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Life Sciences Reporting Summary

Nature Research wishes to improve the reproducibility of the work we publish. This form is published with all life science papers and is intended to promote consistency and transparency in reporting. All life sciences submissions use this form; while some list items might not apply to an individual manuscript, all fields must be completed for clarity.

For further information on the points included in this form, see Reporting Life Sciences Research. For further information on Nature Research policies, including our data availability policy, see Authors & Referees and the Editorial Policy Checklist.

Experimental design

1. Sample size

   Describe how sample size was determined.

   Sample sizes were chosen to be 3 or 4 because they are generally considered as sufficient for 96-well plate based experiments, and generated acceptable P values in statistic analysis.

2. Data exclusions

   Describe any data exclusions.

   No data were excluded from the analysis.

3. Replication

   Describe whether the experimental findings were reliably reproduced.

   All attempts at replication were successful.

4. Randomization

   Describe how samples/organisms/participants were allocated into experimental groups.

   Randomization is not relevant to our study. No research animals, human research participants or clinical studies are involved in our study. The samples we used are aqueous solutions. The allocations of each sample were extracted from a single falcon tube, eliminating differences in sample preparation.

5. Blinding

   Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

   Blinding was not relevant to our study, because all experiments were done on 96-well plates and quantified by plate reader. No subjective analysis were required.

Note: all studies involving animals and/or human research participants must disclose whether blinding and randomization were used.

6. Statistical parameters

   For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or the Methods section if additional space is needed).

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)
☐	☒	A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly.
☐	☒	A statement indicating how many times each experiment was replicated
☐	☒	The statistical test(s) used and whether they are one- or two-sided (note: only common tests should be described solely by name; more complex techniques should be described in the Methods section)
☐	☒	A description of any assumptions or corrections, such as an adjustment for multiple comparisons
☐	☒	The test results (e.g. *p* values) given as exact values whenever possible and with confidence intervals noted
☐	☒	A summary of the descriptive statistics, including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)
☐	☒	Clearly defined error bars

See the web collection on statistics for biologists for further resources and guidance.

Software

Policy information about availability of computer code

7. Software

Describe the software used to analyze the data in this study.

Graphs were plotted in Excel 2016 (version 15.29.1), KI and IC50 was calculated using GraphPad Prism (version 7.0c). Statistical significance was calculated by online t test calculator GraphPad QuickCalcs. Diffraction data was indexed, merged and scaled with XDS and XSCALE (version May 1, 2016). Molecular replacement was performed with Phaser (version 2.5.5), and refinements were performed using Phenix (version 1.12.2829) and Coot (veriosn 0.8.9.1). NMR spectra were processed with TopSpin (version 3.5 pl 2) and analyzed with Sparky (version 3.114). Computational docking was performed by Rosetta software package (version 3.5) and high-throughput docking was performed by Glide Maestro (version 5.6) in Schrödinger suite package. The CD spectra were analyzed by the online software BeStSel. The intensity of cofilin bands were measured by ImageJ (version 1.51j8). The cell confluency, integrated intensity of green and red fluorescence in each well was calculated by Celigo (version 4.1.3.0).

For all studies, we encourage code deposition in a community repository (e.g. GitHub). Authors must make computer code available to editors and reviewers upon request. The *Nature Methods* guidance for providing algorithms and software for publication may be useful for any submission.

Materials and reagents

Policy information about availability of materials

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company.

No unique materials were used.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).

i) clone name, 6E10; provide supplier name, BioLegend (previously Convance); catalog number, SIG-39320; host species, mouse; application, ELISA, WB, IHC, IP; dilution, 1:5000; application reference (selected), 1. Thakker DR, et al. Intracerebroventricular amyloid-beta antibodies reduce cerebral amyloid angiopathy and associated micro-hemorrhages in aged Tg2576 mice. Proc Natl Acad Sci USA Feb 25, 2009. 2. Klyubin I, et al. Amyloid beta protein immunotherapy neutralizes Abeta oligomers that disrupt synaptic plasticity in vivo. Nat Med 11(5):556-61, 2005.
ii) clone name, 4G8; provide supplier name, BioLegend (previously Convance); catalog number, SIG-39200; host species, mouse; application, ELISA, WB, IHC, IP; dilution, 1:1000; application reference (selected), 1. Thakker DR, et al. Intracerebroventricular amyloid-beta antibodies reduce cerebral amyloid angiopathy and associated micro-hemorrhages in aged Tg2576 mice. Proc Natl Acad Sci USA Feb 25, 2009. 2. Kimura N, et al. Age-related changes of intracellular Abeta in cynomolgus monkey brains. Neuropath Appl Neurobiol 31(2):170-80, 2005.
iii) clone name, β 37-42; provide supplier name, Millipore Sigma; catalog number, AB5306; host species, rabbit; application, ELISA, IH(P); dilution, 1:500; application reference (selected), 1. Marksteiner, J; Humpel, C. Beta-amyloid expression, release and extracellular deposition in aged rat brain slices.
Molecular psychiatry 13 939-52 2008. 2. Takashi Togo, Dennis W Dickson, Takashi Togo, Dennis W Dickson. Tau accumulation in astrocytes in progressive supranuclear palsy is a degenerative rather than a reactive process. Acta neuropathologica 104 398-402 2002
iv) name, Anti-Mouse IgG (whole molecule)-Peroxidase antibody; provide supplier name, Sigma-Aldrich; catalog number, A4416; dilution, 1:5000.
v) name, Anti-Rabbit IgG (whole molecule)-Peroxidase antibody; provide supplier name, Sigma-Aldrich; catalog number, A0545; dilution, 1:5000.
vi) name, Cofilin (D3F9) XP Rabbit mAb #5175; provide supplier name, Cell Signaling Technology; catalog number, 5175S; host species, rabbit; application, FC/FACS, ICC, IF, IHC, WB; dilution, 1:1000; application reference (selected), Megaw R. et al., Gelsolin dysfunction causes photoreceptor loss in induced pluripotent cell and animal retinitis pigmentosa models. Nature Communications, 2017.
vii) name, phospho-Cofilin (Ser3) (77G2) Rabbit mAb #3313; provide supplier name, Cell Signaling Technology; catalog number, 3313S; host species, rabbit; application, IF and WB; dilution, 1:500; application reference (selected), Megaw R. et al., Gelsolin dysfunction causes photoreceptor loss in induced pluripotent cell and animal retinitis pigmentosa models. Nature Communications, 2017.
viii) name, Anti-Tubulin β-3 (TUBB3) antibody; provide supplier name, BioLegend; catalog number, 802001; host species, rabbit; clone name, Poly18020; dilution, 1:5000; application reference (selected) Feuer R, et al. 2005. J. Neurosci. 25(9):2434-44. Mozzetti S, et al. 2005. Clin. Cancer Res. 11(1):298-305.

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.

HEK293T cell line was from Prof. Samuel W. French's lab at UCLA

b. Describe the method of cell line authentication used.

None of the cell lines used were authenticated by us

c. Report whether the cell lines were tested for mycoplasma contamination.

None of the cell lines used were tested for mycoplasma contamination by us

d. If any of the cell lines used in the paper are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use.

No commonly misidentified cell lines were used

Animals and human research participants

Policy information about studies involving animals; when reporting animal research, follow the ARRIVE guidelines

11. Description of research animals

Provide details on animals and/or animal-derived materials used in the study.	Male and female embryos (embryonic day 15) from pregnant CD-1 mouse dams.

Policy information about studies involving human research participants

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.	The study did not involve human research participants