

Figure S1

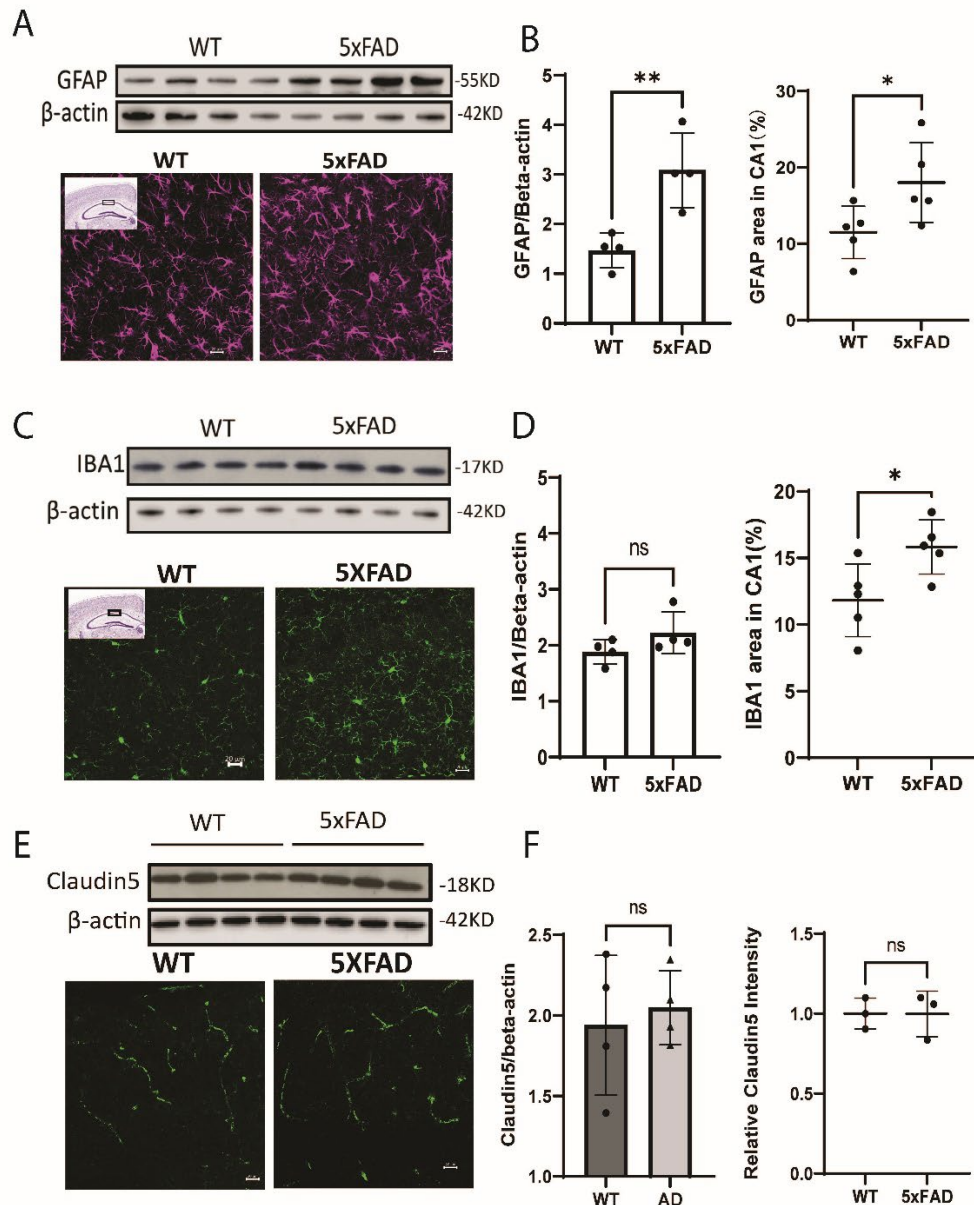


Figure S1. Gliosis is detected in 3 months old 5XFAD mice. (A) GFAP Western blots and representative immunofluorescent images reveal astrogliosis in the hippocampus of 3 months old 5XFAD. (B) Quantification of GFAP protein levels from Western blots shows a significant increase in 5XFAD mice compared to controls, $n=4$. (** $p < 0.01$, Student's t-test). (C) Western blots and immunofluorescent staining of the microglial marker IBA1 indicate activated