Supporting Information.

A novel BODIPY-based theranostic agent for in vivo fluorescent imaging of cerebral Aβ and ameliorating Aβ-associated disorders in Alzheimer's disease transgenic mice†

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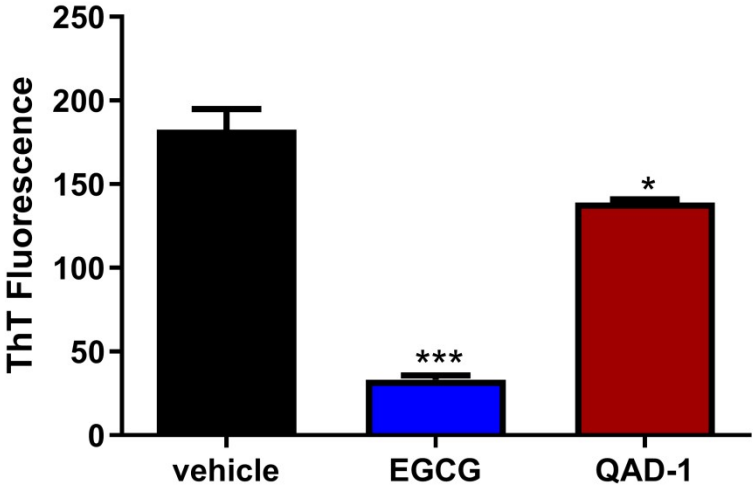
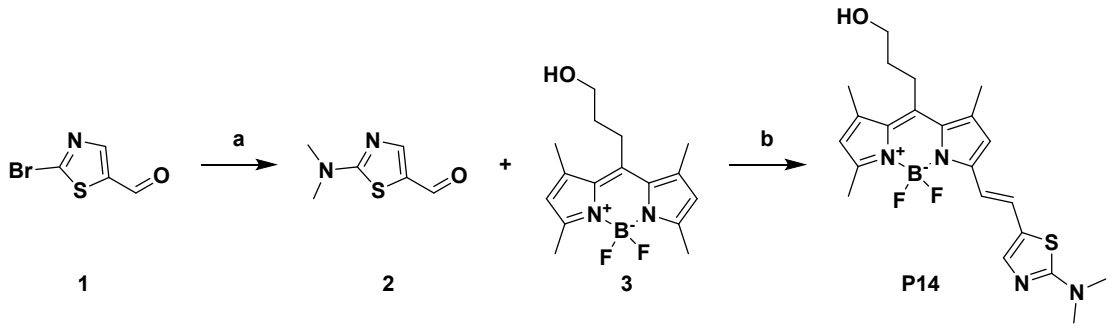


Figure S1. ThT fluorescence of Aβ incubated with QAD-1. Final concentration of Aβ is 4.25 μM; Final concentration of QAD-1 and EGCG is 1 μM Data were presented as the mean ± SD, n = 4, * $P < 0.05$, *** $P < 0.001$ compared with the Aβ42 group.

Synthesis Details



Scheme S1. Synthesis route of probe **P14**: a) Dimethylamine solution (33% w/w), reflux, 4h; b) CH_3COOH/piperidine, toluene/$CHCl_3$, reflux, 4h.

Experimental procedures and compound characterization

5-(dimethylamino)thiophene-2-carbaldehyde (**3**) To a solution of 2-Bromo-5-formylthiazole (2.00 g, 10.42 mmol) in H_2O/DMSO (v:v=4:1, 50 mL) was added dimethylaniline (5.00 mL, 33% aqueous solution, 36.74 mmol). The mixture was stirred at 50 °C for 4 h, and then cooled to room temperature. After extraction with EtOAc, the organic layer was washed with brine, dried over Na_2SO_4, and concentrated to dryness. The residue was purified by silica gel flash chromatography (EtOAc/hexanes) to give **2** (1.30 g, 80%) as a light yellow powder. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.67 (s, 1H), 7.87 (s, 1H), 3.22 (s, 6H).

