

dementia and Parkinson's disease (Dong Hee Choi *et al.*, *Brain & NeuroRehabilitation*, 4, 21-29, 2011).

However, the human tau protein consisting of 441 amino acids has a wide variety of locations where post-translational modification may occur, which makes it difficult to find, in the tau protein, a target portion that exhibits a preventive or therapeutic effect on dementia. Due to such various modifications, there are also difficulties in developing a therapeutic agent.

Disclosure of Invention

Technical Problem

Accordingly, the present inventors have studied to develop an effective therapeutic agent for a degenerative neurological disease. As a result, the present inventors have found that an antibody, which specifically binds to a fragment of the tau protein in which the 280th lysine is acetylated, decreases aggregation of tau proteins. In addition, the present inventors have found that in experiments using a dementia-induced animal model, the animal model into which the antibody has been administered exhibits improved motor function and cognitive function.

Solution to Problem

In order to solve the above problems, in an aspect of the present disclosure, there is provided an anti-tau antibody or an antigen-binding fragment thereof, which comprises (i) a heavy chain variable region (VH) that includes a heavy chain CDR1 having the amino acid sequence represented by SEQ ID NO: 1, a heavy chain CDR2 having the amino acid sequence represented by SEQ ID NO: 2, and a heavy chain CDR3 having the amino acid sequence represented by SEQ ID NO: 3 and (ii) a light chain variable region (VL) that includes a light chain CDR1 having the amino acid sequence represented by SEQ ID NO: 4, a light chain CDR2 having the amino acid sequence represented by SEQ ID NO: 5, and a light chain CDR3 having the amino acid sequence

represented by SEQ ID NO: 6.

In another aspect of the present disclosure, there is provided a polynucleotide that encodes the anti-tau antibody or antigen-binding fragment thereof as defined herein. The present disclosure also provides a polynucleotide that encodes a heavy chain variable region and/or light chain variable region of the anti-tau antibody. In another aspect of the present disclosure, there is provided a polynucleotide that encodes a heavy or light chain of an antibody that includes the heavy chain variable region and the light chain variable region as defined herein.

In another aspect of the present disclosure, there is provided an expression vector comprising the polynucleotide as defined herein.

The present disclosure also provides a host cell into which the expression vector is introduced. In another aspect of the present disclosure, there is provided a host cell comprising the expression vector as defined herein.

In still yet another aspect of the present disclosure, there is provided a method for producing an anti-tau antibody or an antigen-binding fragment thereof as defined herein, the method comprising a step of culturing the host cell as defined herein.

In still yet another aspect of the present disclosure, there is provided a hybridoma having accession number KCTC 14155BP.

The present disclosure also provides a pharmaceutical composition for preventing or treating a degenerative neurological disease, the pharmaceutical composition comprising, as an active ingredient, the anti-tau antibody or antigen-binding fragment thereof. In another aspect of the present disclosure, there is provided a pharmaceutical composition for treating a tau protein-mediated neurological disease, the pharmaceutical composition comprising as an active ingredient the anti-tau antibody or antigen-binding fragment thereof as defined herein.

The present disclosure also provides a composition for diagnosing a degenerative neurological disease, the

composition comprising the anti-tau antibody or antigen-binding fragment thereof. In another aspect of the present disclosure, there is provided a composition for diagnosing a tau protein-mediated neurological disease, the composition comprising the anti-tau antibody or antigen-binding fragment thereof as defined herein.

5 The present disclosure also provides a kit for preventing, treating, or diagnosing a degenerative neurological disease, the kit comprising the antibody or antigen-binding fragment thereof, the polynucleotide, the expression vector, or the host cell. In another aspect of the present disclosure, there is provided a kit for treating, or diagnosing a tau protein-mediated neurological disease, the kit comprising the antibody or antigen-
10 binding fragment thereof as defined herein, the polynucleotide as defined herein, the expression vector as defined herein, or the host cell as defined herein.

In another aspect of the present disclosure, there is provided an antibody or antigen-binding fragment as defined herein for use in therapy.

In another aspect of the present disclosure, there is provided use of the antibody
15 or antigen-binding fragment thereof as defined herein in the manufacture of a medicament for treating a tau protein-mediated neurological disease.

Advantageous Effects of Invention

The anti-tau antibody according to the present invention can specifically bind to

CLAIMS

1. An anti-tau antibody or an antigen-binding fragment thereof, comprising:
a heavy chain variable region (VH) that includes:
a heavy chain CDR1 having the amino acid sequence represented by SEQ ID NO: 1;
a heavy chain CDR2 having the amino acid sequence represented by SEQ ID NO: 2; and
a heavy chain CDR3 having the amino acid sequence represented by SEQ ID NO: 3, and
a light chain variable region (VL) that includes:
a light chain CDR1 having the amino acid sequence represented by SEQ ID NO: 4;
a light chain CDR2 having the amino acid sequence represented by SEQ ID NO: 5; and
a light chain CDR3 having the amino acid sequence represented by SEQ ID NO: 6.
2. The anti-tau antibody or antigen-binding fragment thereof of claim 1, wherein the heavy chain variable region includes any one amino acid sequence selected from the group consisting of SEQ ID NOs: 7 to 11, and the light chain variable region includes any one amino acid sequence selected from the group consisting of SEQ ID NOs: 12 to 15.
3. The anti-tau antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or the antigen-binding fragment thereof is any one selected from the group consisting of:

an anti-tau antibody or antigen-binding fragment thereof which comprises a heavy chain variable region having the amino acid sequence represented by SEQ ID NO: 7 and a light chain variable region having the amino acid sequence represented by SEQ ID NO: 12;

