

## Supplementary figure legends

**Figure S1** (A) Schematic representation of luciferase reporter construct containing PPRE. BV2 cells (B) and primary microglia (C) were treated with increasing concentrations of JuA (0–50  $\mu$ M) for 24 h, then cell viability was measured by MTT assay.

**Figure S2** Male APP/PS1 mice at 8-month-age were treated with solvent, rosiglitazone (Rog) (30 mg/kg/d) or jujuboside A (JuA) at different concentration through intragastric administration (i.g) for 6 weeks. (A) Escape latency during spatial acquisition training. (B) The representative motion track, (C) the distance in target quadrant, (D) time spent in target quadrant, and (E) the platform crossing number in spatial probe test were shown respectively (n = 10). After MWM test, animals were sacrificed and the brain tissues were collected. The A $\beta$ 42 levels in cortex (F) and hippocampus (G) were detected by ELISA. ###  $p < 0.001$ , \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$  versus control.

**Figure S3** APP/PS1 transgenic mice were administrated with JuA (5 mg/kg, i.t.) alone or treated with JuA and GW9662 (0.1 mg/kg, i.t., 30 minutes before the JuA administration) once daily for 7 days. (A) Escape latency during spatial acquisition training, (B) the distance in target quadrant, (C) time spent in target quadrant, (D) the platform crossing number, and (E) the representative motion track in spatial probe test were shown respectively. (F) The A $\beta$ 42 levels in cortex and hippocampus were detected by ELISA. \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$  versus control.

**Figure S4** (A) Male APP/PS1 mice at 8-month-old were treated with solvent (i.t.) or JuA (5 mg/kg, i.t.) once daily for 7 days. The p-tau and tau levels were detected by

western blot. (B) SHSY5Y cells were pretreated with 0.1 % DMSO, specific GSK3 inhibitor CHIR-99021 (10  $\mu$ M) or JuA at indicated concentration for 30 min, and followed by administrated with homocysteine (Hcy) (50  $\mu$ M) for 24 h. The whole cell proteins were subjected into western blot with the antibodies as indicated. #  $p < 0.05$ , ##  $p < 0.01$ , \* $p < 0.05$ , \*\*\* $p < 0.001$  versus control.