3-(5,5-difluoro-1,3,7,9-tetramethyl-5H-4l4,5l4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl)propan-1-ol (3) was prepared according to the literature procedures[1].

(E)-3-(3-(2-(2-(dimethylamino)thiazol-5-yl)vinyl)-5,5-difluoro-1,7,9-trimethyl-5H-5λ^4,6λ^4-dipyrrolo[1,2-*c*:2',1'-*f*][1,3,2]diazaborinin-10-yl)propan-1-ol (P14) To a solution of alcohol 3 (980 mg, 3.20 mmol) in toluene/$CHCl_3$ mixture (v:v=6:1, 70 mL) was added aldehyde 2 (500 mg, 3.20 mmol), piperidine (200 μL) and acetic acid (200 μL), The mixture was stirred under

reflux for 4 h. After the mixture had cooled to room temperature, H_2O was added and extracted with DCM. The organic phase was dried over Na_2SO_4 and concentrated to dryness. The residue was purified by silica gel flash chromatography (EtOAc/hexanes/DCM=5:1:3) to give dye P14 (480 mg, 34%) as a purple blue powder. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.27 (s, 1H), 7.23 (d, *J* = 15.7 Hz, 1H), 6.96 (d, *J* = 15.7 Hz, 1H), 6.58 (s, 1H), 6.04 (s, 1H), 3.79 (t, *J* = 5.7 Hz, 2H), 3.16 (s, 6H), 3.09 – 3.00 (m, 2H), 2.54 (s, 3H), 2.45 (s, 3H), 2.43 (s, 3H), 1.90 – 1.82 (m, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 171.51, 152.33, 143.52, 143.23, 140.37, 138.84, 132.96, 131.47, 127.32, 126.93, 121.25, 118.04, 115.54, 62.49, 40.26, 34.62, 24.91, 16.75, 16.40, 14.55. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{28}BF_2N_4OS^+$: 445.2039; found: 445.2082. HPLC purity: 98.9%.

