

CLAIMS

1. A monoclonal antibody, or an epitope-binding fragment thereof, capable of immunospecifically binding to the phosphorylated residue 396 of human tau (**SEQ ID NO:33**).
2. The monoclonal antibody according to claim 1 consisting of an intact antibody.
3. The monoclonal antibody or epitope-binding fragment thereof according to claim 1 comprising or consisting of an epitope-binding fragment selected from the group consisting of: an Fv fragment (*e.g.* single chain Fv and disulphide-bonded Fv); a Fab-like fragment such as Fab fragment, Fab' fragment and F(ab)₂ fragment; and a domain antibody such as a single V_H variable domain or V_L variable domain.
4. The monoclonal antibody or epitope-binding fragment thereof according to any preceding claims, wherein the antibody is selected from the group consisting of antibodies of subtype IgG1, IgG2, IgG3 or IgG4.
5. The monoclonal antibody or epitope-binding fragment thereof according to any of the previous claims which is human or humanized.
6. The monoclonal antibody, or epitope-binding fragment thereof, according to any one of the preceding claims, wherein said antibody is substantially incapable of binding to the phosphorylated 404 residue on tau (**SEQ ID NO:33**).
7. A monoclonal antibody, or epitope-binding fragment thereof, comprising:
 - (a) a Light Chain CDR1 having the amino acid sequence of **SEQ ID NO:1**;
 - (b) a Light Chain CDR2 having the amino acid sequence of **SEQ ID NO:2**;
 - (c) a Light Chain CDR3 having the amino acid sequence of **SEQ ID NO:3**;
 - (d) a Heavy Chain CDR1 having the amino acid sequence of **SEQ ID NO:4**;
 - (e) a Heavy Chain CDR2 having the amino acid sequence of **SEQ ID NO:5**; and
 - (f) a Heavy Chain CDR3 having the amino acid sequence of **SEQ ID NO:6**.
8. The monoclonal antibody, or epitope-binding fragment thereof according to claim 7, comprising the heavy chain of **SEQ ID NO:8** or the light chain of **SEQ ID NO:7**.
9. The monoclonal antibody, or epitope-binding fragment thereof according to claim 7, comprising the heavy chain of **SEQ ID NO:8** and the light chain of **SEQ ID NO:34**.

10. A monoclonal antibody, or epitope-binding fragment thereof, according to any one of claims 1 to 6, comprising:
 - (a) a Light Chain CDR1 having the amino acid sequence of **SEQ ID NO:9**;
 - (b) a Light Chain CDR2 having the amino acid sequence of **SEQ ID NO:10**;
 - (c) a Light Chain CDR3 having the amino acid sequence of **SEQ ID NO:11**;
 - (d) a Heavy Chain CDR1 having the amino acid sequence of **SEQ ID NO:12**;
 - (e) a Heavy Chain CDR2 having the amino acid sequence of **SEQ ID NO:13**; and
 - (f) a Heavy Chain CDR3 having the amino acid sequence of **SEQ ID NO:14**.
11. The monoclonal antibody according to claim 10, comprising the heavy chain of **SEQ ID NO:16** and/or the light chain of **SEQ ID NO:15**.
12. A monoclonal antibody, or epitope-binding fragment thereof, according to any one of claims 1 to 6, comprising:
 - (a) a Light Chain CDR1 having the amino acid sequence of **SEQ ID NO:17**;
 - (b) a Light Chain CDR2 having the amino acid sequence of **SEQ ID NO:18**;
 - (c) a Light Chain CDR3 having the amino acid sequence of **SEQ ID NO:19**;
 - (d) a Heavy Chain CDR1 having the amino acid sequence of **SEQ ID NO:20**;
 - (e) a Heavy Chain CDR2 having the amino acid sequence of **SEQ ID NO:21**; and
 - (f) a Heavy Chain CDR3 having the amino acid sequence of **SEQ ID NO:22**.
13. The monoclonal antibody according to claim 12, comprising the heavy chain of **SEQ ID NO:24** and/or the light chain of **SEQ ID NO:23**.
14. A monoclonal antibody, or epitope-binding fragment thereof, according to any one of claims 1 to 6, comprising:
 - (a) a Light Chain CDR1 having the amino acid sequence of **SEQ ID NO:25**;
 - (b) a Light Chain CDR2 having the amino acid sequence of **SEQ ID NO:26**;
 - (c) a Light Chain CDR3 having the amino acid sequence of **SEQ ID NO:27**;
 - (d) a Heavy Chain CDR1 having the amino acid sequence of **SEQ ID NO:28**;
 - (e) a Heavy Chain CDR2 having the amino acid sequence of **SEQ ID NO:29**; and
 - (f) a Heavy Chain CDR3 having the amino acid sequence of **SEQ ID NO:30**.
15. The monoclonal antibody according to claim 14, comprising the heavy chain of **SEQ ID NO:32** and/or the light chain of **SEQ ID NO:31**.
16. The monoclonal antibody, or epitope-binding fragment thereof, according to any one of claims 1 to 6, wherein the Heavy Chain is selected from the group consisting of **SEQ ID NO:8**, **SEQ ID NO:16**, **SEQ ID NO:24**, **SEQ ID NO:32**, and **SEQ ID NO:35**

and the Light Chain is selected from the group consisting of **SEQ ID NO:7**, **SEQ ID NO:15**, **SEQ ID NO:23**, and **SEQ ID NO:36**.

