

Supplemental Figures

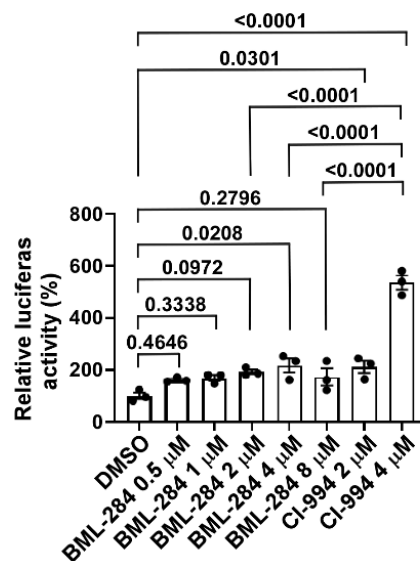


Fig. S1. Comparison of Wnt/ β -catenin signaling activation by CI-994 and BML-284.

Wnt reporter assay in Wnt3A-expressing HEK293 cells with the treatment of CI-994 and BML-284 at indicated concentrations for 24 h. All the values are mean $\pm$ SEM of triplicate determinations. *P* values were calculated using one-way ANOVA with Tukey's multiple comparison test.

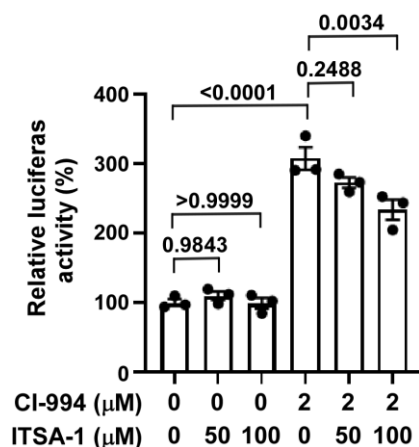


Fig. S2. ITSA-1 attenuates Wnt/ β -catenin signaling induced by CI-994. Wnt reporter

assay in Wnt3A-expressing HEK293 cells with the treatment of CI-994 and ITSA-1 at

indicated concentrations for 24 h. All the values are mean $\pm$ SEM of triplicate determinations. *P* values were calculated using one-way ANOVA with Tukey's multiple comparison test.

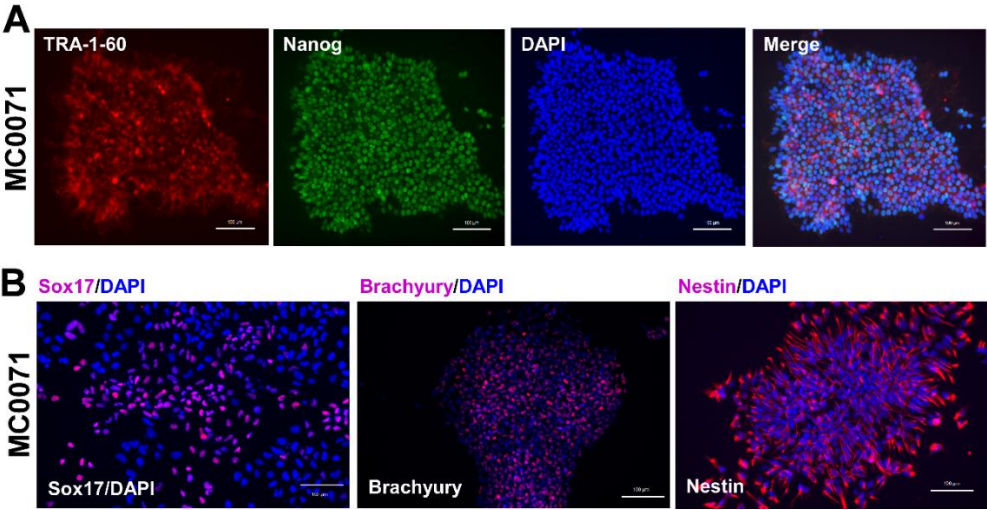


Fig. S3. The pluripotency of the iPSC line MC0071. (A) Immunostaining of pluripotency markers (TRA-1-60 and Nanog) in iPSC line MC0071 carrying MAPT P301L mutation and MC0127 carrying PSEN1 M146V mutation. (B) *In vitro* differentiation of iPSC line MC0071 into cells of all three germ layers. Cells were for Sox17 (endoderm), Brachyury (mesoderm), Nestin (ectoderm), and DAPI (nucleus). Scale bar:100 μ m.

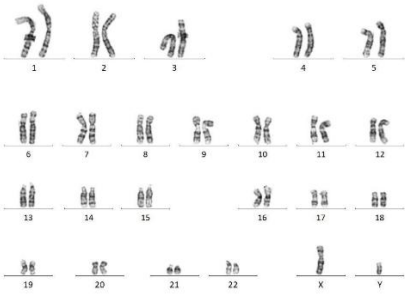


Fig. S4. Karyotyping analysis of the iPSC line MC0071.

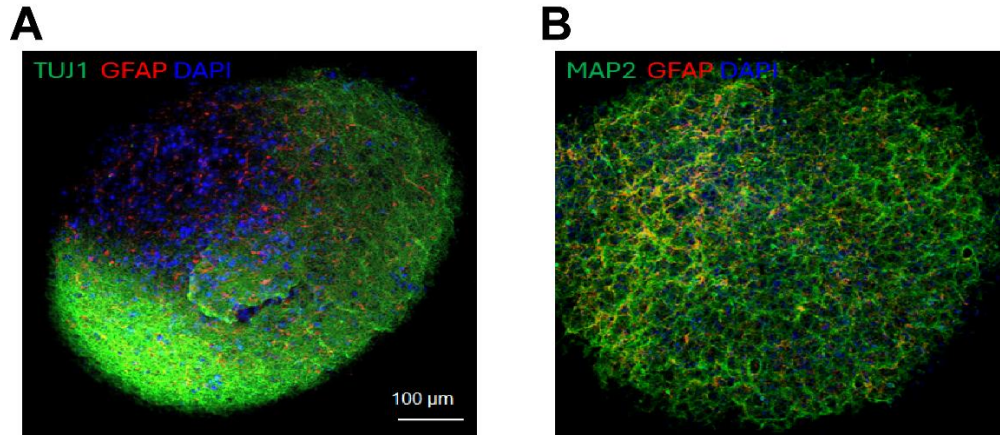


Fig. S5. Characterization of cerebral organoids Patient-specific iPSC-derived cerebral organoids carrying *APOE* $\epsilon 4/\epsilon 4$ (MC0020) (A) or *APOE* $\epsilon 3/\epsilon 3$ and *MAPT* p.P301L mutation (B) at 3 months of age were fixed with 4% paraformaldehyde (PFA) at 4°C overnight and then permeabilized with 0.25% Triton-X 100 in phosphate-buffered saline (PBS) for 15 min. Organoids were blocked with 3% bovine serum albumin (BSA) and incubated with primary antibodies against neuronal marker Tuj1 (T8578, Sigma), neuronal marker MAP2 (AB2290A4, Sigma) and astrocytic marker GFAP (N206A/8, Antibodies Inc.) at 4°C overnight. After washing with PBS, organoids were incubated with secondary antibodies (A11001 and A11041, ThermoFisher Scientific) and DAPI for 2 h. Images were captured by the Zeiss LSM 880 confocal microscope (Leica Biosystems).