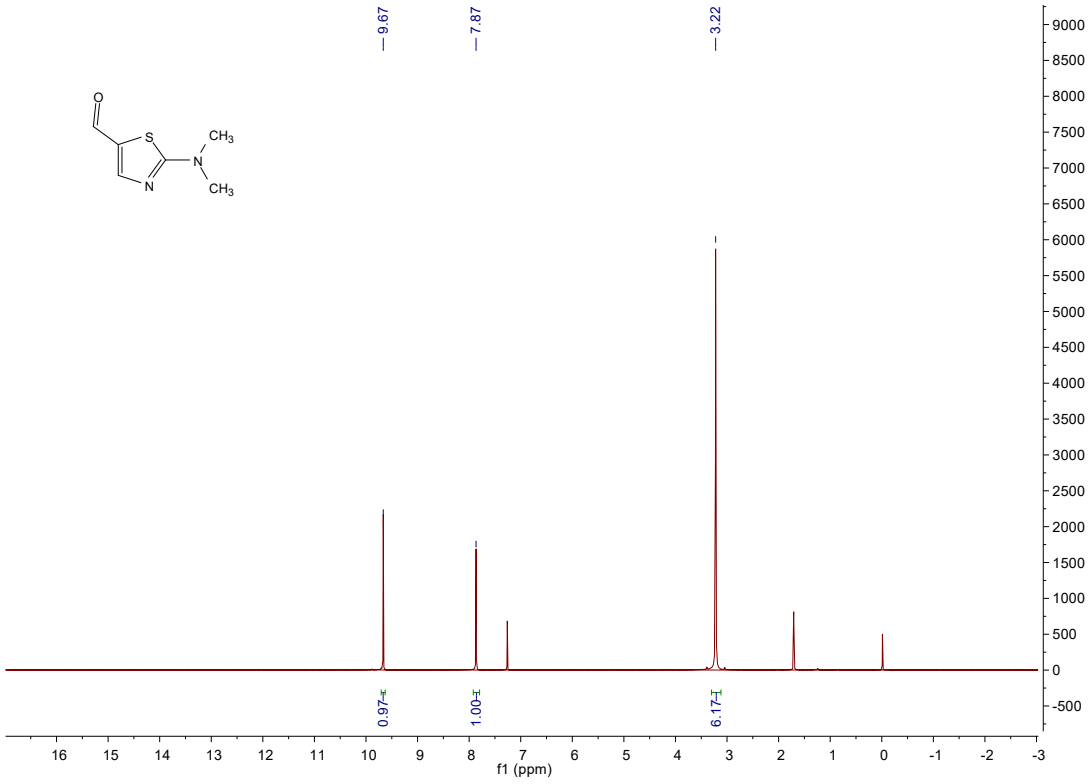


Figure S2. ^{1}**H** NMR spectrum of **2**.

