

### Supporting Information

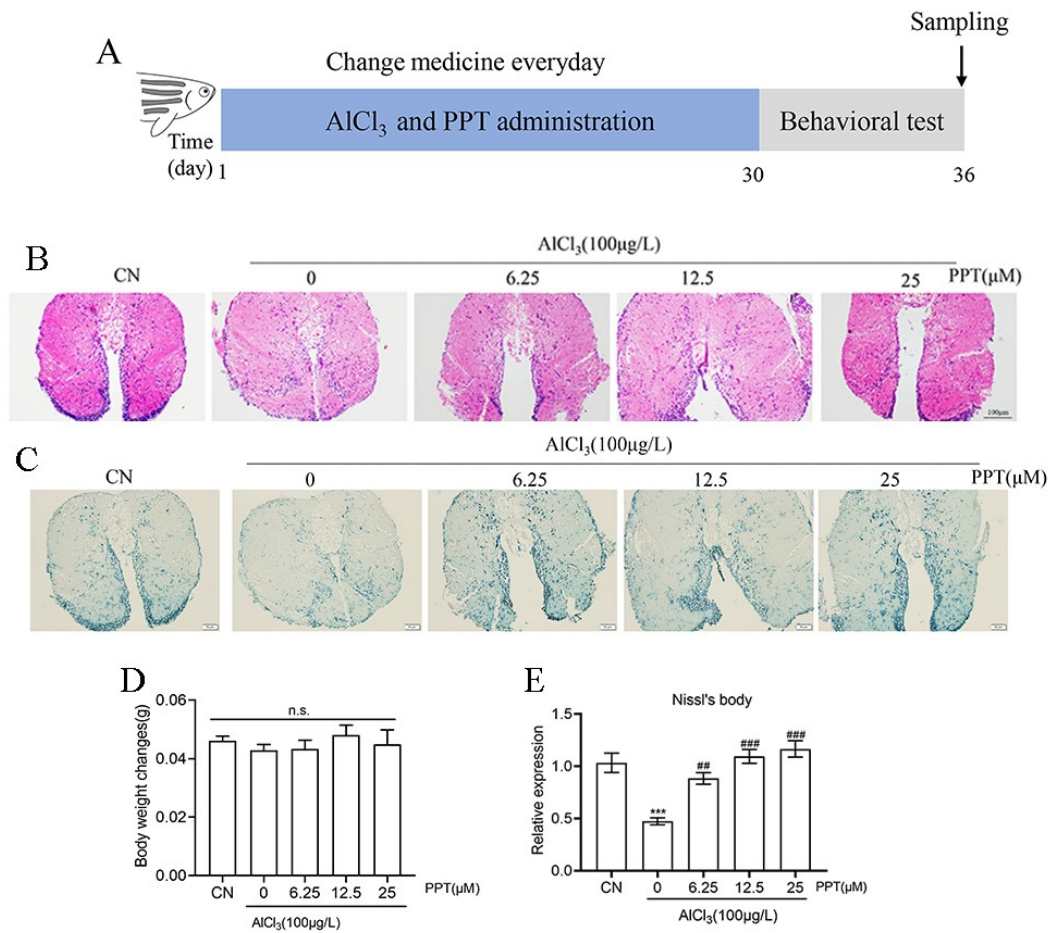
Supporting information Table S1. Primers of target genes used in this study

Species	Target gene	Sequence of primer
zebrafish	<i>gapdh</i>	F 5'- ACCACAGTCCATCAC-3'
		R 5'- TCCACCACCCTGTTGCTGTA-3'
zebrafish	<i>huc</i>	F 5'- AGACAAGATCACAGGCCAGAGCTT-3'
		R 5'- TGGTCTGCAGTTTGAGACCGTTGA-3'
zebrafish	<i>neurod1</i>	F 5'-ATGCCTCCAACCTGAACCC-3'
		R 5'-AGACCCGCTGCCTGATAG-3'
mouse	<i>18s</i>	F 5'-AGTCCCTGCCCTTTGTACACA-3'
		R 5'-CGATCCGAGGGCCTCACTA-3'
mouse	<i>gfap</i>	F 5'- TCTCGAATGACTCCTCCACTC-3',
		R 5'-AAGCTCCGCCTGGTAGACAT-3'
mouse	<i>dcx</i>	F 5'-GGCCAAGAAGGTACGTTTCTAC-3'
		R5'-AGCAACGCATCAAACTACGAA-3'
mouse	$\beta$ III tubulin	F 5'-GCGCCTTTGGACACCTATTCA-3'
		R 5'-GCCCTCCGTATAGTGCCCT -3'
human	<i>app</i>	F 5'-CAAGCAGTGCAAGACCCATC-3'
		R 5'-AGAAGGGCATCACTTACAACTC-3'

