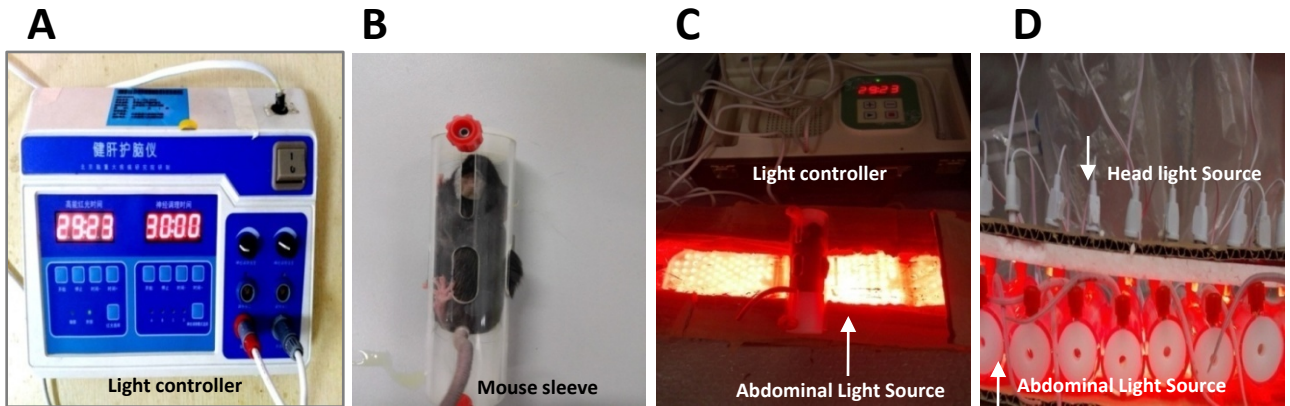# Supplementary Figure 1

Figure S1. Light-emitting diode with red light (LED-RL, 630 nm) illuminates in the brains and livers of APP/SI1 mice. **A,** The device of LED-RL. **B,** Mouse was fixed in the plastic sleeve. **C, D,** Mice were illuminated with a head light source (**C**) and an abdomen light source (**D**) for consecutive 2 months (n = 10).
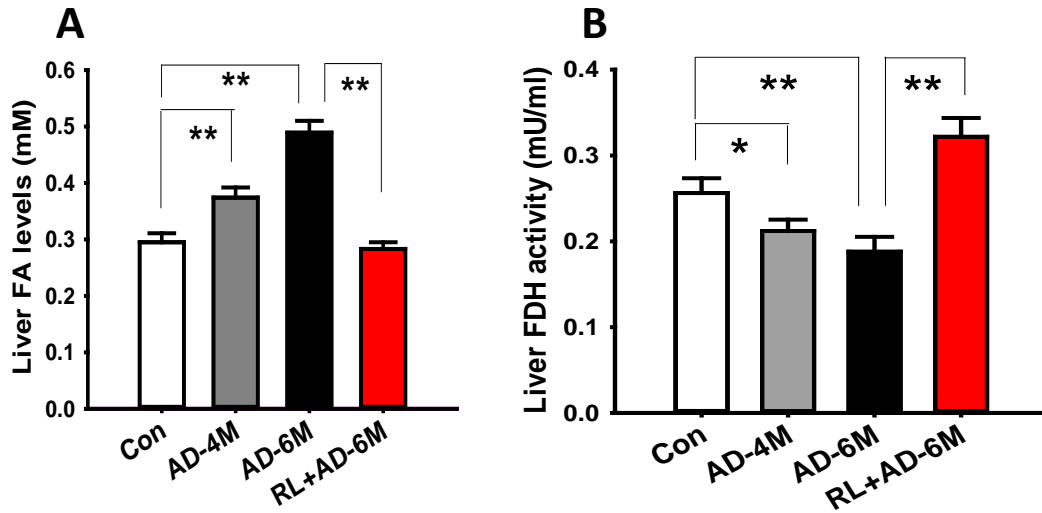
Supplementary Figure 2

