

## Claims

1. An isolated antibody or antigen binding fragment thereof which binds to PHF tau comprising: a) a heavy chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:7, b) a heavy chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:8, c) a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:9, d) a light chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:19, e) a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:20, and f) a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:21.

2. The isolated antibody or antigen binding fragment thereof of claim 1 comprising: a) the heavy chain variable region CDR1 having the amino acid sequence of SEQ ID NO:7, b) the heavy chain variable region CDR2 having the amino acid sequence of SEQ ID NO:8, c) the heavy chain variable region CDR3 having the amino acid sequence of SEQ ID NO:9, d) the light chain variable region CDR1 having the amino acid sequence of SEQ ID NO:19, e) the light chain variable region CDR2 having the amino acid sequence of SEQ ID NO:20, and f) the light chain variable region CDR3 having the amino acid sequence of SEQ ID NO:21.

3. The isolated monoclonal antibody or antigen-binding fragment of claim 2 comprising a human heavy chain IgG1 constant region and a human light chain kappa constant region.

4. An isolated nucleic acid encoding the monoclonal antibody or antigen-binding fragment of claim 2.

5. A vector comprising the isolated nucleic acid of claim 4.

6. A host cell comprising the nucleic acid of claim 5.

7. A pharmaceutical composition comprising the isolated monoclonal antibody or antigen-binding fragment of claim 2 and a pharmaceutically acceptable carrier.

8. Use of the pharmaceutical composition of claim 7 in the manufacture of a medicament to reduce pathological tau aggregation or spreading of tauopathy in a subject in need thereof,.

9. Use of the pharmaceutical composition of claim 7 in the manufacture of a

medicament to slow progression of a tauopathy in a subject in need thereof, .

10. The use of claim 9 wherein the tauopathy is selected from the group consisting of Alzheimer's disease, frontotemporal dementia, and progressive supranuclear palsy.

11. The use of claim 10 wherein the tauopathy is Alzheimer's disease.

12. The use of claim 11 wherein the Alzheimer's disease is familial Alzheimer's disease.

13. The use of claim 11 wherein the Alzheimer's disease sporadic Alzheimer's disease.

14. The use of claim 10 wherein the tauopathy is frontotemporal dementia.

15. The use of claim 14 wherein the frontotemporal dementia is frontotemporal dementia with parkinsonism linked to chromosome 17 (FTDP-17).

16. The use of claim 10 wherein the tauopathy is progressive supranuclear palsy.

17. A method of producing the monoclonal antibody or antigen-binding fragment of claim 2 comprising culturing a cell comprising a nucleic acid encoding the antibody or antigen-binding fragment under conditions to produce the antibody or antigen-binding fragment, and recovering the antibody or antigen-binding fragment from the cell or cell culture.

18. A method of detecting the presence of PHF-tau in a biological sample from a subject, comprising contacting the biological sample with the antibody or antigen-binding fragment of claim 2 and detecting binding of the antibody or antigen-binding fragment to PHF-tau in the sample from the subject.

19. The method of claim 18 wherein the biological sample is a blood, serum, plasma, interstitial fluid, or cerebral spinal fluid sample.

20. An isolated antibody or antigen binding fragment thereof which binds to PHF tau comprising: a) a heavy chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:80, b) a heavy chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:81, c) a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:9, d) a light chain variable region CDR1 comprising the amino acid sequence of SEQ ID

NO:70, e) a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:20, and f) a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:21.

21. The isolated antibody or antigen binding fragment thereof of claim 20 comprising: a) the heavy chain variable region CDR1 having the amino acid sequence of SEQ ID NO:80, b) the heavy chain variable region CDR2 having the amino acid sequence of SEQ ID NO:81, c) the heavy chain variable region CDR3 having the amino acid sequence of SEQ ID NO:9, d) the light chain variable region CDR1 having the amino acid sequence of SEQ ID NO:70, e) the light chain variable region CDR2 having the amino acid sequence of SEQ ID NO:20, and f) the light chain variable region CDR3 having the amino acid sequence of SEQ ID NO:21.

22. An isolated antibody or antigen binding fragment thereof which binds to PHF tau comprising: a) a heavy chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:71, b) a heavy chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:72, c) a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:73, d) a light chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:70, e) a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:20, and f) a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:21.

23. The isolated antibody or antigen binding fragment thereof of claim 22 comprising: a) the heavy chain variable region CDR1 having the amino acid sequence of SEQ ID NO:71, b) the heavy chain variable region CDR2 having the amino acid sequence of SEQ ID NO:72, c) the heavy chain variable region CDR3 having the amino acid sequence of SEQ ID NO:73, d) the light chain variable region CDR1 having the amino acid sequence of SEQ ID NO:70, e) the light chain variable region CDR2 having the amino acid sequence of SEQ ID NO:20, and f) the light chain variable region CDR3 having the amino acid sequence of SEQ ID NO:21.

24. An isolated monoclonal antibody or antigen-binding fragment thereof comprising a heavy chain variable region having the polypeptide sequence of amino acids 1-188 of SEQ ID

NO:74, and a light chain variable region having the polypeptide sequence of amino acids 1-107 of SEQ ID NO:75.

25. An isolated monoclonal antibody or antigen-binding fragment thereof comprising a heavy chain variable region having the polypeptide sequence of amino acids 1-118 of SEQ ID NO:76, and a light chain variable region having the polypeptide sequence of amino acids 1-107 of SEQ ID NO:77.

26. An isolated monoclonal antibody or antigen-binding fragment thereof comprising a heavy chain variable region having the polypeptide sequence of SEQ ID NO:27, and a light chain variable region having the polypeptide sequence of SEQ ID NO:31.

27. An isolated nucleic acid encoding the monoclonal antibody or antigen-binding fragment of claim 26.

28. A vector comprising the isolated nucleic acid of claim 27.

29. A host cell comprising the nucleic acid of claim 28.

30. A pharmaceutical composition comprising the isolated monoclonal antibody or antigen-binding fragment of claim 26 and a pharmaceutically acceptable carrier.

31. Use of the pharmaceutical composition of claim 30 in the manufacture of a medicament to reduce pathological tau aggregation or spreading of tauopathy in a subject in need thereof.

32. Use of the pharmaceutical composition of claim 30 in the manufacture of a medicament to slow progression of a tauopathy in a subject in need thereof.

33. The use of claim 32 wherein the tauopathy is selected from the group consisting of Alzheimer's disease, frontotemporal dementia, and progressive supranuclear palsy.

34. The use of claim 33 wherein the tauopathy is Alzheimer's disease.

35. The use of claim 34 wherein the Alzheimer's disease is familial Alzheimer's disease.

36. The use of claim 34 wherein the Alzheimer's disease is sporadic Alzheimer's disease.

37. The use of claim 33 wherein the tauopathy is frontotemporal dementia.
38. The use of claim 37 wherein the frontotemporal dementia is frontotemporal dementia with parkinsonism linked to chromosome 17 (FTDP-17).
39. The use of claim 33 wherein the tauopathy is progressive supranuclear palsy.
40. A method of producing the monoclonal antibody or antigen-binding fragment of claim 26 comprising culturing a cell comprising a nucleic acid encoding the antibody or antigen-binding fragment under conditions to produce the antibody or antigen-binding fragment, and recovering the antibody or antigen-binding fragment from the cell or cell culture.
41. The pharmaceutical composition of claim 7 or claim 30 for use in:
- a) reducing pathological tau aggregation or spreading of tauopathy; or
  - b) slowing progression of a tauopathy in a subject in need thereof.