CLAIMS

1. An isolated human monoclonal anti-tau antibody, or a tau-binding fragment thereof which specifically binds a tau epitope which comprises the amino acid sequence of SEQ ID NO: 7 and

   (i) is capable of binding pathologically modified tau;

   (ii) binds to pathologically aggregated tau at the pre-tangle stage, in neurofibrillary tangles (NFT), neuropil threads and/or dystrophic neurites in the brain; and

   (iii) does not substantially bind to physiological forms of tau in the brain of a healthy donor when assessed by immunohistochemical staining.

2. An isolated human monoclonal anti-tau antibody, or a tau-binding fragment thereof comprising:

   (a) a heavy chain variable region comprising a heavy chain CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NO: 23, 24, and 25, respectively, and a light chain variable region comprising a light chain CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NO: 26, 27, and 28, respectively; or

   (b) a heavy chain variable region comprising a heavy chain CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NO: 35, 36, 37, respectively, and a light chain variable region comprising a light chain CDR1, CDR2, and CDR3 comprising the amino acid sequences of SEQ ID NO: 38, 39, and 40, respectively.

3. The antibody or tau-binding fragment thereof of claim 2 wherein

   (a) the heavy chain variable region and the light chain variable region comprises the amino acid sequences of SEQ ID NO: 9 and 11, respectively;

   (b) the heavy chain variable region and the light chain variable region comprises the amino acid sequences of SEQ ID NO: 93 and 11, respectively; or

   (c) the heavy chain variable region and the light chain variable region comprises the amino acid sequences of SEQ ID NO: 17 and 19, respectively.

4. The antibody or tau-binding fragment thereof of any one of claims 1 to 3, 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.

5. A polynucleotide or polynucleotides encoding the antibody or tau-binding fragment thereof of any one of claims 1 to 4.

6. A vector or vectors comprising the polynucleotide or polynucleotides of claim 5.

7. A host cell comprising the polynucleotide or polynucleotides of claim 5 or the vector or vectors of claim 6.

8. A method for preparing an anti-tau antibody or tau-binding fragment thereof, the method comprising
   (a) culturing the host cell of claim 7; and
   (b) isolating said antibody or tau binding fragment thereof from the culture.

9. An anti-tau antibody or tau-binding fragment thereof encoded by the polynucleotide or polynucleotides of claim 5 or obtainable by the method of claim 8.

10. The antibody or tau-binding fragment thereof of any one of claims 1 to 4 or 9, which is
   (a) detectably labeled wherein the detectable label is selected from the group consisting of an enzyme, a radioisotope, a fluorophore and a heavy metal; or
   (b) which is attached to a drug.

11. A composition comprising the antibody or tau-binding fragment thereof of any one of claims 1 to 4, 9 or 10, the polynucleotide or polynucleotides of claim 5, the vector or vectors of claim 6 or the host cell of claim 7, wherein the composition is
   (i) a pharmaceutical composition further comprising a pharmaceutically acceptable carrier; or

(ii) a diagnostic composition further comprising one or more reagents conventionally used in immune- or nucleic acid-based diagnostic methods.

12. The composition of claim 11 further comprising a neuroprotective agent useful for treating a neurodegenerative tauopathy.

13. Use of the anti-tau antibody or tau-binding fragment thereof of any one of claims 1 to 4, 9 or 10, in the manufacture of a medicament for the prophylactic or therapeutic treatment of a neurodegenerative tauopathy in a human subject, 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, Gerstmann-Sträussler-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, Tangle only dementia, multi-infarct dementia, and ischemic stroke.

14. The use according to claim 13, wherein the neurodegenerative tauopathy is Alzheimer's disease.

15. Use of the anti-tau antibody or tau-binding fragment thereof of any one of claims 1 to 4, 9 or 10, in the manufacture of a medicament for monitoring the progression of a neurodegenerative tauopathy in a human subject, or the response to a treatment of a neurodegenerative tauopathy in a human subject, 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, Gerstmann-Sträussler-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, Tangle only dementia, multi-infarct dementia, and ischemic stroke.

16. A method of diagnosing or monitoring the progression of a neurodegenerative tauopathy in a human subject, the method comprising

(a) assessing the level of pathologically modified or aggregated tau in a sample from the human subject to be diagnosed with at least one antibody of any one of claims 1 to 4, 9 or 10; 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 human 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, 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, Gerstmann-Sträussler-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, Tangle only dementia, multi-infarct dementia and ischemic stroke.

17. Use of the antibody or tau-binding fragment thereof of any one of claims 1 to 4, 9 or 10, in the manufacture of a medicament for *in vivo* detection of or targeting a therapeutic or diagnostic agent to tau in the human or animal body, wherein said *in vivo* detection comprises positron emission tomography (PET), single photon emission tomography (SPECT), near infrared (NIR) optical imaging or magnetic resonance imaging (MRI).

18. A method for diagnosing a neurodegenerative tauopathy in a human subject, comprising detecting the presence of tau that binds to the antibody of claims 2 or 3 in a biological sample of said human subject.

19. A kit useful in the diagnosis of a neurodegenerative tauopathy, said kit comprising the antibody or tau-binding fragment thereof of any one of claims 1 to 4, 9 or 10, the polynucleotide or polynucleotides of claim 5, the vector or vectors of claim 6 or the host cell of claim 7, with reagents or instructions for use.

20. The anti-tau antibody or tau-binding fragment thereof of any one of claims 1 to 4, 9 or 10 or the composition of claim 11 or 12 for use in therapy.