

Supplementary Figures

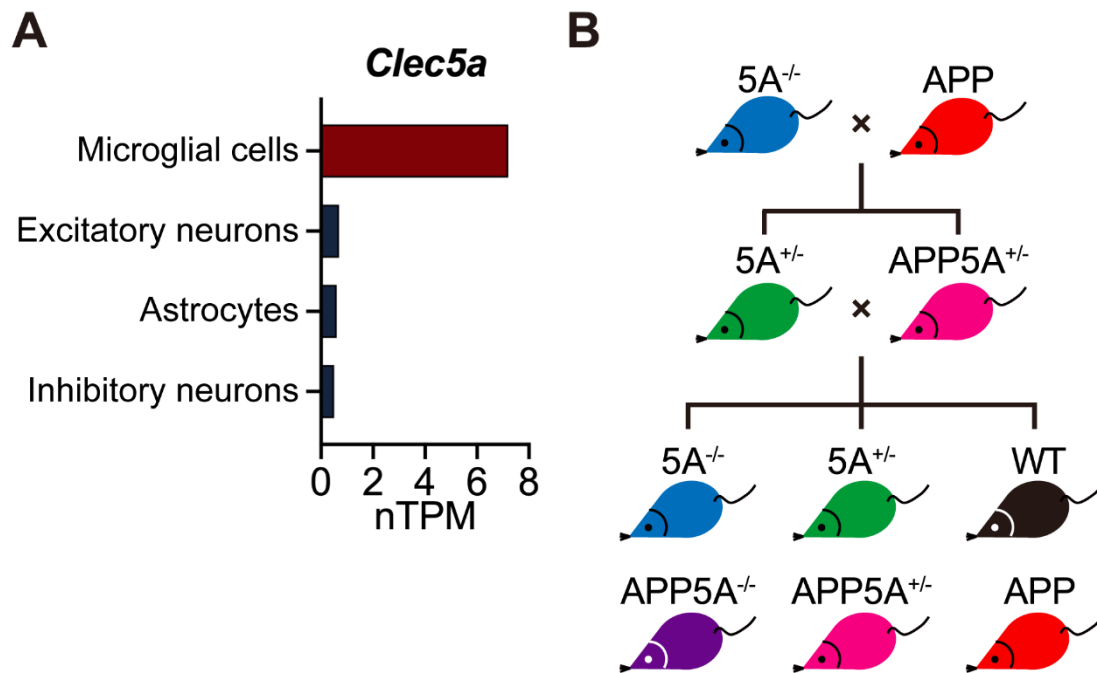


Figure S1. (A) The *Clec5a* is mainly expressed in microglial cells in the mouse brain based on the online database, The Human Protein Atlas, Protein Atlas version 23.0 (proteintlas.org). **(B)** Breeding schematic to generate APP mice with *Clec5a* knockout and other 5 genotypes of littermate controls.