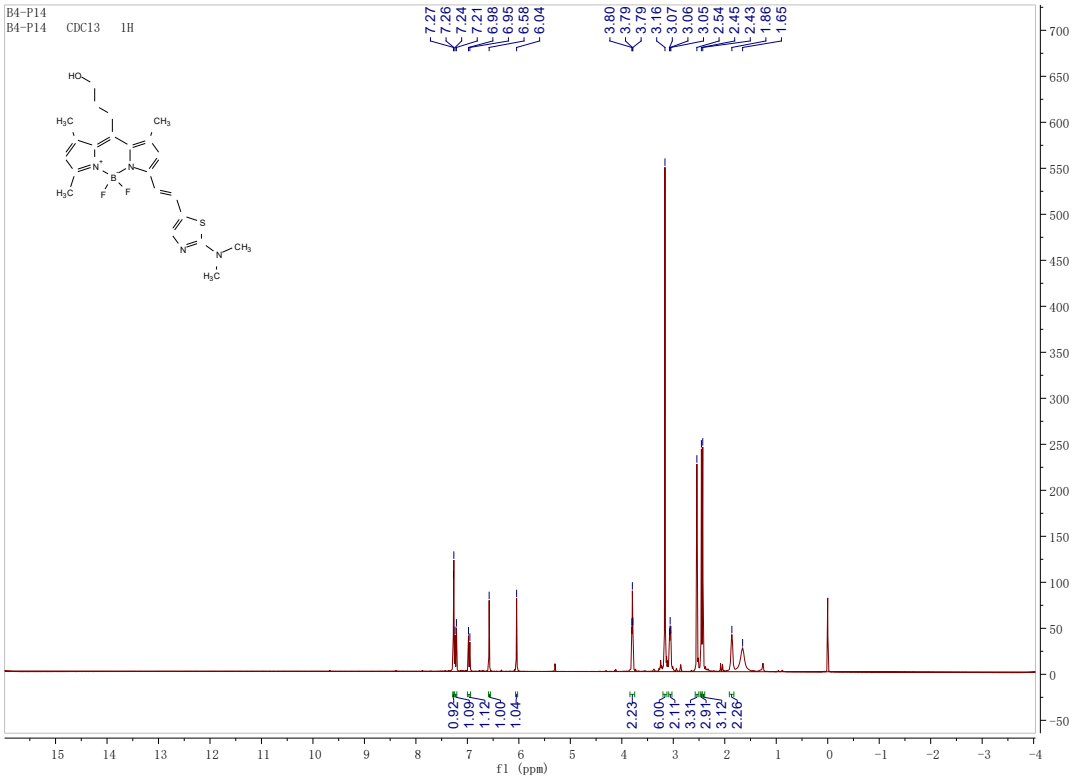


Figure S3. ^{1}**H** NMR spectrum of **P14**

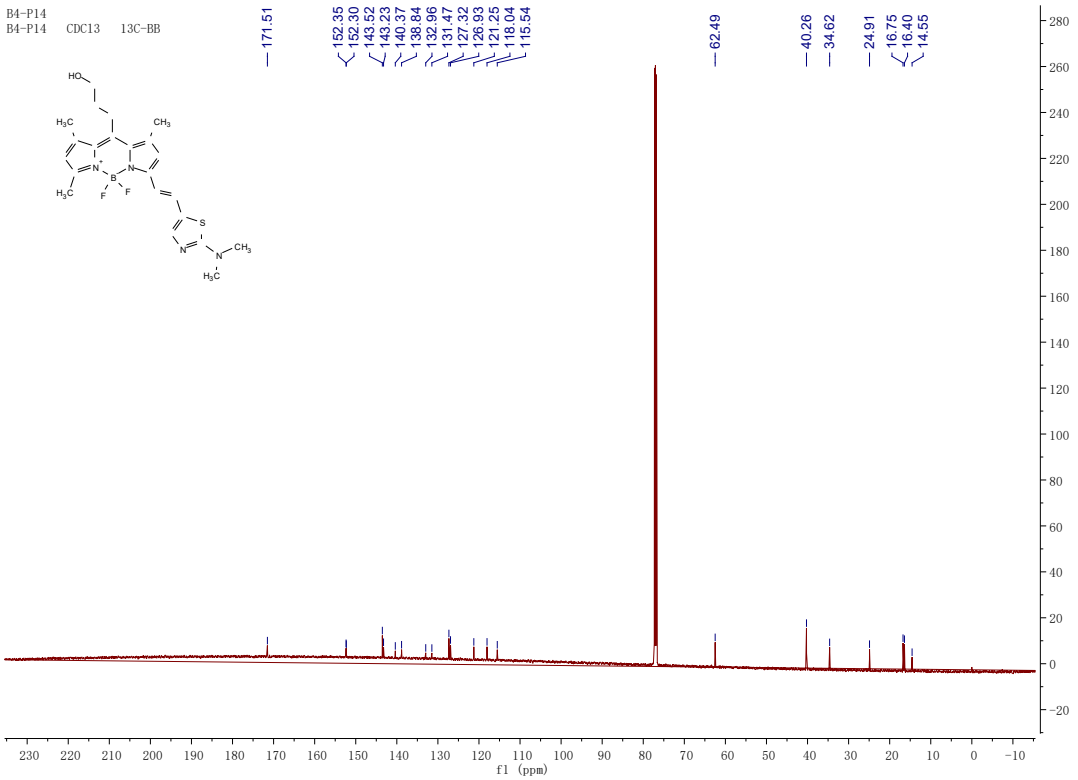


Figure S4. ^{13}**C** NMR spectrum of **P14**.

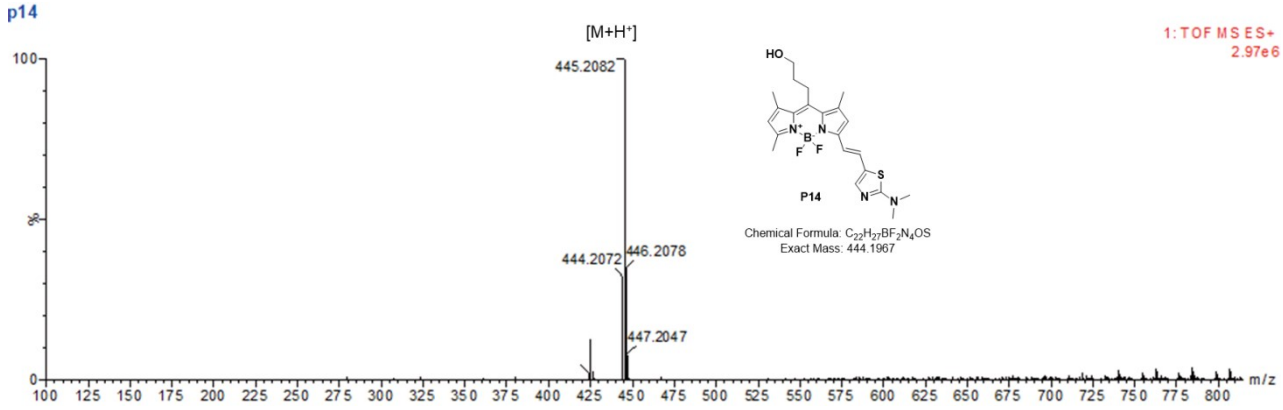


Figure S5. MS spectrum of **P14**.

