and/or diagnostic agent to α-synuclein in the human or animal body.

30. The use of claim 29, wherein said, wherein said in vivo imaging comprises positron emission tomography (PET), single photon emission tomography (SPECT), near infrared (NIR) optical imaging or magnetic resonance imaging (MRI).

CLAIMS

1. An isolated human monoclonal anti-α-synuclein antibody, or an α-synuclein binding fragment thereof comprising:

a VH CDR1 comprising residues 31-35 of SEQ ID NO:9,

a VH CDR2 comprising residues 50-68 of SEQ ID NO:9,

a VH CDR3 comprising residues 101-102 of SEQ ID NO:9,

a VL CDR1 comprising residues 23-33 of SEQ ID NO:12,

a VL CDR2 comprising residues 49-55 of SEQ ID NO:12, and

a VL CDR3 comprising residues 88-98 of SEQ ID NO:12.

2. An isolated human monoclonal anti-α-synuclein antibody, or an α-synuclein binding fragment thereof comprising:

a VH CD1l comprising residues 31-35 of SEQ ID NO:3,

a VH CDR2 comprising residues 50-66 of SEQ ID NO:3,

a VH CDR3 comprising residues 99-110 of SEQ ID NO:3,

a VL CDR1 comprising residues 23-33 of SEQ ID NO:6,

a VL CDR2 comprising residues 49-55 of SEQ ID NO:6, and

a VL CDR3 comprising residues 88-98 of SEQIDNO:6.

3. An isolated human monoclonal anti-α-synuclein antibody, or an α-synuclein binding fragment thereof comprising:

a VH CDR1 comprising residues 31-35 of SEQ ID NO:15,

a VH CDR2 comprising residues 50-66 of SEQ ID NO:15,

a VH CDR3 comprising residues 99-112 of SEQ ID NO:15,

a VL CDR1 comprising residues 24-34 of SEQ ID NO:18,

a VL CDR2 comprising residues 50-56 of SEQ ID NO:18, and

a VL CDR3 comprising residues 89-96 of SEQ ID NO:18.

4. An isolated human monoclonal anti-α-synuclein antibody, or an α-synuclein binding fragment thereof comprising:

a VH CDR1 comprising residues 31-35 of SEQ ID NO:15,

a VH CDR2 comprising residues 50-66 of SEQ ID NO:15,

a VH CDR3 comprising residues 99-112 of SEQ ID NO:15,

a VL CDR1 comprising residues 24-34 of SEQ ID NO:21,

a VL CDR2 comprising residues 50-56 of SEQ ID NO:21, and

a VL CDR3 comprising residues 89-97 of SEQ ID NO:21.

5. An isolated human monoclonal anti-α-synuclein antibody, or an α-synuclein binding fragment thereof comprising:

a) a VH region comprising the amino acid sequence of SEQ ID NO:10 and

b) a VL region comprising the amino acid sequence of SEQ ID NO:13.

6. An isolated human monoclonal anti-α-synuclein antibody, or an α-synuclein binding fragment thereof comprising:

a) a VH region comprising the amino acid sequence of SEQ ID NO:4 and

b) a VH region comprising the amino acid sequence of SEQ ID NO:7.

7. An isolated human monoclonal anti-α-synuclein antibody, or an α-synuclein binding fragment thereof comprising:

a) a VH region comprising the amino acid sequence of SEQ ID NO:16 and

b) a VL region comprising the amino acid sequence of SEQ ID NO:19.

8. An isolated human monoclonal anti-α-synuclein antibody, or an α-synuclein binding fragment thereof comprising:

a) a VH region comprising the amino acid sequence of SEQ ID NO:16 and

b) a VL region comprising the amino acid sequence of SEQ ID NO:22.

9. The antibody or α-synuclein binding fragment thereof of any one of claims 1-8, which is

(i) detectably labeled, wherein the detectable label is selected from the group consisting of an enzyme, a radioisotope, a fluorophore and a heavy metal; or

(ii) attached to a drug.

10. The antibody or α-synuclein binding fragment thereof of any one of claims 1-8 comprising a human IgG 1 heavy chain constant region.

11. The antibody or α-synuclein binding fragment thereof of claim 10 comprising a human lambda light chain constant region.

12. The antibody or α-synuclein binding fragment thereof of any one of claims 1-8 comprising a human lambda light chain constant region.

