

Fig. 26 illustrates expression levels of the phosphorylated tau protein (pSer396) in the brain tissues of normal mice, a dementia-induced mouse model, and a dementia-induced mouse model into which the ADEL-Y01m antibody is intracerebroventricularly administered (** $p < 0.01$).

5 Fig. 27 illustrates expression levels of the acetylated tau protein (Tau-acK280) in the brain tissues of normal mice, a dementia-induced mouse model, and a dementia-induced mouse model into which the ADEL-Y01m antibody is intracerebroventricularly administered.

10 Fig. 28 illustrates photographs showing brain tissues immunostained with phosphorylated tau protein (AT8, pT231), wherein the brain tissues are obtained from normal mice, a dementia-induced mouse model, and a dementia-induced mouse model (Tau-P301L-ADEL-Y01m) into which the ADEL-Y01m antibody is intracerebroventricularly administered.

15 Fig. 29 illustrates expression levels of AT8 and phosphorylated tau protein (pT231) in brain tissues of normal mice, a dementia-induced mouse model, and a dementia-induced mouse model (Tau-P301L-ADEL-Y01m) into which the ADEL-Y01m antibody is intracerebroventricularly administered (* $p < 0.05$).

20 Fig. 30 illustrates expression levels of the entire tau protein (Tau5), an acetylated tau protein (Tau-acK280), and phosphorylated tau protein (pT231) in brain tissues of normal mice, a dementia-induced mouse model, and a dementia-induced mouse model (Tau-P301L-ADEL-Y01m) into which the ADEL-Y01m antibody is intraperitoneally administered.

25 Fig. 31 illustrates expression levels of the entire tau protein (Tau5) in the brain tissues of normal mice, a dementia-induced mouse model, and a dementia-induced mouse model into which the ADEL-Y01m antibody is intraperitoneally administered (* $p < 0.05$).

Fig. 32 illustrates expression levels of the acetylated tau protein (Tau-acK280) in the brain tissues of normal mice, a dementia-induced mouse model, and a dementia-induced mouse model into which the ADEL-Y01m antibody is intraperitoneally

intraperitoneally administered, and whether the antibody is bound to tau protein.

Fig. 41 illustrates an experimental schedule for identifying a behavior-improving effect achieved upon intraperitoneal administration of the ADEL-Y01m antibody using an aged dementia-induced mouse model.

5 Fig. 42 illustrates the result of a nesting building test (* $p < 0.05$) in which the ADEL-Y01m antibody is intraperitoneally administered into an aged dementia-induced mouse model.

10 Fig. 43 illustrates the result of a Y-maze test (* $p < 0.05$) in which the ADEL-Y01m antibody is intraperitoneally administered into an aged dementia-induced mouse model.

Fig. 44 illustrates the time spent staying in each zone in a water maze test (* $p < 0.05$) in which the ADEL-Y01m antibody is intraperitoneally administered into an aged dementia-induced mouse model.

15 Fig. 45 illustrates expression levels of the entire tau protein (Tau5), an acetylated tau protein (Tau-acK280), and a phosphorylated tau protein (pT231) in brain tissues of normal mice, an aged dementia-induced mouse model, and an aged dementia-induced mouse model into which the ADEL-Y01m antibody is intraperitoneally administered.

20 Fig. 46 illustrates expression levels of the entire tau protein (Tau5) in the brain tissues of normal mice, an aged dementia-induced mouse model, and an aged dementia-induced mouse model into which the ADEL-Y01m antibody is intraperitoneally administered (* $p < 0.05$, ** $p < 0.01$).

25 Fig. 47 illustrates expression levels of the acetylated tau protein (Tau-acK280) in the brain tissues of normal mice, an aged dementia-induced mouse model, and an aged dementia-induced mouse model into which the ADEL-Y01m antibody is intraperitoneally administered (** $p < 0.01$).

Fig. 48 illustrates expression levels of the entire phosphorylated tau protein (pT231) in the brain tissues of normal mice, an aged dementia-induced mouse model, and an aged dementia-induced mouse model into which the ADEL-Y01m antibody is

As a result, for the affinity between the ADEL-Y01m antibody and the K280-ac protein fragment, the antigen dissociation constant (K_d) value was measured as 2.57×10^{-10} M (Fig. 7).