Figure S2. Red light illumination decreases FA levels and improves FDH activity in the livers of APP/SI1 mice. **A**, Quantitative assessment of liver FA levels detected by using high-performance liquid chromatography(HPLC). $n= 8$. **B**, Quantitative results of liver FDH activity analyzed by FDH kit. $n =8$;. ** $p< 0.01$; values are mean ± s.e.m.
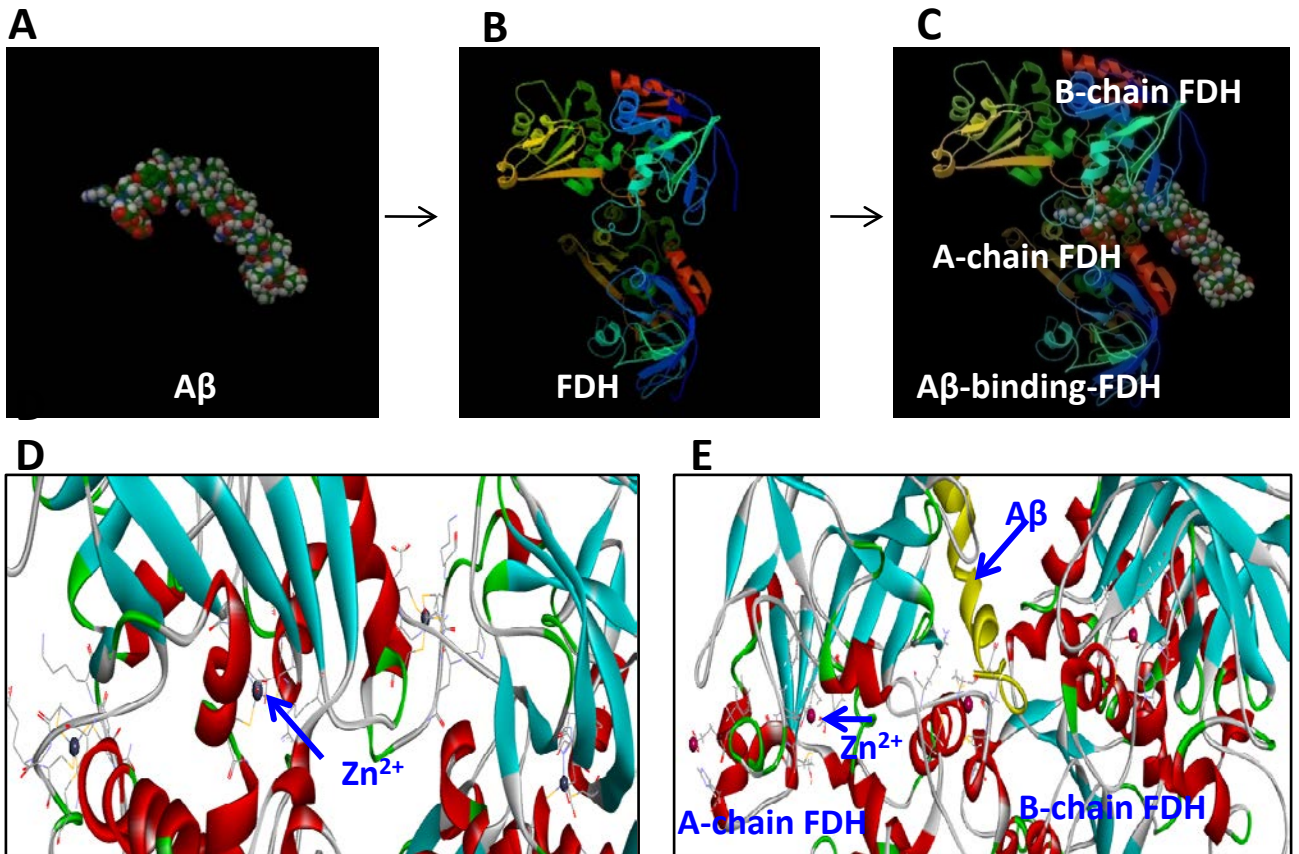
Supplementary Figure 3

