CLAIMS

1. An anti-tau antibody or tau-binding fragment thereof that comprises a heavy chain variable region (VH) comprising heavy chain variable region (VH) complementarity determining regions (CDRs) 1, 2, and 3 and a light chain variable region (VL) comprising light chain variable region (VL) complementarity determining regions (CDRs) 1, 2, and 3, wherein:

(a) the VH CDRs 1, 2, and 3 consist of the amino acid sequences set forth in SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 87, respectively, and the VL CDRs 1, 2, and 3 consist of the amino acid sequences set forth in SEQ ID NO: 88, SEQ ID NO: 89, and SEQ ID NO: 90, respectively; or

(b) the VH CDRs 1, 2, and 3 consist of the amino acid sequences set forth in SEQ ID NO: 103, SEQ ID NO: 104, SEQ ID NO: 105, respectively, and the VL CDRs 1, 2, and 3 consist of the amino acid sequences set forth in SEQ ID NO: 106, SEQ ID NO: 107, and SEQ ID NO: 108, respectively.

2. The anti-tau antibody or tau-binding fragment thereof of claim 1, wherein:

(a) the VH consists of an amino acid sequence that has at least 90% identity to the amino acid sequence set forth in SEQ ID NO: 48 and

the VL consists of an amino acid sequence that has at least 90% identity to the amino acid sequence set forth in SEQ ID NO: 49; or

(b) the VH consists of an amino acid sequence that has at least 90% identity to the amino acid sequence set forth in SEQ ID NO: 47 and

the VL consists of an amino acid sequence that has at least 90% identity to the amino acid sequence set forth in SEQ ID NO: 49;

(c) the VH consists of an amino acid sequence that has at least 90% identity to the amino acid sequence set forth in SEQ ID NO: 54 and

the VL consists of an amino acid sequence that has at least 90% identity to the amino acid sequence set forth in SEQ ID NO: 55; or

(d) the VH consists of an amino acid sequence that has at least 90% identity to the amino acid sequence set forth in SEQ ID NO: 220 and

the VL consists of an amino acid sequence that has at least 90% identity to the amino acid sequence set forth in SEQ ID NO: 55.

3. The anti-tau antibody or tau-binding fragment thereof of claim 1 or 2, wherein:

(a) the VH consists of the amino acid sequence set forth in SEQ ID NO: 48 and

the VL consists of the amino acid sequence set forth in SEQ ID NO: 49; or

(b) the VH consists of the amino acid sequence set forth in SEQ ID NO: 47 and

the VL consists of the amino acid sequence set forth in SEQ ID NO: 49;

(c) the VH consists of the amino acid sequence set forth in SEQ ID NO: 54 and

the VL consists of the amino acid sequence set forth in SEQ ID NO: 55; or

(d) the VH consists of the amino acid sequence set forth in SEQ ID NO: 220 and

the VL consists of the amino acid sequence set forth in SEQ ID NO: 55.

4. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain and a light chain, wherein the heavy chain consists of the amino acid sequence set forth in SEQ ID NO: 218 and the light chain consists of the amino acid sequence set forth in SEQ ID NO: 219.

5. The anti-tau antibody or tau-binding fragment thereof of any of claims 1 to 3, wherein the anti-tau antibody or tau-binding fragment is selected from the group consisting of a Fab, a Fab', a $F(ab')_2$, an Fd, an Fv, a single-chain Fv (scFv), a single-chain antibody, and a disulfide-linked Fv (sdFv).

6. The anti-tau antibody or tau-binding fragment thereof of any of claims 1 to 3, wherein the anti-tau antibody or tau-binding fragment thereof further comprises a human IgG1 heavy chain constant region and a human lambda light chain constant region.

7. The anti-tau antibody or tau-binding fragment thereof of any of claims 1 to 3, 5, and 6, wherein the anti-tau antibody or tau-binding fragment thereof further comprises a human lambda light chain constant region.

8. The anti-tau antibody or tau-binding fragment thereof of any one of claims 1 to 6, wherein the anti-tau antibody or tau-binding fragment thereof further comprises polyethylene glycol or a detectable label selected from the group consisting of an enzyme, a radioisotope, a fluorescent compound, a chemiluminescent compound, a bioluminescent compound, and a heavy metal.

9. A pharmaceutical composition comprising the anti-tau antibody or tau-binding fragment thereof of any one of claims 1 to 7 and a pharmaceutically acceptable carrier.