In addition, binding of the K280-ac protein fragment prepared in Preparation Example 1 with the ADEL-Y01h (v01 to v12) antibodies prepared in Preparation Example 2 was measured by ELISA.

First, plates were treated with the K280-ac protein fragment at 250 ng/well and reaction was allowed to proceed at 4°C overnight. The next day, washing with a washing buffer was performed three times, and then treatment with a primary antibody was performed with 8 concentrations (2 µg, 1 µg, 0.5 µg, 0.25 µg, 0.12 µg, 0.06 µg, 0.03 µg, 0.01 µg). As a secondary antibody, HRP-labeled anti-human IgG antibody was used.

As a result, it was identified that the ADEL-Y01h (v01 to v10) antibodies exhibited a high antibody affinity for the K280-ac protein fragment (Fig. 8).

II. Identification of therapeutic effects caused by ADEL-Y01m antibody using animal model

Preparation Example 3. Preparation of dementia mouse model

JNPL3 mice expressing Tau-P301L mutant gene were purchased from Taconic, and back-crossed with C57BL/6 mice for five generations in the experimental animal room of the Asan Institute for Life Sciences, South Korea. Then, the mice were raised under a specific pathogen free (SPE) condition.

Experimental Example 3. Identification of characteristics of dementia mouse model

The Tau-P301L dementia mouse model used in experiments exhibited a difference in accumulation of the tau protein in brain tissue with aging, as compared with the normal mice. Immunoblotting using the ADEL-Y01m antibody prepared in Preparation Example 2 was conducted.

The brains were extracted from normal mice and Tau-P301L dementia mice, and then soluble and insoluble proteins were separated through Sarkosyl fractions from

intraperitoneally administered. On the other hand, remarkably decreased expression levels of the entire tau protein, the phosphorylated tau protein, and the acetylated tau protein were observed in the brain tissues of the Tau-P301L dementia mice, into which the ADEL-Y01m antibody had been intraperitoneally administered, as compared with
5 the brain tissues of the Tau-P301L dementia mice, into which IgG had been intraperitoneally administered (Figs. 45 to 48).

In addition, brain tissues of the aged Tau-P301L dementia mice, into which IgG or ADEL-Y01m antibody had been intracerebroventricularly administered in an amount of 50 mg/kg, and the normal mice were extracted, and cerebral cortical tissues were
10 partially isolated therefrom using formic acid. In the cerebral cortical tissues, insoluble tau aggregates were checked through semi-denaturing western blotting. Here, the semi-denaturing western blotting was performed in the same manner as in Experimental Example 9.

As a result, an increase in insoluble tau aggregates was observed in the brain
15 tissues of the Tau-P301L dementia mice, into which IgG had been intraperitoneally administered. On the other hand, a remarkable decrease in insoluble tau aggregates was observed in the brain tissues of the Tau-P301L dementia mice, into which the ADEL-Y01m antibody had been intraperitoneally administered administered, as compared with the brain tissues of the Tau-P301L dementia mice, into which IgG had been
20 intraperitoneally administered (Fig. 49).

III. Identification of Tau seeding inhibitory effect of anti-tau antibody

Experimental Example 15. Identification of tau aggregation and seeding of acetylated tau protein

First, the wild-type tau protein (Tau) was reacted *in vitro* with the P300 enzyme,
25 an acetyltransferase. Cultured nerve cells were treated with acetylated tau protein (Tau-K280-ac), which had been reacted with the P300. In order to identify whether the acetylated tau protein induces intracellular aggregation, treatment with the acetylated tau protein or wild-type tau protein was performed, and western blotting was performed on the donor cell lysate using anti-HA antibody (Sigma-Aldrich, #11867423001) when

fraction were mixed, and the mixture was allowed to react at room temperature for 20 minutes. Thereafter, each well was subjected to treatment with the mixture, and then incubation was performed at a temperature of 37°C for 24 hours. Then, fluorescence wavelength analysis was performed using the CLARIOstar® (BMG Labtech) instrument.