microglia morphology in 5XFAD mice. (D) Quantification of IBA1 protein levels between AD and control mice. $n=4$. (E) Western blot analysis and immunofluorescent staining of the tight junction protein Claudin 5 indicate alterations in BBB integrity in 5XFAD mice. (F) Quantification of Claudin 5 protein levels from the Western blots. $n=4$. Statistical analysis confirms no significant changes (ns, Student's t-test).

Figure S2

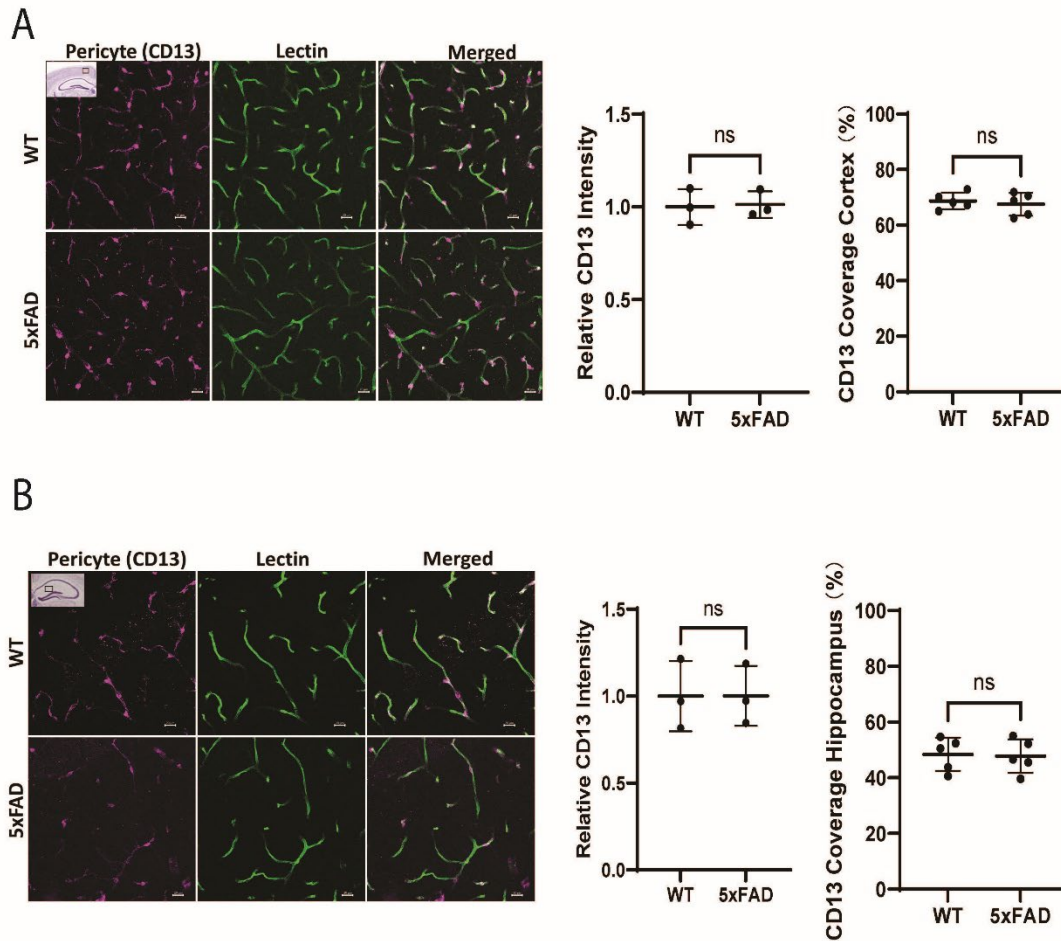
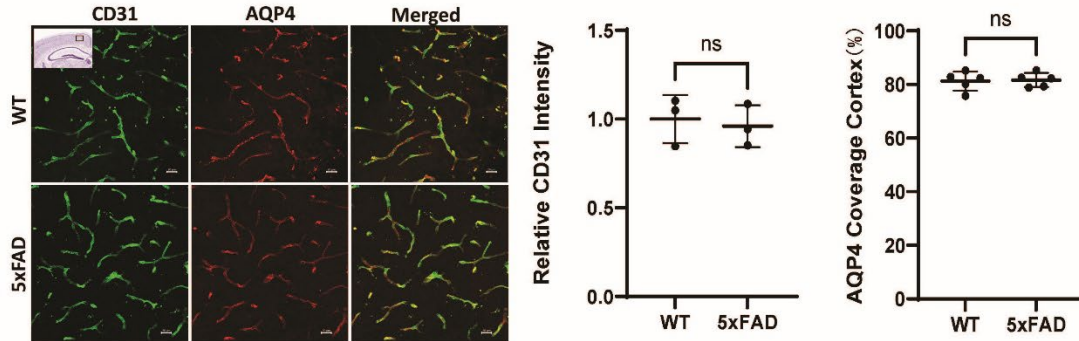