Supporting information Table S2. Interaction energies after computational alanine scanning of the

residues

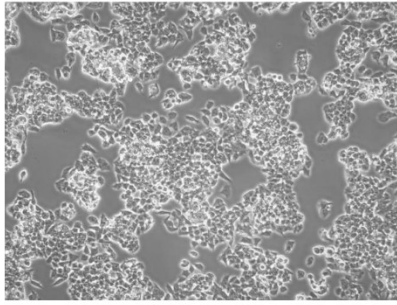
	<b>Residue</b>	<b>Interaction Energy (kcal/mol)</b>	<b>VDW Interaction Energy (kcal/mol)</b>	<b>Electrostatic Interaction Energy (kcal/mol)</b>
2RD0-E821A	A_LYS271	-1.524960	-4.654240	3.129280
	A_ARG818	-22.157976	-5.524761	-16.633215
	A_PRO835	-4.269438	-2.354823	-1.914615
2RD0-K271A	A_ARG818	-22.157976	-5.524761	-16.633215
	A_GLU821	-8.876178	-1.881095	-6.995083
	A_PRO835	-4.269438	-2.354823	-1.914615
2RD0P835A	A_LYS271	-1.524960	-4.654240	3.129280
	A_ARG818	-22.157976	-5.524761	-16.633215
	A_GLU821	-8.876178	-1.881095	-6.995083
2RD0-R818A	A_LYS271	-1.524960	-4.654240	3.129280
	A_GLU821	-8.876178	-1.881095	-6.995083
	A_PRO835	-4.269438	-2.354823	-1.914615



Supporting information Fig. S1. PPT improves cognitive function and neurogenesis in AD zebrafish. (A) Flowchart of the zebrafish experiment. (B) HE staining results. (C) Nissl's staining results.

(D) Changes in body weight of zebrafish before and after drug administration. (E) Quantitative results of Nissl bodies. Nissl's staining results presented as *mean*  $\pm$  *SD* ( $n=3$ ; compared with the control group, \*\*\* $P < 0.001$ ; compared with the model group, ## $P < 0.01$ , ###  $P < 0.001$ ).

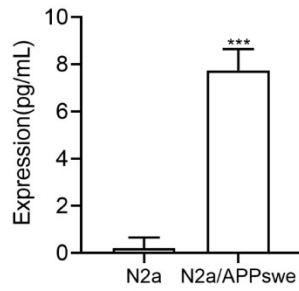
A



B

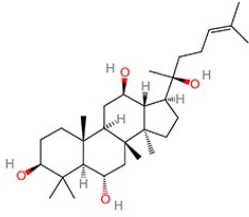
	<i>18s</i> CT	<i>app</i> CT
N2a	18.548	Undetermined
	17.812	Undetermined
	19.360	Undetermined
	18.559	Undetermined
N2a/APPswe	20.722	25.100
	20.734	25.281
	20.714	24.023
	20.778	25.683

C

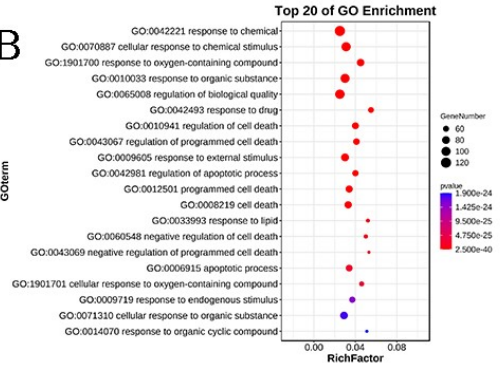


Supporting information Fig. S2. The verification of N2a/APPswe cell line. (A) Cellular morphology photograph of N2a/APPswe cell line. (B) CT value of *app* between N2a and N2a/APPswe cell line. (C) A $\beta$  secretion of N2a/APPswe cell in conditioned medium.