As a result, in a case where the ADEL-Y01h01_v01 antibody was administered, the cells treated with the K280-ac protein fragment exhibited a decreased integrated FRET density; and in a case where the ADEL-Y01h01_v01 antibody was administered, the cells treated with the aggregate of the K280-ac protein fragments also exhibited a decreased integrated FRET density (Fig. 54). In addition, in a case where the ADEL-Y01h antibody was administered, the cells treated with the Sarkosyl insoluble fraction in brain tissues of patients with Alzheimer's disease exhibited a decreased integrated FRET density (Fig. 55). From these results, it was identified that in a case where the ADEL-Y01h01_v01 antibody was administered, tau seeding was inhibited.

Experimental Example 17. Identification of tau seeding inhibitory effect caused by ADEL-Y01h antibody: In vivo

In order to identify an *in vivo* tau seeding inhibitory effect caused by the ADEL-Y01h antibody, IgG or ADEL-Y01h antibody had been intravenously injected starting from 2 weeks before the Sarkosyl insoluble fraction from patients with Alzheimer's disease was administered to CA1 layer in the left hippocampus of the Tau-P301L dementia mice produced in Preparation Example 3. The Sarkosyl insoluble fraction was administered to the CA1 layer in the left hippocampus of the Tau-P301L dementia mice. Subsequently, brain tissue was extracted at the expense of each mouse, and then sectioned frozen. The brain sections were subjected to immunohistological staining with an anti-AT8 antibody, and a level of tau seeding was checked.

Specifically, a Sarkosyl insoluble fragment (3 µl, 3.3 µg/µl) in brain tissue from a patient with Alzheimer's disease at Braak stage IV was subjected to sonication and injected into CA1 layer (anterior-posterior: -1.9 mm, inside-outside: 1.5 mm, left: -1.8 mm) in the left hippocampus of 6-month-old Tau-P301L dementia mice. The Tau-

P301L dementia mice had been intravenously injected with IgG or ADEL-Y01h antibody in an amount of 20 mg/kg/week starting from 2 weeks before administration of the Sarkosyl insoluble fragment; and the mice were intravenously administered IgG or ADEL-Y01h antibody once a week from the week of administration of the Sarkosyl insoluble fragment to Week 12. Here, the Sarkosyl insoluble fragment was injected at a rate of 0.2 μ l/min using a 10 μ l glass syringe (Hamilton, 0.49 mm, Reno, NV), and the needle was removed after 5 minutes of waiting before removal in order to prevent backflow. After 12 weeks, brain tissue was extracted at the expense of each mouse and cut into 30 μ m thick frozen sections using Leica CM1860.

For immunohistological staining, each of the brain sections was washed with Buffer A (1% NGS, 0.2% Triton X-100 and 30% H₂O₂, and PBS). The brain section was subjected to treatment with PBS containing 1% NGS and 0.2% Triton X-100, and IgG or ADEL-Y01m antibody, and allowed to react at 4°C overnight. The brain section was washed several times with PBS solution, and then reacted with a secondary antibody (Vector Laboratories) at room temperature for 1 hour. Thereafter, the brain section was subjected to immunostaining using the Vectastain ABC kit (Vector Laboratories), and the immunostaining was performed according to the manufacturer's manual. The stained brain sections were analyzed using the ImageJ software (NIH, Bethesda, MD), and three brain sections containing the hippocampus were quantified. For nerve cells stained with the anti-AT8 antibody, measurement was performed by three blind testers with the brain sections used in the experiment, and quantitative analysis was performed at specific threshold levels. Three brain sections between Bregma -1.75 and Bregma -2.25 in 7 Tau-P301L dementia mice, into which IgG had been administered, and 8 Tau-P301L dementia mice, into which the ADEL-Y01h antibody had been administered, were used for analysis. A t-test was used for statistical analysis.

As a result, for the Tau-P301L dementia mice, into which IgG had been administered, staining of nerve cell bodies was strongly observed in brain regions (cortex, hippocampus) opposite to the side where the patient's insoluble fragment had been administered. On the other hand, for the Tau-P301L dementia mice, into which

the ADEL-Y01h antibody had been administered, decreased staining was observed in the hippocampus and cortex (Figs. 56 to 59).

