

Description of Additional Supplementary Files

Supplementary Movie 1-3

ER ballooning in genome-edited iPSC-derived homozygous AD mutant neurons

Red: ER-tracker, staining the ER. Mutant AD-iPSCs carry the APP KM670/671NL mutation, which was made by genome editing from normal iPSCs. Therefore, the backgrounds of the three lines of iPS cells were identical.

- (1) Normal iPSC-derived neurons
- (2) Heterozygous mutant AD-iPSC-derived neurons
- (3) Homozygous mutant AD-iPSC-derived neurons

Supplementary Movie 4-6

Chronological and spatial relationships between intracellular A β and YAP

Red: NucRed, staining of the nucleus; green: EGFP-YAPdeltaC, staining of YAPdeltaC; blue: BTA1, staining of intracellular A β .

- (4) Homozygous mutant AD-iPSC-derived neurons
- (5) Heterozygous mutant AD-iPSC-derived neurons
- (6) Heterozygous mutant AD-iPSC-derived neurons

Supplementary Movie 7-18

Necrosis after ER ballooning in genome-edited iPSC-derived homozygous AD mutant neurons

Red: ER-tracker, staining the ER; green: BTA1, staining intracellular A β . Mutant AD-iPSCs carry the APP KM670/671NL mutation, which was made by genome editing from normal iPSCs. Therefore, the backgrounds of the three lines of iPS cells were identical.

- (7) Normal iPSC-derived neurons before treatment
- (8) Heterozygous mutant AD-iPSC-derived neurons before treatment
- (9) Homozygous mutant AD-iPSC-derived neurons before treatment
- (10) Normal iPSC-derived neurons after S1P treatment
- (11) Heterozygous mutant AD-iPSC-derived neurons after S1P treatment
- (12) Homozygous mutant AD-iPSC-derived neurons after S1P treatment
- (13) Normal iPSC-derived neurons after AAV-YAPdeltaC infection
- (14) Heterozygous mutant AD-iPSC-derived neurons after AAV-YAPdeltaC infection
- (15) Homozygous mutant AD-iPSC-derived neurons after AAV-YAPdeltaC infection
- (16) Normal iPSC-derived neurons after AAV-NINS infection (negative control)
- (17) Heterozygous mutant AD-iPSC-derived neurons after AAV-NINS infection (negative control)
- (18) Homozygous mutant AD-iPSC-derived neurons after AAV-NINS infection (negative control)