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样品名称：P14

操作者 : JXY
仪器 : 仪器 2 位置 : 样品瓶 14
进样日期 : 2022-7-3 7:39:34 下午
进样量 : 20 µl
采集方法 : C:\CHEM32\2\METHODS\MYJ-2.M
最后修改 : 2022-7-3 6:16:36 下午 : JXY
(调用后修改)
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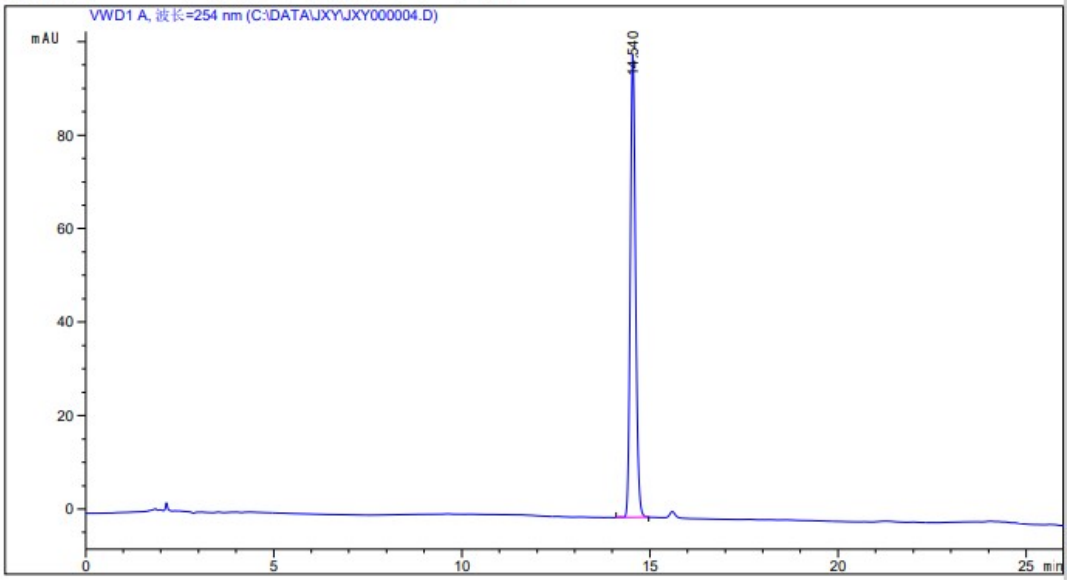

面积百分比报告

排序 : 信号
乘积因子 : 1.0000
稀释因子 : 1.0000
内标使用乘积因子和稀释因子

信号 1: VWD1 A, 波长=254 nm

峰 #	保留时间 [min]	类型	峰宽 [min]	峰面积 mAU *s	峰高 [mAU]	峰面积 %
1	14.540	BB	0.1497	960.77997	98.93221	100.0000
总量 :				960.77997	98.93221	

Figure S6. HPLC purity of **P14**.