17. The monoclonal antibody, or epitope-binding fragment thereof, according to any one of claims 1 to 6, comprising
 - (a) a Heavy Chain CDR1 comprising the amino acid sequence selected from the group consisting of **SEQ ID NO:4**, **SEQ ID NO:12**, **SEQ ID NO:20**, and **SEQ ID NO:28**;
 - (b) a Heavy Chain CDR2 comprising the amino acid sequence selected from the group consisting of **SEQ ID NO:5**, **SEQ ID NO:13**, **SEQ ID NO:21**, and **SEQ ID NO:29**; and
 - (c) a Heavy Chain CDR3 comprising the amino acid sequence selected from the group consisting of **SEQ ID NO:6**, **SEQ ID NO:14**, **SEQ ID NO:22**, and **SEQ ID NO:30**; and
 - (d) a Light Chain CDR3 comprising the amino acid sequence selected from the group consisting of **SEQ ID NO:3**, **SEQ ID NO:11**, **SEQ ID NO:19**, and **SEQ ID NO:27**.
18. The monoclonal antibody, or epitope-binding fragment thereof, according to any one of claims 1 to 6, comprising:
 - (a) a Heavy Chain CDR1 comprising the amino acid sequence of **SEQ ID NO:20**;
 - (b) a Heavy Chain CDR2 comprising the amino acid sequence of **SEQ ID NO:21**;
 - (c) a Heavy Chain CDR3 comprising the amino acid sequence of **SEQ ID NO:22**; and
 - (d) a Light Chain CDR3 comprising the amino acid sequence of **SEQ ID NO:19**.
19. A monoclonal antibody, or epitope-binding fragment thereof, selective for an amino acid motif of hyperphosphorylated tau comprising of a phosphorylated serine two residues removed from a tyrosine residue.
20. A monoclonal antibody or epitope-binding fragment thereof according to claim 19, wherein the amino acid motif has the sequence:

-Y - X - S(phosphorylated) - P -

wherein Y is tyrosine, X is a naturally occurring amino acid, P is proline and S(phosphorylated) is serine with a phosphorylated hydroxyl side chain.

21. The monoclonal antibody or epitope-binding fragment thereof according to any one of the preceding claims wherein the antibody or epitope-binding fragment thereof further comprises a detectable moiety.

22. The monoclonal antibody or epitope-binding fragment thereof according to claim 21 wherein the detectable moiety is a fluorescent label, a chemiluminescent label, a paramagnetic label, a radioisotopic label or an enzyme label.
24. A nucleic acid encoding a monoclonal antibody or epitope-binding fragment thereof according to any one of claims 1 to 20, or encoding a constituent chain thereof.
25. The monoclonal antibody, or epitope-binding fragment thereof, according to any one of claims 1 to 20, for use in therapy.
26. Use of the monoclonal antibody, or epitope-binding fragment thereof according to any one of claims 1 to 20, in the manufacture of a medicament for treating a tauopathy selected from the group consisting of of Alzheimer's disease, Argyrophilic Grain Disease (AGD), Psychosis, particularly Psychosis due to AD or Psychosis in patients with AD, psychiatric symptoms of patients with Lewy body dementia, Progressive Supranuclear Palsy (PSP), Frontotemporal dementia (FTD or variants thereof), TBI (traumatic brain injury, acute or chronic), Corticobasal Degeneration (CBD), Picks Disease, Primary age-related tauopathy (PART), Neurofibrillary tangle-predominant senile dementia, Dementia pugilistica, Chronic traumatic encephalopathy, stroke, stroke recovery, neurodegeneration in relation to Parkinson's disease, Parkinsonism linked to chromosome, Lytico-Bodig disease (Parkinson-dementia complex of Guam), Ganglioglioma and gangliocytoma, Meningioangiomatosis, Postencephalitic parkinsonism, Subacute sclerosing panencephalitis, Huntington's disease, lead encephalopathy, tuberous sclerosis, Hallervorden-Spatz disease and lipofuscinosis.
27. A kit comprising the antibody, or fragment thereof, according to any one of claims 1-20, for use in therapy.