Figure S2. Preservation of pericyte intensity in 3 months old 5XFAD mice. (A) Representative immunofluorescent staining of the pericyte marker protein CD13, alongside the vascular marker lectin, shows no significant difference in CD13 fluorescence intensity or coverage in the cerebral cortex of 5XFAD mice compared to controls. $n=3$. (B) Representative immunofluorescent staining and quantification of CD13 fluorescence intensity and coverage in the hippocampus show no significant difference between the two groups. $n=3$. Statistical analysis confirms no significant changes (ns, Student's t-test).

Figure S3

A



B

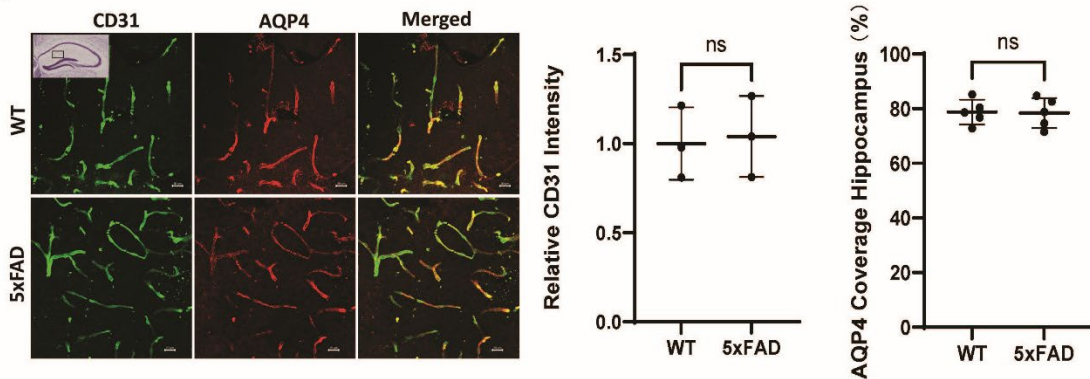
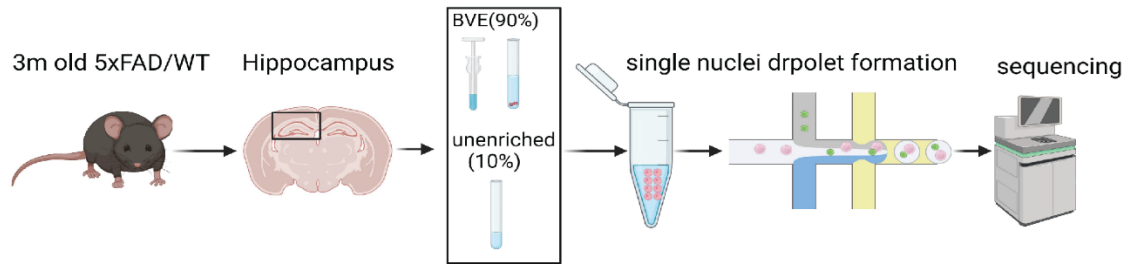