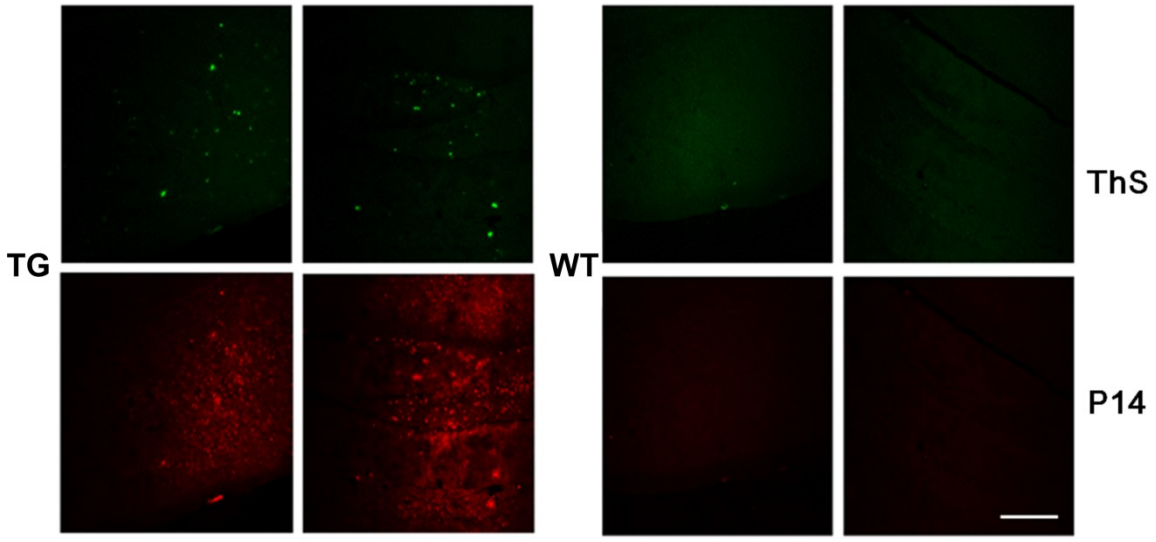

Figure S7. *Ex vivo* fluorescence imaging of APP/PS1 (TG) and wild-type mice (WT) after i.v. injection of **P14**. The excitation channel for **P14** imaging = 589 nm, emission channel = 641 nm; the excitation channel for ThS imaging = 488 nm, emission channel = 550 nm; scale bar= 250 μm; n = 3.

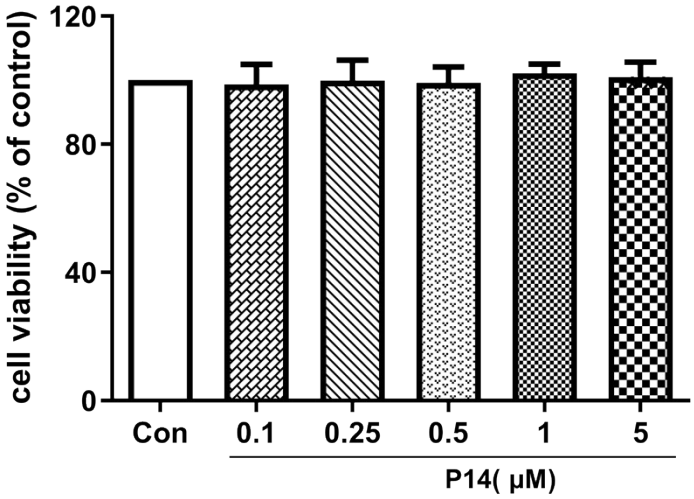

Figure S8. Effect of **P14** on cell viability of primary neurons. Cell viability conducted by MTT assay. Data were presented as the mean ± SD, n = 5; Con: control group.