Experimental Example 18. Identification of tau aggregation and seeding inhibitory effects caused by ADEL-Y01m antibody

5 In order to identify a tau aggregation inhibitory effect caused by the ADEL-Y01m antibody, an *in vitro* tau aggregation assay was performed. K18 protein fragment produced *in vitro* was acetylated by being reacted with 1.5 µg of P300 and 1 mM Acetyl-CoA at a temperature of 30°C for 3 hours. Thereafter, monomeric K18 protein fragment was reacted with 25 µM acetylated K18 protein fragment (K18-P301L) at room
10 temperature for 1 hour. Then, the resultant was treated with 25 mM heparin 57, HEPES (10 mM, pH 7.4), and NaCl (100 mM), and stirred at a condition of 700 rpm to induce aggregation of the tau proteins. Then, tau aggregation and seeding inhibitory effects thereof were analyzed, using the ADEL-Y01m antibody, through western blotting and thioflavin-T assay. It was identified by thioflavin-T assay that aggregation of acetylated
15 tau proteins is inhibited in a case where treatment with the ADEL-Y01h antibody is performed, as compared with a case where the acetylated tau proteins are aggregated.

 First, for fibrillation reaction, 10 M to 20 M acetylated tau protein (2N4R) was incubated at 37°C in a solution obtained by adding heparin (Sigma-Aldrich) and DTT at a concentration of 2 mM in 100 mM sodium acetate buffer (pH 7.0). The protein and
20 ThT solution (at a ratio of 1:1) was added to each well. ThT fluorescence analysis at different time points was measured using CLARIOstar® (BMG Labtech, Ortenberg, Germany) at 450 nm (excitation) and 510 nm (emission) wavelengths.

 Cultured mouse nerve cells were treated with the aggregate of acetylated proteins, and western blotting was performed to identify the results.

25 For the experiment, primary cerebral cortical neurons (DIV10) were treated with monomeric K18-P301L, aggregated K18-P301L, or acetylated K18-P301L at a concentration of 3 µg/ml for 24 hours. The neurons were pretreated with the ADEL-Y01m antibody at 3 µg/ml for 30 minutes prior to the K18 protein treatment.

 As a result, it was seen that many tau aggregates enter the nerve cells and induce

aggregation of intrinsic tau proteins; however, it was identified that in a case of being treated simultaneously with the ADEL-Y01m antibody, such phenomena are decreased (Figs. 60 and 61).

Experimental Example 19. Identification of nerve cell protective effect caused by ADEL-Y01h antibody

In order to identify a nerve cell protective effect caused by the ADEL-Y-1h antibody, cerebral cortical nerve cells were first isolated from the mouse brain during embryonic days. Specifically, brain tissue was extracted at the expense of a 16-day-old mouse, and the cerebral cortex was isolated therefrom. Thereafter, the cerebral cortical tissue was dissected in calcium- and magnesium-free Hank's balanced salt solution (HBSS) and incubated in a 0.125% trypsin solution at 37°C for 15 minutes. Trypsin was inactivated by treatment with Dulbecco's modified Eagle's medium (DMEM) containing 20% fetal bovine serum, and the cerebral cortical tissue was pulverized using a pipette. The resulting cell suspension was diluted in NB medium (neurobasal medium) supplemented with B27 supplement (GibcoBRL), and dispensed onto a plate coated with poly-D-lysine (Sigma) at 50 µg/ml and laminin (GibcoBRL) at 1 µg/ml. The nerve cells were cultured at a condition of 37°C and 5% CO₂ for 10 days. Then, the cultured nerve cells were treated with an aggregate of acetylated K18 protein fragments at 3 µg/ml and IgG or ADEL-Y01h antibody, and allowed to react for 24 hours.

After 24 hours, the supernatant was collected and analyzed using a cytotoxicity detection kit (LDH, Roche Applied Sciences). As a colorimetric assay for quantifying cell death, a method of measuring activity of lactate dehydrogenase (LDH), which was released into the supernatant from the cytosol of damaged nerve cells, was used. Absorbance at a wavelength of 490 nm was measured using the Tecan Infinite® 200 instrument. The results were expressed in percentage of cell viability as compared with a negative control (Blank).

In addition, the cell viability was measured using MTT (Thiazolyl Blue Tetrazolium Bromide, Sigma-Aldrich, St. Louis, MO, USA) reduction assay.

Absorbance at a wavelength of 540 nm was measured using the TecanInfinite®200 instrument, and the results were expressed in percentage as compared with a negative control (Blank).

In addition, the results were obtained under a condition of two independent cultures and 6 wells, and all values were expressed as mean $\pm$ s.e. of the mean. One-way ANOVA with Tukey's multiple comparison test was used for statistical analysis.