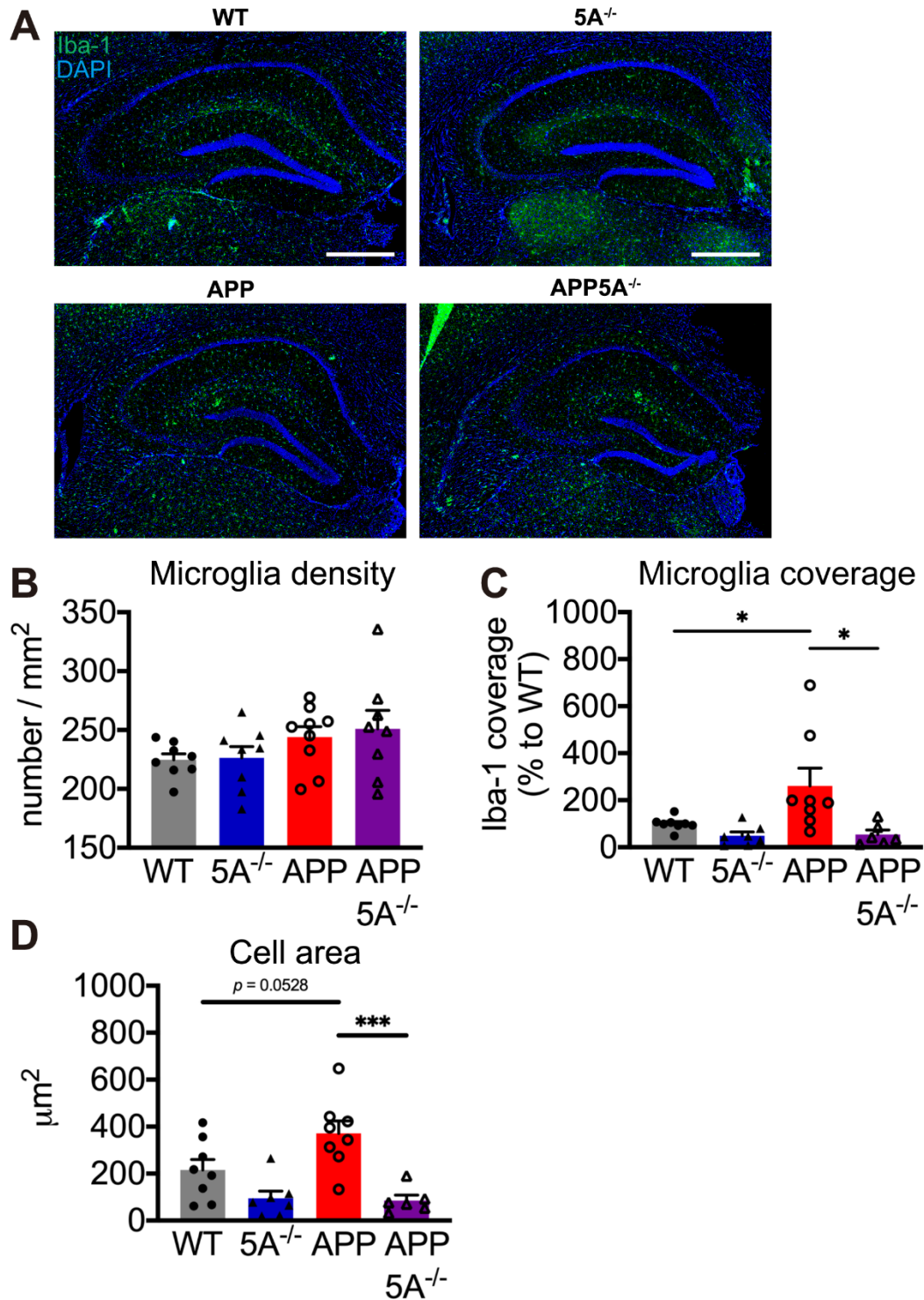


Figure S2. The *Clec5a* knockout altered the microglial coverage and cell size, but not cell density, in the hippocampus. **(A)** The representative images of hippocampal sections staining with Iba-1 staining (green) and DAPI (blue). Scale bar: 500 μ m. **(B)** The microglia density in the hippocampus was calculated as number/mm². **(C)** The microglia coverage was calculated as the Iba-1⁺ area normalized to the hippocampus area. The result in the WT group was set as 100. **(D)** The average area of each microglia in the hippocampus. n = 8-14 slices per mouse and 7-9 mice for each genotype. * $p \leq 0.05$, *** $p \leq 0.001$.