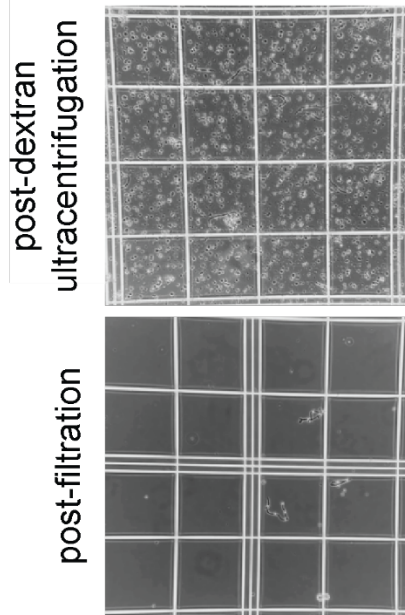
Figure S3. Preservation of endothelial cell intensity and AQP4 polarization in 3 months old 5XFAD mice. (A) Representative immunofluorescent staining of the endothelial marker protein CD31 and the water channel protein AQP4 shows no significant difference in fluorescence intensity in the cerebral cortex of 5XFAD mice compared to controls. $n=3$. (B) Representative immunofluorescent staining and quantification of CD31 and AQP4 fluorescence intensity in the hippocampus show no significant difference between groups. $n=3$. Statistical analysis confirms no significant changes (ns, Student's t-test).

A



B

Blood vessel enrichment



C

qPCR following blood vessel enrichment

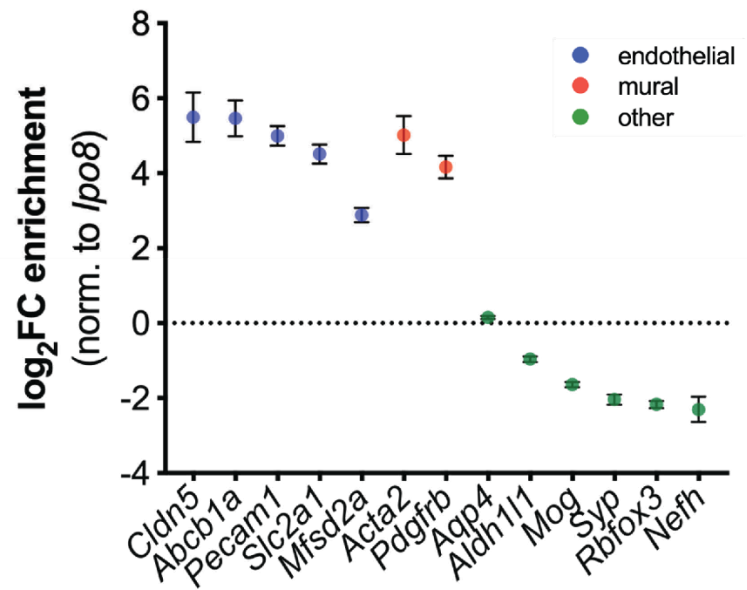


Figure S4. Optimized blood vessel enrichment protocol. (A) Schematic representation of the single-nucleus RNA sequencing (snRNA-Seq) workflow used to analyze the mouse hippocampus. (B) Representative images of mouse cortex homogenates following dextran ultracentrifugation and filtration. Blood vessels are visibly enriched. (C) Quantitative PCR (qPCR) results on n=3 samples of flash-frozen mouse cortex.