Figure S3. Molecular simulation: Aβ-binding with FDH by using Autodock software. **A,** Human Aβ (PDB ID: 1Z0Q). **B,** human FDH (PDB ID: 1TEH). **C.** Aβ-binding with FDH. **D,** Zn^{2+} in the A and B chains of FDH. **E,** Aβ-binding with A and B chains of FDH by Hydrogen -bond connection. FDH: formaldehyde dehydrogenase
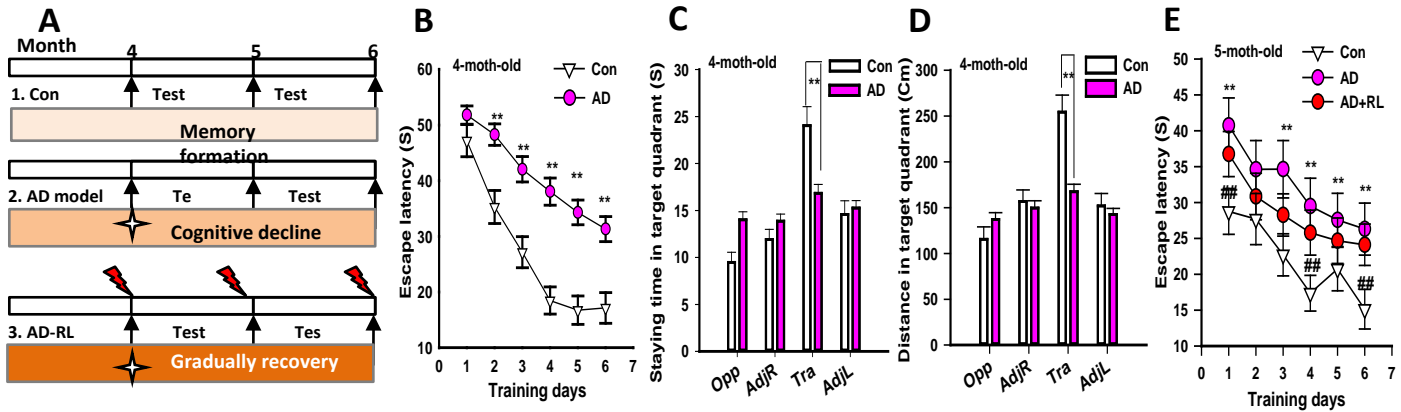
Supplementary Figure 4

Figure S4. The changes in spatial memory in APP/PS1 mice with or without 630-nm red light illumination.