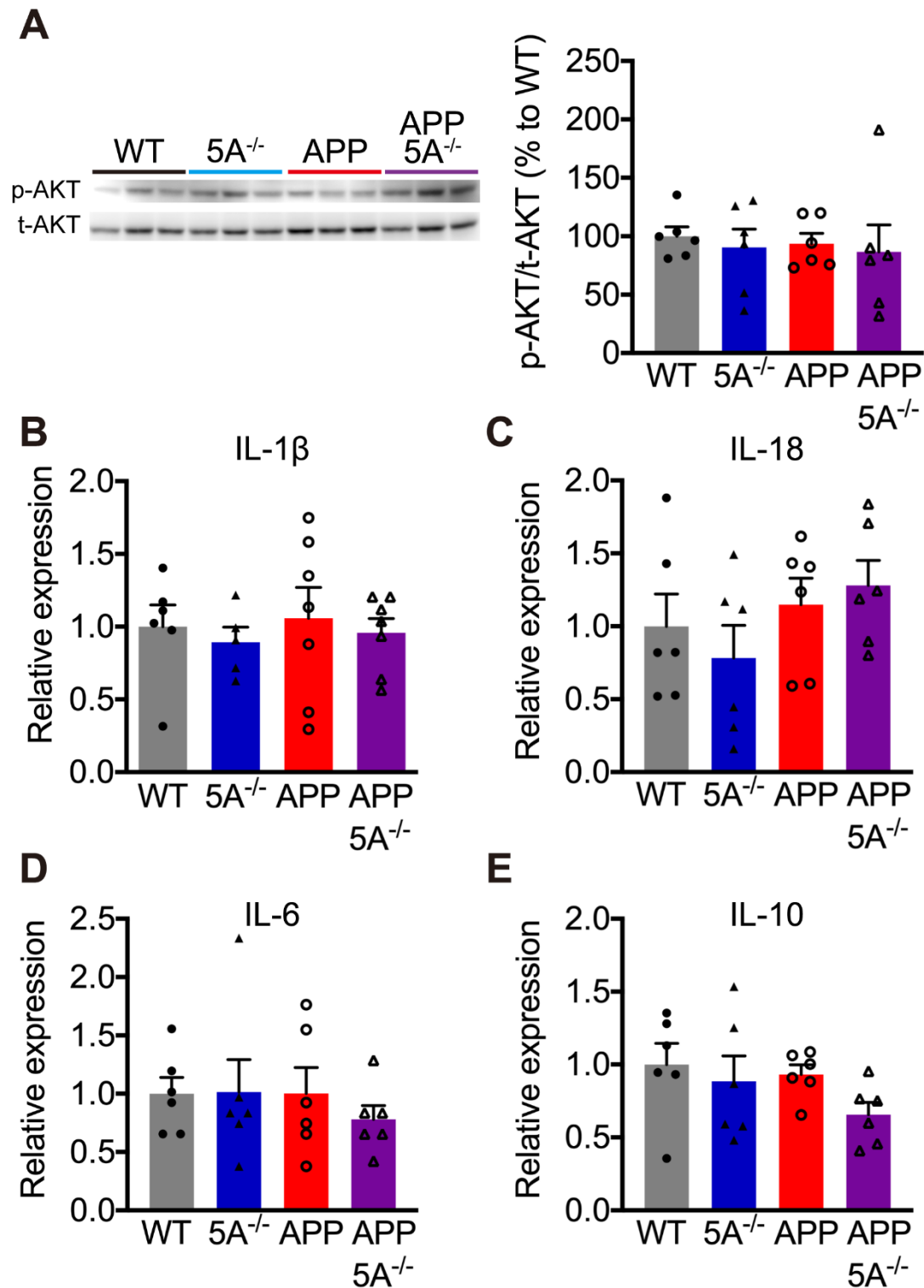


Figure S3. The AKT activation and inflammatory cytokines were not altered in *Clec5a* knockout mice. **(A)** The AKT phosphorylation was measured by western blotting. The activity of AKT was calculated by the ratio of p-AKT to t-AKT. $n = 6$ mice for each genotype. **(B)** The IL-1 β protein level in mice hippocampus was measured by ELISA and normalized to the WT group. $n = 5-7$ mice for each genotype. **(C-E)** The protein levels of IL-18 **(C)**, IL-6 **(D)**, and IL-10 **(E)** were measured by the Multi-Plex immunoassay. $n = 6$ mice for each genotype.

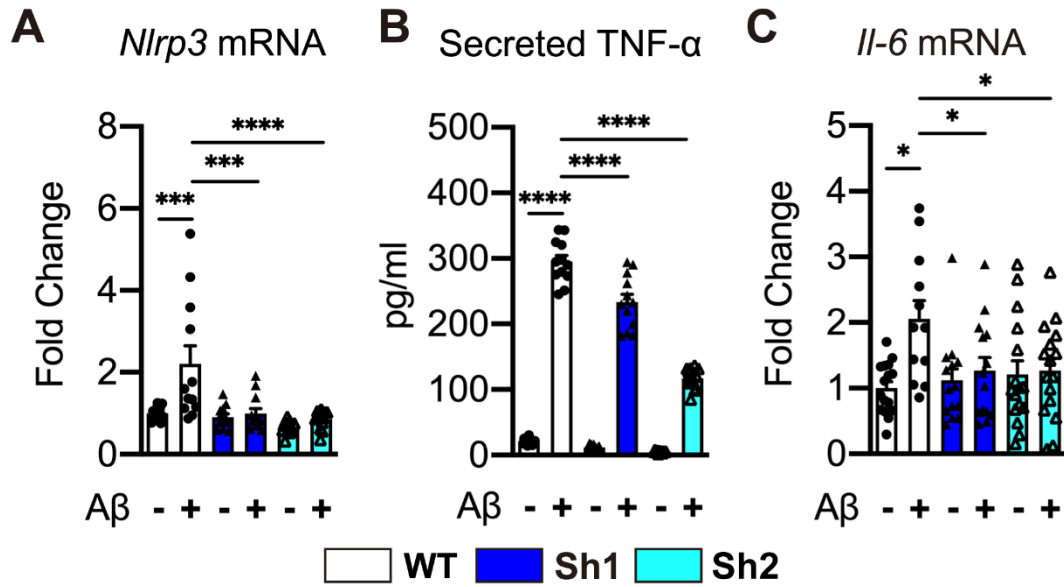


Figure S4. *Clec5a* knockdown decreases the A β -induced inflammatory signals in BV2 microglial cells. The BV2 cells (WT, Sh1, Sh2) were treated with or without oA β for 24 hours. **(A)** The mRNA level of *Nlrp3* in the treated cells was analyzed by qPCR. n = 12-16 wells from 4 independent experiments in each group. **(B)** The level of TNF- α secreted from the cells was examined by ELISA. n = 12 wells from 3 independent experiments in each group. **(C)** The mRNA level of *Il-6* in the treated cells was analyzed by qPCR. n = 12-16 wells from 4 independent experiments in each group. All data were normalized to the WT without oA β treatment group. * $p \leq 0.05$, *** $p \leq 0.001$, **** $p \leq 0.0001$.