Figure S5

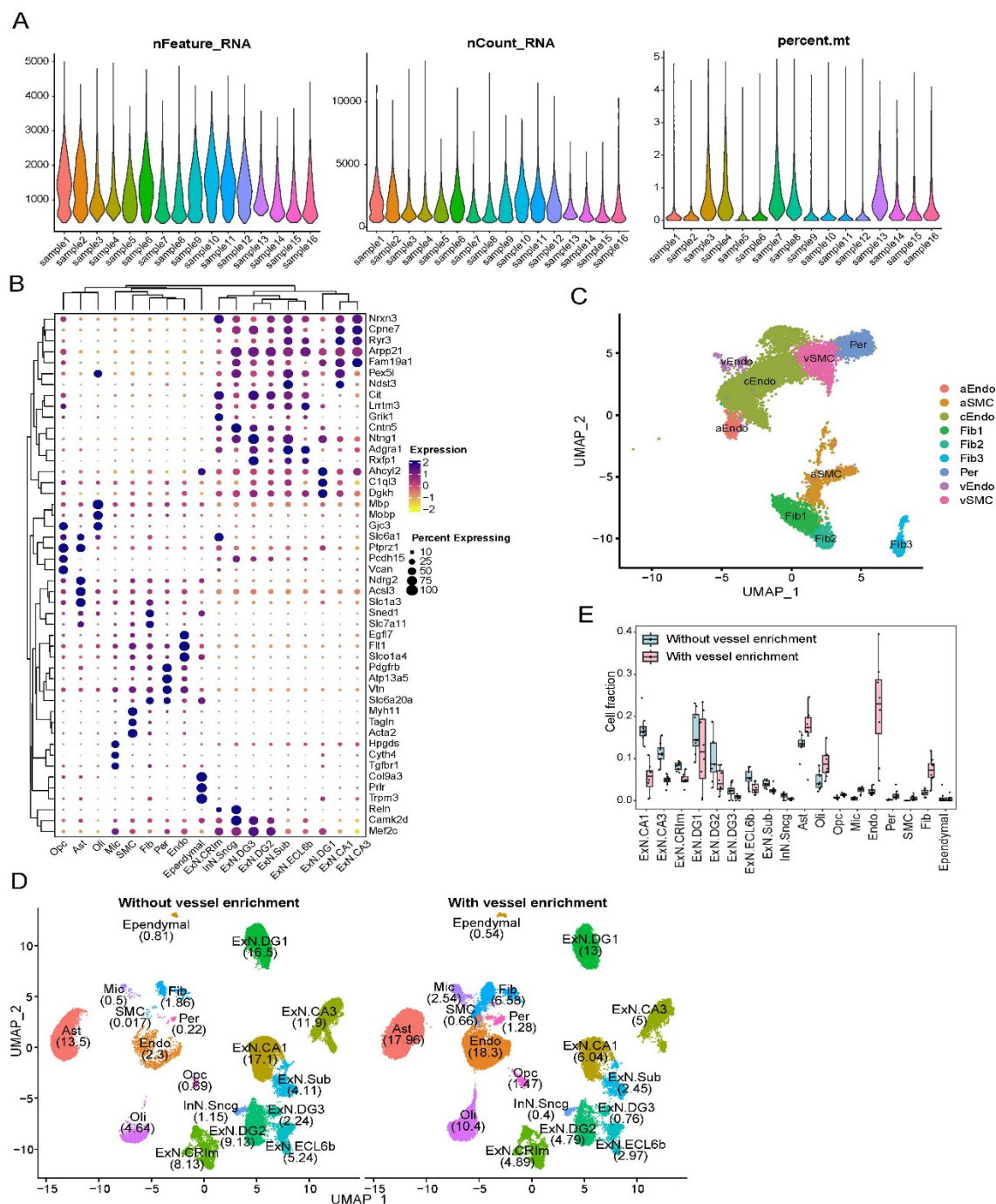


Figure S5. Transcriptional profiling of the hippocampus in 3 months old 5xFAD mice at single-cell resolution. (A) Quality metrics. (B) marker genes for different cell type indicated. (C) UMAP plot visualizing vascular single nuclei annotated by subtypes. (D) UMAP visualization comparing conditions with (left) or without (right) blood vessel enrichment with cell type percentages included. (E) Cell proportion analysis indicates significant fractional differences in cell type proportions between conditions (with and without vessel enrichment).