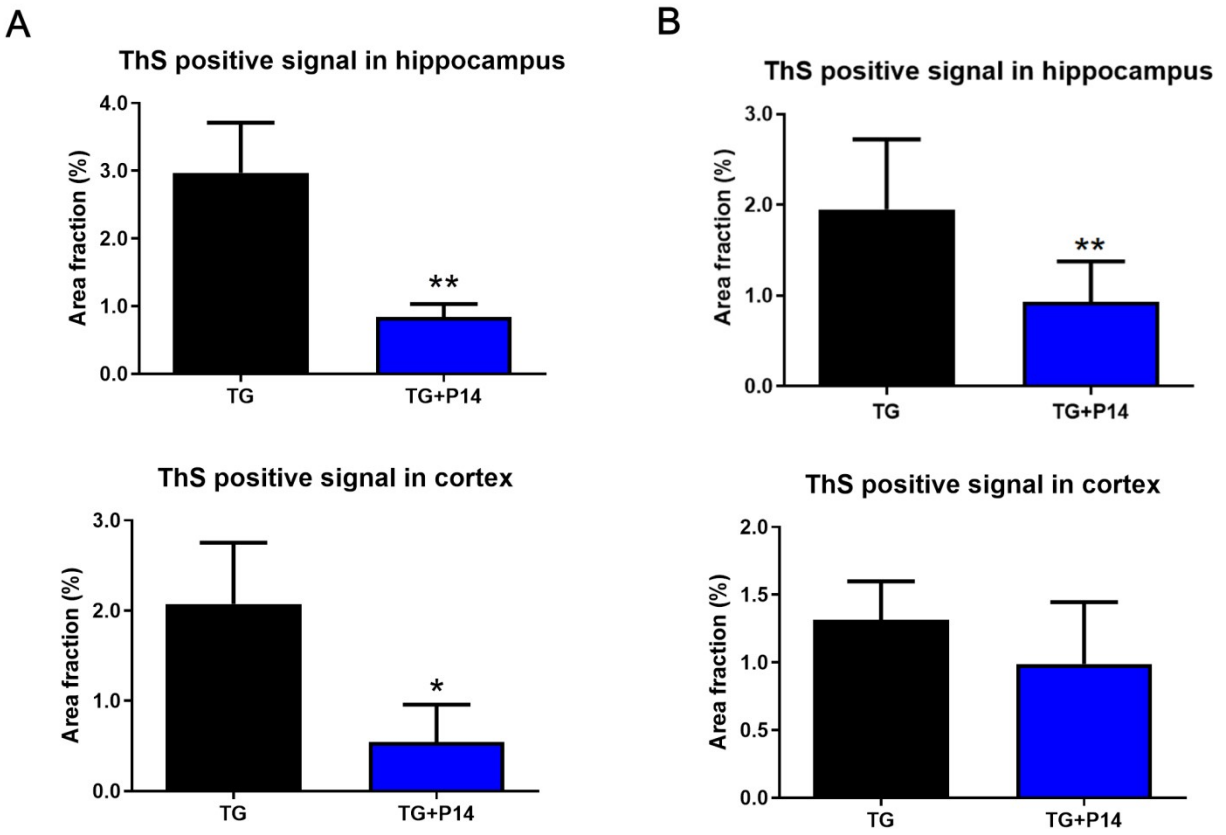

Figure S9. Quantitative analysis of ThS positive signals in brain sections. (A) The results of quantitative analysis of ThS positive signals in brain sections of APP/PS1 mice (n = 3). (B) The results of quantitative analysis of ThS positive signals in brain sections of 5×FAD mice (n = 9-10). Data are shown as mean ± SD. *P < 0.05, **P < 0.01 compared with the TG group. WT: wild type mice; TG: APP/PS1 mice in Panel A； 5× FAD mice in Panel B.

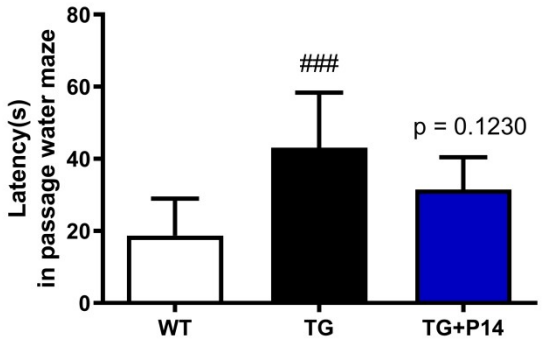

Figure S10. Latency of passage water maze of APP/PS1 transgenic mice and wild type mice. Data were presented as the mean ± SD, ### $P < 0.001$ compared with the WT group; n = 6-10. WT: wild type mice; TG: APP/PS1 mice.

1 W. M. Ren, M. M. Xu, S. H. Liang, H. J. Xiang, L. Tang, M. K. Zhang, D. J. Ding, X. Li, H. Y. Zhang and Y. H. Hu, *Biosens Bioelectron*, 2016, **75**, 136-141.