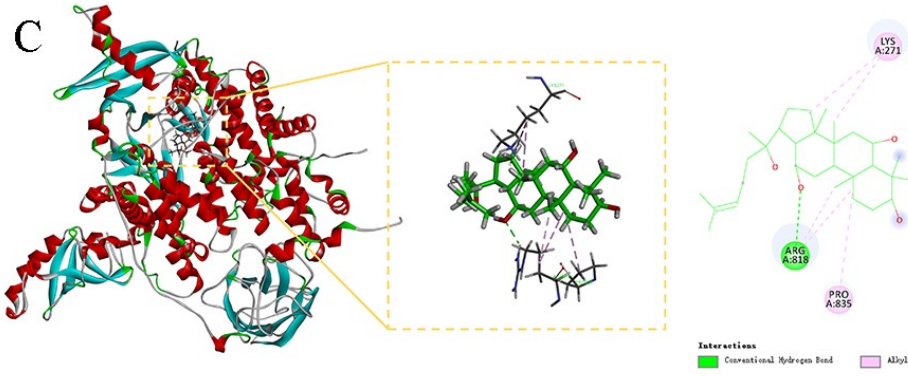
A



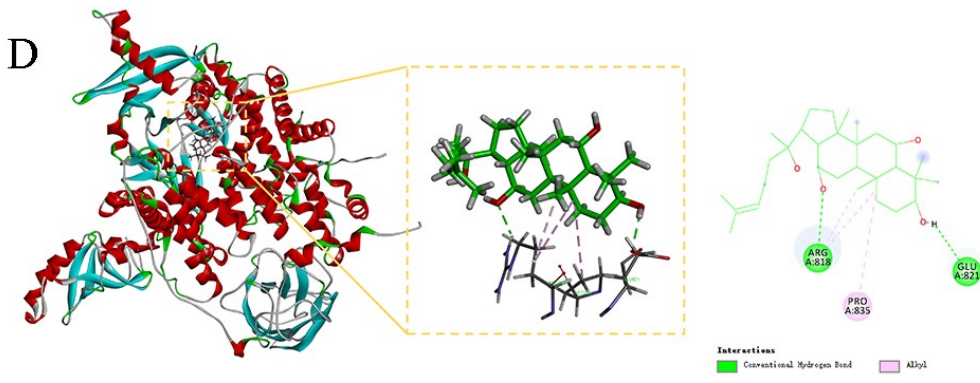
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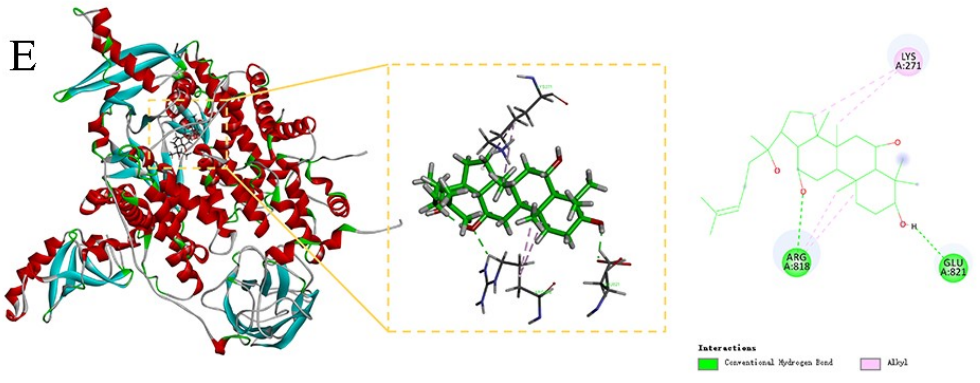
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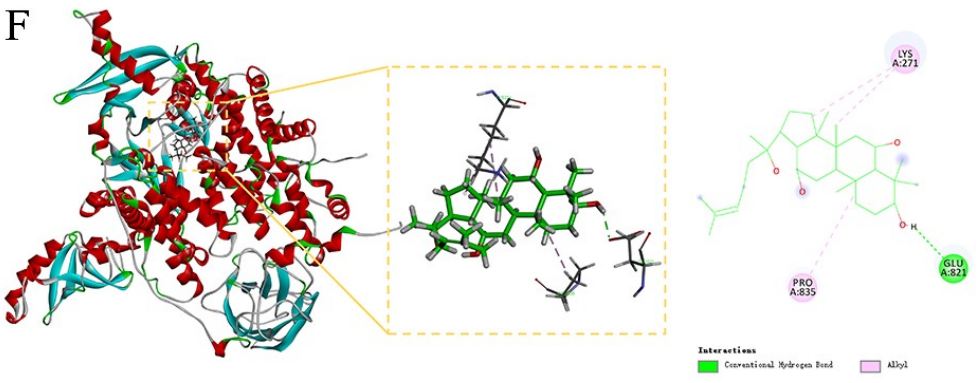
D



E



F



Supporting information Fig. S3. Signaling pathways of PPT in treating AD predicted by network pharmacology and site-directed mutagenesis analysis of PI3CA1 and PPT. (A) The chemical structure of PPT is shown. (B) Distribution of potential targets in GO enrichment analysis. Top 20 pathways with corresponding p-values, displayed in a dot plot. The color indicated p-values and the sizes of the dots represented the gene count of each term. (C) 2RD0-E821A. (D) 2RD0-K271A. (E) 2RD0-P835A. (F) 2RD0-R818A.