(**A**) The time schedule for R-LED irradiation on the three groups' APP/PSI mice. (**B, C, D**) APP/PSI mice without red light treatment exhibited a longer escape latency, a shorter time and shorter swimming distance in target quadrant than healthy control mice (n = 10). (**E**) One-month R-LED irradiation on APP/PSI mice improved the ability of spatial learning in than APP/PSI mice without R-LED treatments (n = 10).
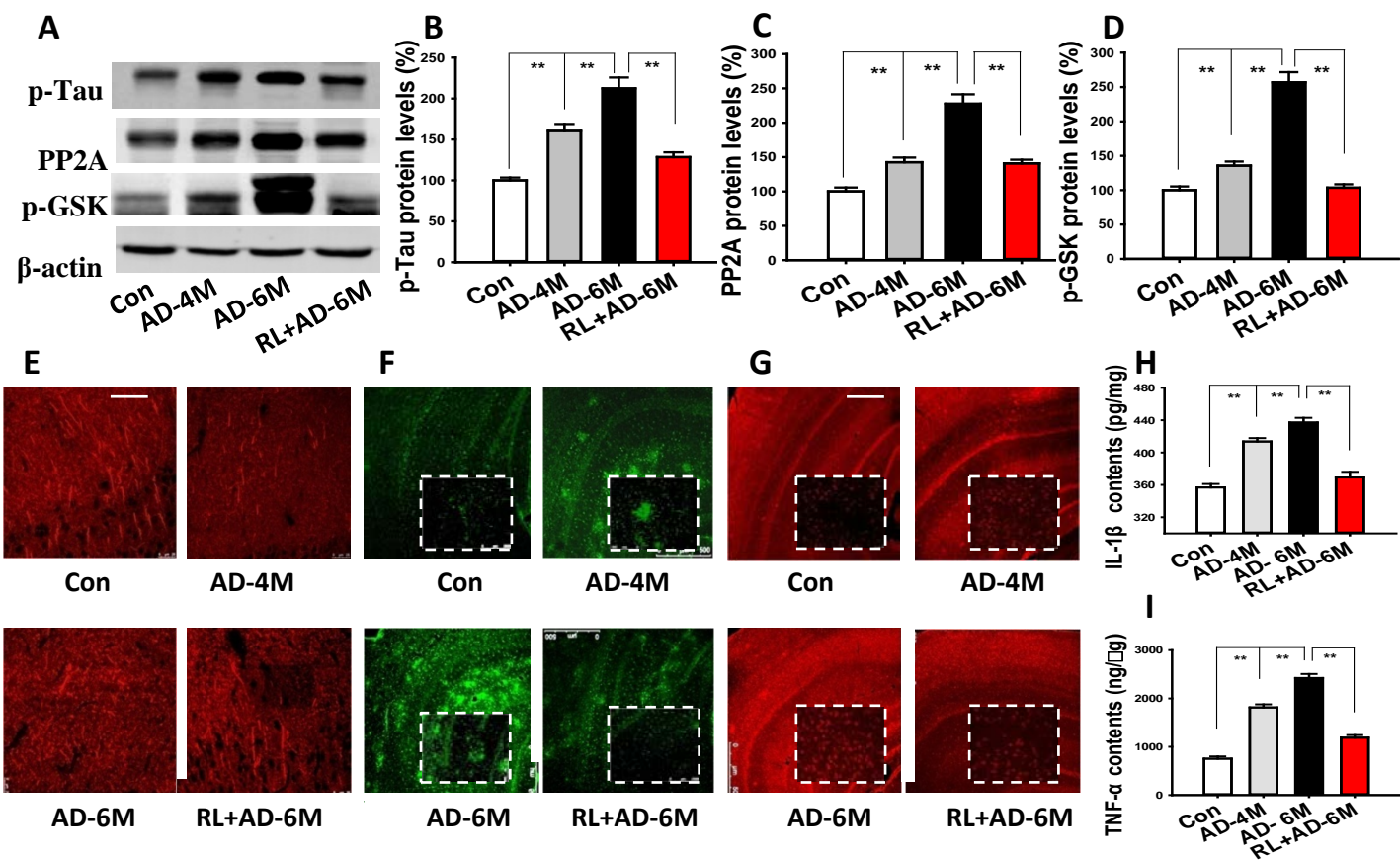
Supplementary Figure 5

Figure S5. Red light inhibits tau hyperphosphorylation and other AD-associated phenotypes in APP/PS1 transgenic mice**. A-D,** Representative Western blotting images (**A**) and quantification of the Alzheimer' disease-related proteins expression, Tau p-Tyr181 (**B**) PP2A (**C**), and GSKα/β p-Tyr279/216 (**D**) in these four groups of mice. Con: wild C57BL/6 mice; AD-4M: 4-month old APP/PS1 mice; AD-6M: 6-month old APP/PS1 mice; RL+AD-6M: 6-month old APP/PS1 mice with 2-month RL illumination. (n =6-9 mice each). **E-G,** Representative immunohistochemical images depicting the synapse expression strained by MAP2 antibody (**E**), the over-proliferation of astrocytes strained by GFAP antibody (**F**) and microglia stained by CD45 antibody (**G**) in the hippocampus and cortex. Scale bar, 500 μm. n=3-6 sections from 3-4 mice each. **H, I,** Quantitative assessment of brain IL-β levels (**H**) and TNFα (**I**) detected by ELISA kits (n = 8). ** $p < 0.01$; values are mean ± SEM.