As a result, as illustrated in Fig. 62, high LDH activity was observed in the IgG-treated nerve cells. On the other hand, decreased LDH activity was observed in the ADEL-Y01h antibody-treated nerve cells as compared with the IgG-treated nerve cells.

In addition, as illustrated in Fig. 63, greatly decreased viability was observed in the IgG-treated nerve cells. On the other hand, significantly increased viability was observed in the ADEL-Y01m antibody-treated nerve cells as compared with the IgG-treated nerve cells. From these results, it was identified that the ADEL-Y01h antibody exhibited a protective effect against damages in nerve cells caused by aggregation of acetylated tau proteins.

Experimental Example 20. Identification of microglial phagocytosis promotion effect caused by ADEL-Y01h antibody

In order to identify a microglial phagocytosis promotion effect caused by the ADEL-Y01h antibody, primary microglia were first isolated from the cerebral cortex of 2- to 3-day-old mice and cultured according to the method described in McDonald DR *et al.*, *J Neurosci.* 1997; 17: 2284-94.

Thereafter, for analysis of the microglial phagocytosis, the acetylated K18 protein fragment was labeled with HiLyte™ Fluor 488 according to the manufacturer's instructions. For aggregation of HiLyte™ Fluor 488-labeled acetylated K18 proteins, the proteins were respectively incubated at 37°C in 100 mM sodium acetate buffer (pH 7.0) containing heparin (Sigma-Aldrich, St. Louis, MO, USA) and 2 mM DTT so that aggregation thereof was induced.

The microglia were dispensed in a 12-well-plate at 5×10^4 cells/well, and then the aggregate of acetylated K18 protein fragments (3 μ g/ml) was allowed to react at 37°C

for 2 hours. Pretreatment with IgG or the ADEL-Y01h antibody at a concentration of 4.5 µg/ml was performed 30 minutes before treatment with the aggregate of acetylated K18 protein fragments. For analysis of phagocytosis, the cells were separated by treatment with trypsin, and then fixed with 1% paraformaldehyde (PFA). For flow cytometry, treatment with an HBSS solution containing 200 µl of 2% fetal bovine serum was performed and analysis was performed using the FACSCanto™ II (BD Biosciences) instrument and 488 fluorescence filter.

As a result, promoted phagocytosis was observed in the ADEL-Y01h antibody-treated microglia as compared with the IgG-treated microglia (Fig. 64).

Statistical analysis

Statistical analysis was performed using GraphPad software (GraphPad Prism v7.0 and GraphPad Prism v8.0, GraphPad Software, San Diego, CA, USA). Data were analyzed by one-way ANOVA (Tukey's post hoc test) and Student's t-test. P values less than 0.05 were considered significant.

【Accession Number】

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CLAIMS

1. An anti-tau antibody or an antigen-binding fragment thereof, comprising:
a heavy chain variable region (VH) that includes:
5 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
10 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
15 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
20 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.
- 25 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;

5 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
10 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
15 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
20 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;

25 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.
- 5
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 as described in claim 2.
- 10 heavy chain variable region and the light chain variable region as described in claim 2.
10. A hybridoma having accession number KCTC 14155BP.
11. 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 of claim 1.
- 15 the anti-tau antibody or antigen-binding fragment thereof of claim 1.
12. The pharmaceutical composition of claim 11, wherein the degenerative neurological disease is a tau protein-mediated neurological disease.
- 20
13. The pharmaceutical composition of claim 12, 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, meningoangiomatosis, subacute sclerosing panencephalitis, Hallervorden-Spatz disease, or lipofuscinosis.
- 25

14. The pharmaceutical composition of claim 13, 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
5 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.
- 10 15. 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 16. A composition for diagnosing a degenerative neurological disease, the composition comprising the anti-tau antibody or antigen-binding fragment thereof of claim 1.
- 20 17. A kit for preventing, treating, or diagnosing a degenerative 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.
18. The antibody or antigen-binding fragment thereof of claim 1 for use in therapy.
- 25 19. Use of the antibody or antigen-binding fragment thereof of claim 1 in the manufacture of a medicament for treating a degenerative neurological disease.

20. The use of claim 19, wherein the degenerative neurological disease is a tau protein-mediated neurological disease.