13. A composition comprising the antibody or α-synuclein binding fragment thereof of any one of claims 1-8 wherein the composition is

(i) a pharmaceutical composition further comprising a pharmaceutically acceptable carrier; or

(ii) a diagnostic composition further comprising one or more immuno or nucleic acid based diagnostic reagents.

14. A kit for the diagnosis of a synucleinopathic disease, said kit comprising the antibody or α-synuclein binding fragment thereof of any one of claims 1-8 with reagents and/or instructions for use.

15. The kit of claim 14, wherein the synucleinopathic disease is Parkinson's disease.

16. An isolated polynucleotide or polynucleotides encoding the antibody or α-synuclein binding fragment thereof of any one of claims 1-8.

17. An expression vector or vectors comprising the polynucleotide or polynucleotides of claim 16.

18. A host cell comprising the expression vector or vectors of claim 17.

19. A method for preparing an anti-α-synuclein antibody or fragment thereof, said method comprising:

(a) culturing the cell of claim 18; and

(b) isolating said antibody or fragment thereof from the culture.

20. The use of the antibody or α-synuclein binding fragment thereof of any one of claims 1-8 in the manufacture of a medicament for treatment of a synucleinopathic disease in a human subject.

21. The use of claim 20, wherein the synucleinopathic disease is Parkinson's disease.

22. The use of claim 21, wherein the human monoclonal anti-α-synuclein antibody, or an α-synuclein binding fragment thereof, comprises:

a VH CDR1 comprising residues 31-35 of SEQ ID NO:9,

a VH CDR2 comprising residues 50-68 of SEQ ID NO:9,

a VH CDR3 comprising residues 101-102 of SEQ ID NO:9,

a VL CDR1 comprising residues 23-33 of SEQ ID NO:12,

a VL CDR2 comprising residues 49-55 of SEQ ID NO:12, and

a VL CDR3 comprising residues 88-98 of SEQ ID NO:12.

23. The use of claim 21, wherein the human monoclonal anti-α-synuclein antibody, or an α-synuclein binding fragment thereof, comprises:

a) a VH region comprising the amino acid sequence of SEQ ID NO:10 and

b) a VL region comprising the amino acid sequence of SEQ IDNO:13.

24. A method of diagnosing a synucleinopathic disease in a human subject, the method comprising:

(a) assessing a level of α-synuclein in a sample from the subject to be diagnosed with the antibody or α-synuclein binding fragment thereof of any one of claims 1-8; and

(b) comparing the level of the α-synuclein to a control, wherein a difference or similarity between the level of the α-synuclein and the indicates that the subject has a synucleinopathic disease.

25. The method of claim 24, wherein the synucleinopathic disease is Parkinson's disease.

26. The use of the antibody or α-synuclein binding fragment thereof of any one of claims 1-8 attached to a therapeutic or diagnostic agent in the manufacture of a medicament for *in vivo* detection of or targeting a therapeutic and/or diagnostic agent to α-synuclein in a human subject, wherein α-synuclein is detected by positron emission tomography (PET), single photon emission tomography 20 (SPECT), near infrared (NIR) optical imaging, magnetic resonance imaging (MRI), or a combination thereof.

27. The antibody or α-synuclein binding fragment thereof of any one of claims 1-8 for use as a medicament.

28. The antibody or α-synuclein binding fragment thereof for use of claim 27, wherein the human monoclonal anti-α-synuclein antibody, or an α-synuclein binding fragment thereof, comprises:

a VH CDR1 comprising residues 31-35 of SEQ ID NO:9,

a VH CDR2 comprising residues 50-68 of SEQ ID NO:9,

a VH CDR3 comprising residues 101-102 of SEQ ID NO:9,

a VL CDR1 comprising residues 23-33 of SEQ ID NO:12,

a VL CDR2 comprising residues 49-55 of SEQ ID NO:12, and

a VL CDR3 comprising residues 88-98 of SEQ ID NO:12.

29. The antibody or α-synuclein binding fragment thereof for use of claim 27, wherein the human monoclonal anti-α-synuclein antibody, or an α-synuclein binding fragment thereof, comprises:

a) a VH region comprising the amino acid sequence of SEQ ID NO:10 and

b) a VL region comprising the amino acid sequence of SEQ IDNO:13.