**Figure S1**

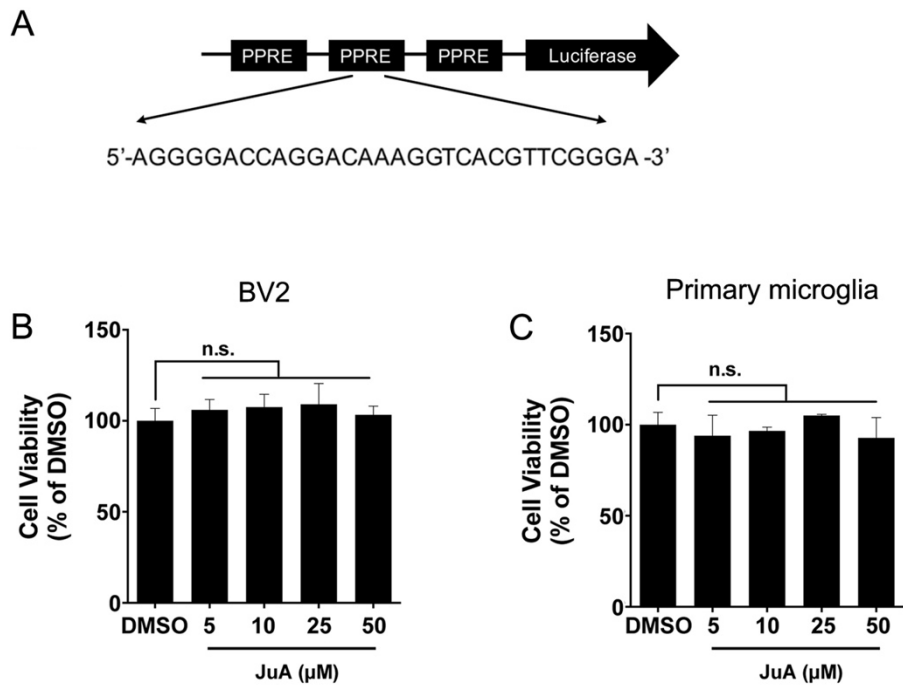


Figure S2

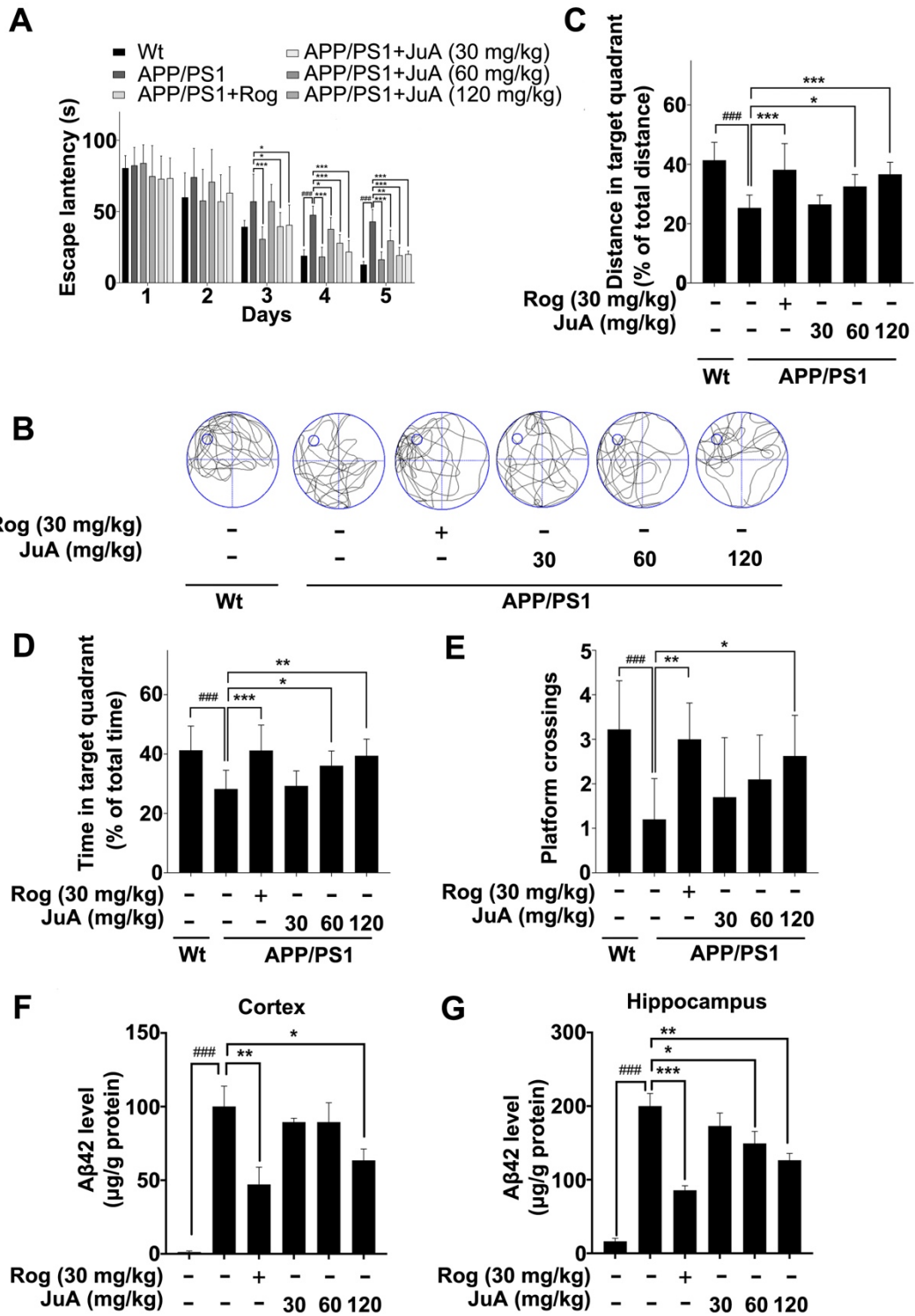
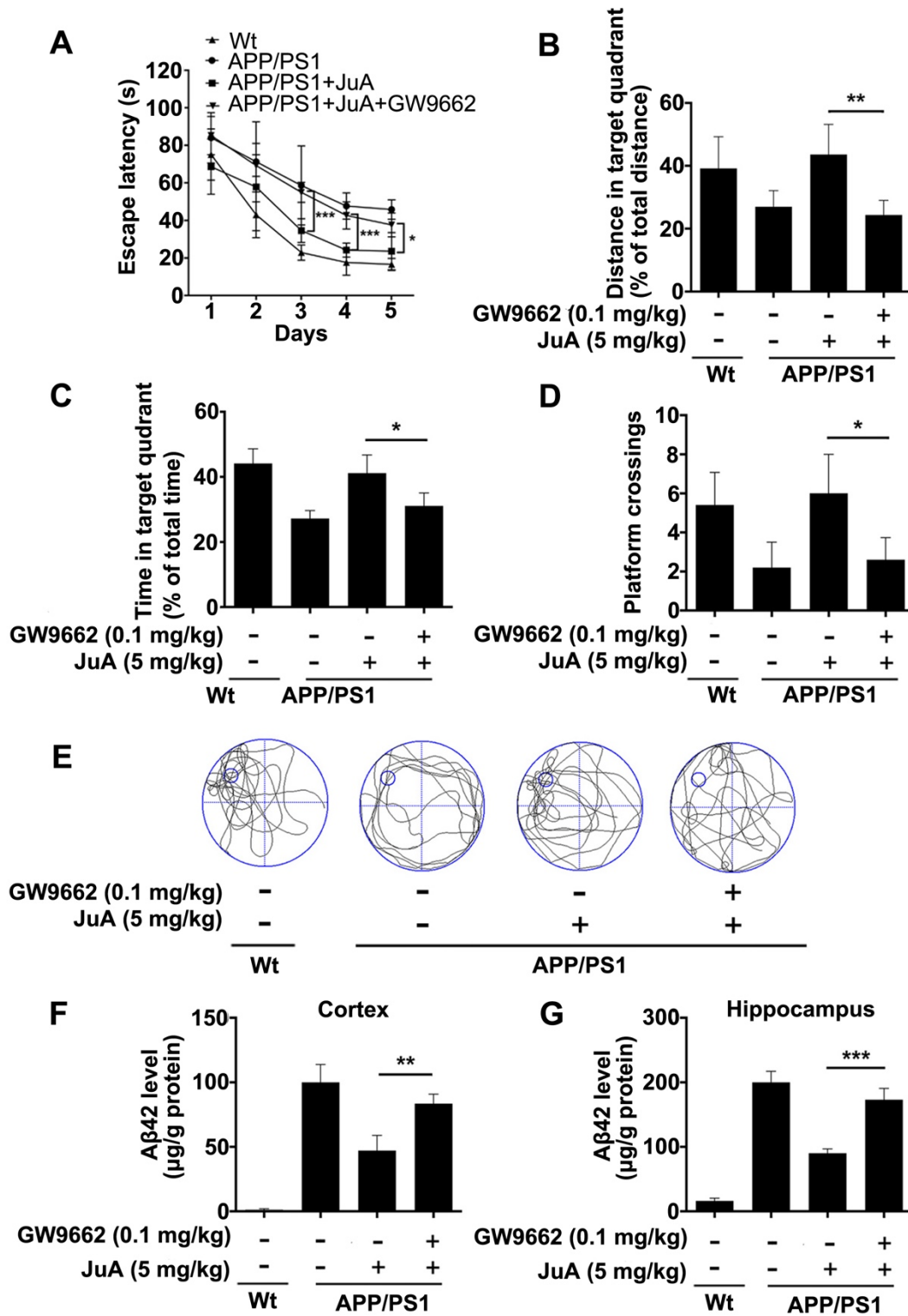
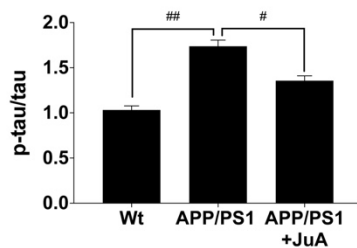
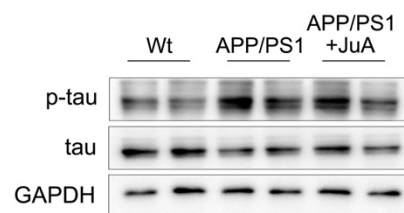


Figure S3



**Figure S4**

**A**



**B**