an anti-tau antibody or antigen-binding fragment thereof which comprises a heavy chain variable region having the amino acid sequence represented by SEQ ID NO: 8 and a light chain variable region having the amino acid sequence represented by SEQ ID NO: 13;

an anti-tau antibody or antigen-binding fragment thereof which comprises a heavy chain variable region having the amino acid sequence represented by SEQ ID NO: 8 and a light chain variable region having the amino acid sequence represented by SEQ ID NO: 14;

an anti-tau antibody or antigen-binding fragment thereof which comprises a heavy chain variable region having the amino acid sequence represented by SEQ ID NO: 8 and a light chain variable region having the amino acid sequence represented by SEQ ID NO: 15;

an anti-tau antibody or antigen-binding fragment thereof which comprises a heavy chain variable region having the amino acid sequence represented by SEQ ID NO: 9 and a light chain variable region having the amino acid sequence represented by SEQ ID NO: 13;

an anti-tau antibody or antigen-binding fragment thereof which comprises a heavy chain variable region having the amino acid sequence represented by SEQ ID NO: 9 and a light chain variable region having the amino acid sequence represented by SEQ ID NO: 14;

an anti-tau antibody or antigen-binding fragment thereof which comprises a heavy chain variable region having the amino acid sequence represented by SEQ ID NO: 9 and a light chain variable region having the amino acid sequence represented by SEQ ID NO: 15;

an anti-tau antibody or antigen-binding fragment thereof which comprises a

heavy chain variable region having the amino acid sequence represented by SEQ ID NO: 10 and a light chain variable region having the amino acid sequence represented by SEQ ID NO: 13;

an anti-tau antibody or antigen-binding fragment thereof which comprises a heavy chain variable region having the amino acid sequence represented by SEQ ID NO: 10 and a light chain variable region having the amino acid sequence represented by SEQ ID NO: 14;

an anti-tau antibody or antigen-binding fragment thereof which comprises a heavy chain variable region having the amino acid sequence represented by SEQ ID NO: 10 and a light chain variable region having the amino acid sequence represented by SEQ ID NO: 15;

an anti-tau antibody or antigen-binding fragment thereof which comprises a heavy chain variable region having the amino acid sequence represented by SEQ ID NO: 11 and a light chain variable region having the amino acid sequence represented by SEQ ID NO: 13;

an anti-tau antibody or antigen-binding fragment thereof which comprises a heavy chain variable region having the amino acid sequence represented by SEQ ID NO: 11 and a light chain variable region having the amino acid sequence represented by SEQ ID NO: 14; and

an anti-tau antibody or antigen-binding fragment thereof which comprises a heavy chain variable region having the amino acid sequence represented by SEQ ID NO: 11 and a light chain variable region having the amino acid sequence represented by SEQ ID NO: 15.

4. The anti-tau antibody or antigen-binding fragment thereof of claim 1, wherein the fragment is any one selected from the group consisting of Fab, scFv, F(ab')₂, and Fv.

5. A polynucleotide encoding the anti-tau antibody or antigen-binding fragment thereof of claim 1.

6. An expression vector comprising the polynucleotide of claim 5.
7. A host cell comprising the expression vector of claim 6.
8. A method for producing the anti-tau antibody or antigen-binding fragment thereof of claim 1, the method comprising a step of culturing the host cell of claim 7.
9. A polynucleotide encoding a heavy or light chain of an antibody that includes the heavy chain variable region and the light chain variable region of claim 2.
10. A hybridoma having accession number KCTC 14155BP.
11. A pharmaceutical composition for treating a tau protein-mediated neurological disease, the pharmaceutical composition comprising as an active ingredient the anti-tau antibody or antigen-binding fragment thereof of claim 1.
12. The pharmaceutical composition of claim 11, wherein the tau protein-mediated neurological disease is tauopathy, primary age-related tauopathy, chronic traumatic encephalopathy, progressive supranuclear palsy, corticobasal degeneration, frontotemporal dementia, Lytico-Bodig disease, Parkinsonism, subacute sclerosing meningitis, lead encephalopathy, tuberous sclerosis, ganglioglioma, gangliocytoma, meningioangiomatosis, subacute sclerosing panencephalitis, Hallervorden-Spatz disease, or lipofuscinosis.
13. The pharmaceutical composition of claim 12, wherein the tauopathy is Alzheimer's disease (AD), progressive supranuclear palsy (PSP), corticobasal

degeneration (CBD), Pick's disease (PiD), a group of related disorders collectively termed frontotemporal dementia with Parkinsonism linked to chromosome 17 (FTDP-17), amyotrophic lateral sclerosis (ALS), Creutzfeld-Jakob disease (CJD), dementia pugilistica (DP), Gerstmann-Sträussler-Scheinker disease (GSSD), Lewy body disease, chronic traumatic encephalopathy (CTE), or Huntington's disease.

14. The pharmaceutical composition of claim 11, wherein the pharmaceutical composition is to be administered through any one route of administration selected from the group consisting of intracerebral, intracerebroventricular, intraperitoneal, percutaneous, intramuscular, intradural, intravenous, subcutaneous, and nasal routes of administration.

15. A composition for diagnosing a tau protein-mediated neurological disease, the composition comprising the anti-tau antibody or antigen-binding fragment thereof of claim 1.

16. A kit for treating, or diagnosing a tau protein-mediated neurological disease, the kit comprising the antibody or antigen-binding fragment thereof of claim 1, the polynucleotide of claim 5, the expression vector of claim 6, or the host cell of claim 7.

17. The antibody or antigen-binding fragment thereof of claim 1 for use in therapy.

18. Use of the antibody or antigen-binding fragment thereof of claim 1 in the manufacture of a medicament for treating a tau protein-mediated neurological disease.