10. An isolated polynucleotide or polynucleotides comprising a nucleotide sequence or nucleotide sequences encoding the anti-tau antibody or tau-binding fragment thereof of any one of claims 1 to 7.

11. The polynucleotide or polynucleotides of claim 10, further comprising:

(a) the nucleic acid sequence set forth in SEQ ID NO: 173 and/or SEQ ID NO: 174; or

(b) the nucleic acid sequence set forth in SEQ ID NO: 179 and/or SEQ ID NO: 180.

12. An expression vector or vectors comprising the polynucleotide or polynucleotides of claim 10 or 11.

13. An isolated host cell comprising the expression vector or vectors of claim 12 or the polynucleotide or polynucleotides of claim 10 or 11.

14. A method for preparing an anti-tau antibody or tau-binding fragment thereof, the method comprising:

culturing the host cell of claim 13 in a cell culture; and

isolating the anti-tau antibody or tau-binding fragment thereof from the cell culture.

15. The method of claim 14, further comprising formulating the anti-tau antibody or tau-binding fragment into a sterile pharmaceutical composition suitable for administration to a human subject.

16. Use of the anti-tau antibody or tau-binding fragment of any one of claims 1 to 7, or the pharmaceutical composition of claim 9 in the manufacture of a medicament for treating a neurodegenerative tauopathy.

17. Use of the anti-tau antibody or tau-binding fragment of any one of claims 1 to 7, or the pharmaceutical composition of claim 9 in the manufacture of a medicament for treating abnormal accumulation or deposition of tau in the central nervous system in a human subject in need thereof,

18. The use according to claim 16, wherein the neurodegenerative tauopathy is selected from the group consisting of Alzheimer's disease, amyotrophic lateral sclerosis/parkinsonism-dementia complex, argyrophilic grain dementia, British type amyloid angiopathy, cerebral amyloid angiopathy, corticobasal degeneration, Creutzfeldt-Jakob disease, dementia pugilistica, diffuse neurofibrillary tangles with calcification, Down's syndrome, frontotemporal dementia, frontotemporal dementia with parkinsonism linked to chromosome 17, frontotemporal lobar degeneration, GerstmannSträussler-Scheinker disease, Hallervorden-Spatz disease, inclusion body myositis, multiple system atrophy, myotonic dystrophy, Niemann-Pick disease type C,

non-Guamanian motor neuron disease with neurofibrillary tangles, Pick's disease, postencephalitic parkinsonism, prion protein cerebral amyloid angiopathy, progressive subcortical gliosis, progressive supranuclear palsy, subacute sclerosing panencephalitis, neurofibrillary tangle-predominant dementia, multi-infarct dementia, and ischemic stroke.

19. The use according to claim 16, wherein the neurodegenerative tauopathy is Alzheimer's disease.

20. The use according to claim 16, wherein the neurodegenerative tauopathy is frontotemporal dementia with parkinsonism linked to chromosome 17.

21. The use according to claim 16, wherein the neurodegenerative tauopathy is frontotemporal lobar degeneration.

22. A composition comprising the anti-tau antibody or tau-binding fragment of any one of claims 1 to 8 for use in *in vivo* diagnosis of a tauopathy in a human subject in need thereof.

23. An *in vitro* method for monitoring the progression of a neurodegenerative tauopathy, the method comprising:

(a) measuring the level of pathologically modified or aggregated tau in a sample obtained from a human subject using the anti-tau antibody or tau-binding fragment thereof of any one of claims 1 to 8, and

(b) comparing the level of modified or aggregated tau to a reference standard that indicates the level of the pathologically modified or aggregated tau in one or more control subjects, wherein

a difference or similarity between the level of pathologically modified or aggregated tau and the reference standard indicates that the human subject has a neurodegenerative tauopathy.

24. An *in vitro* method for using the level of pathologically modified or aggregated tau as an indicator of a neurodegenerative tauopathy, the method comprising:

(a) measuring the level of pathologically modified or aggregated tau in a sample obtained from a human subject using the anti-tau antibody or tau-binding fragment thereof of any one of claims 1 to 8, and

(b) comparing the level of modified or aggregated tau to a reference standard that indicates the level of the pathologically modified or aggregated tau in one or more control subjects, wherein

a difference or similarity between the level of pathologically modified or aggregated tau and the reference standard indicates that the human subject has a neurodegenerative tauopathy.