Figure S6

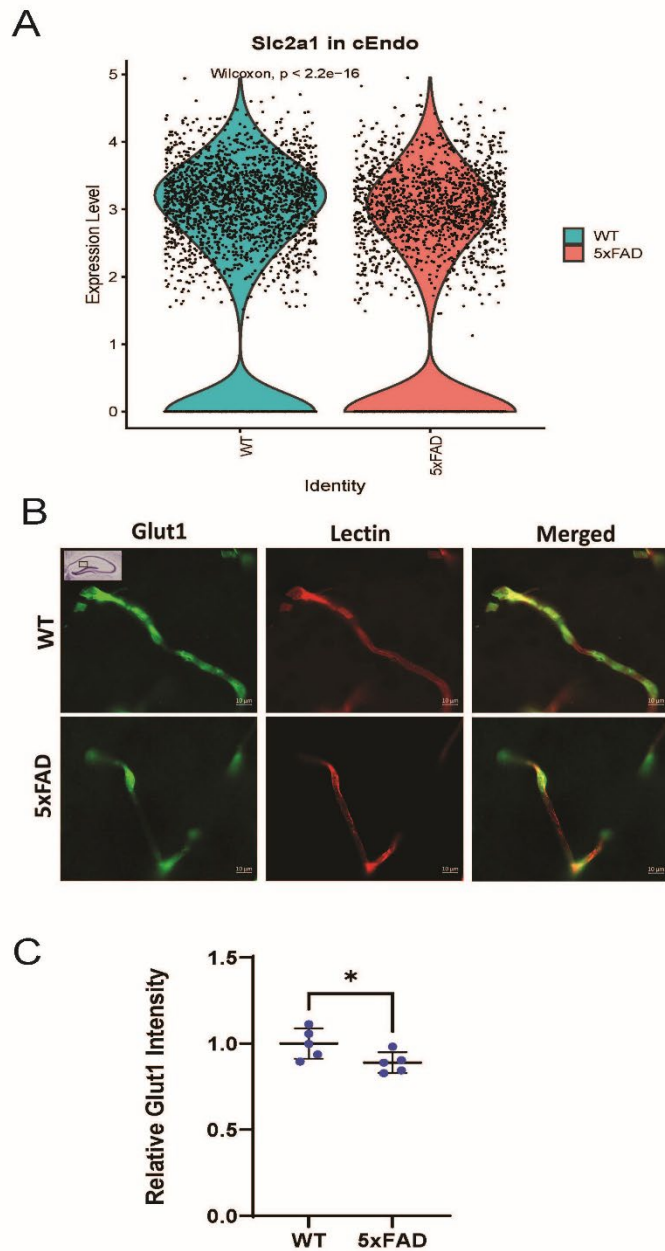


Figure S6. Validation of downregulated Slc2a1 in the blood vessel of 3 months old 5XFAD mice. (A) Violin plot shows the significantly reduced mRNA levels of Slc2a1 in the capillary endothelial cells of the hippocampus in 3-month-old 5XFAD mice. (B) Representative immunofluorescent staining of GLUT1, encoded by Slc2a1, demonstrates a decrease in this glucose transporter within cerebral blood vessels of the hippocampus in 3-month-old 5XFAD mice. (C) Quantification of the immunofluorescent intensity of Glut1 (left panel) and Lectin (right panel) in the hippocampal blood vessels. $n = 5$. * $p < 0.05$ by two-tailed Student's t-test.