Supplementary Figure 6

A

B 630 nm red light penetration into 1.2 cm skull   **C** 630 nm red light penetrating 4 cm meat
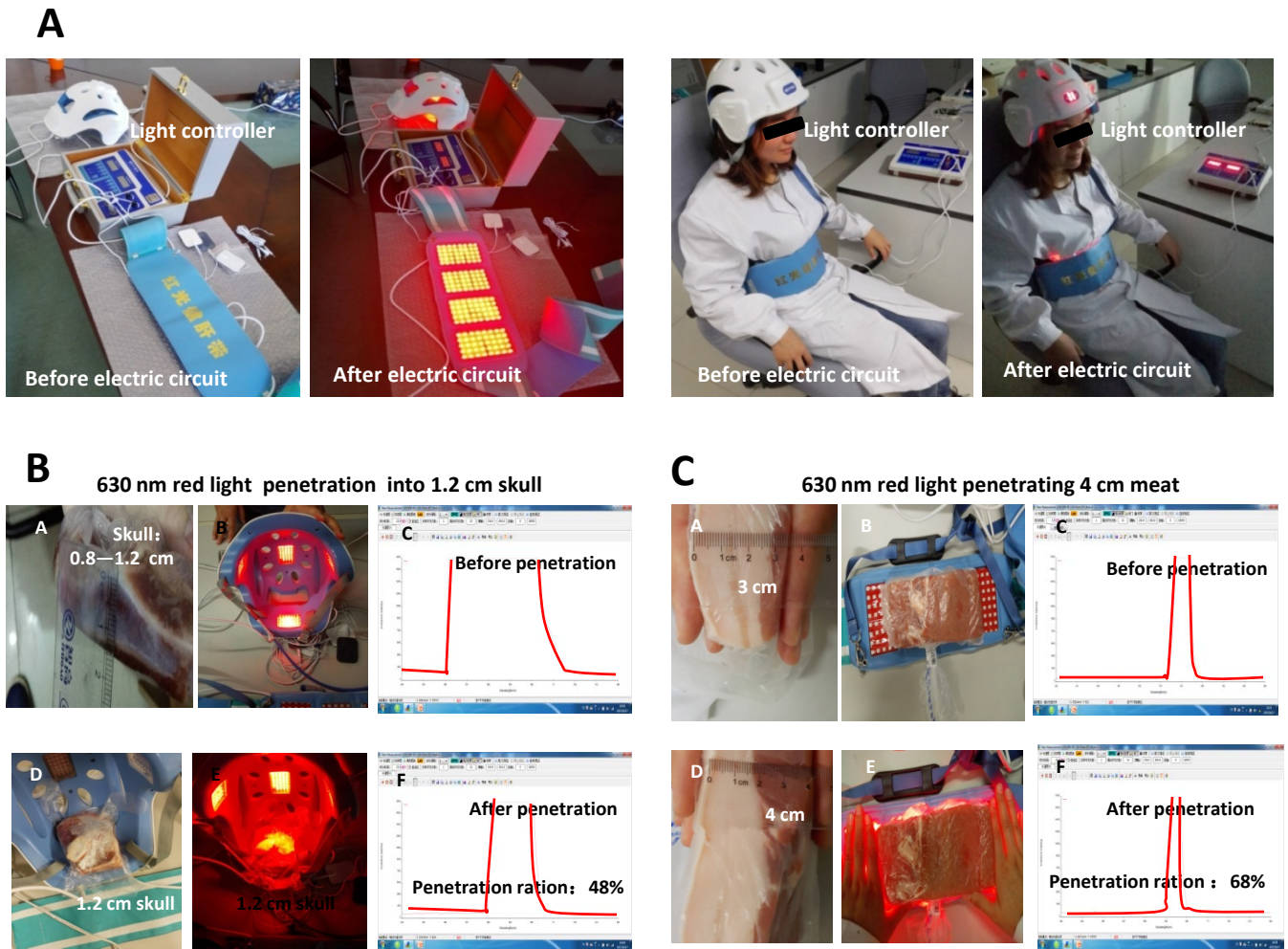

Figure S6. Red light at 630 nm penetrates into 1.2 cm skull and 1.5 cm abdomen which mimicked human samples. **A,** The LED-red light device before or after electric circuit. **B,** The mean thickness of human skull is about 1 cm. A skull with 1.2 cm thickness was selected to be illuminated, and 630 nm-red light can penetrate it with ~48% penetration ratio. **C,** The mean thickness of human abdomen is about 1.5 cm. A piece of meat with 3~4 cm thickness was illuminated, and 630 nm-red light can penetrate it with ~68% penetration ratio.