

## Supporting information for

### TMEM16F exacerbates tau pathology and mediates phosphatidylserine exposure in phospho-tau-burdened neurons

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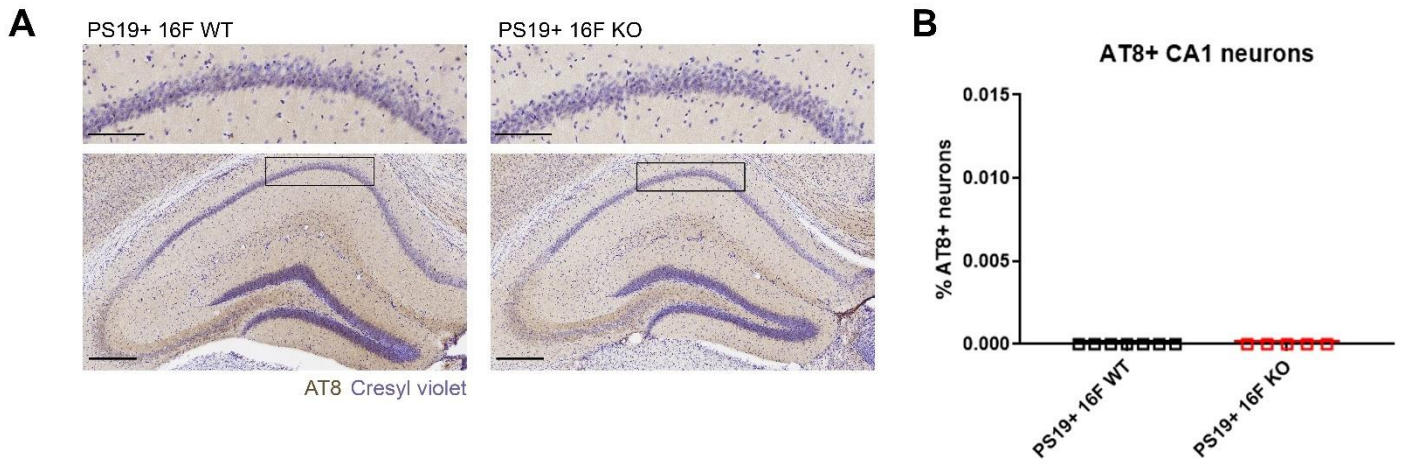
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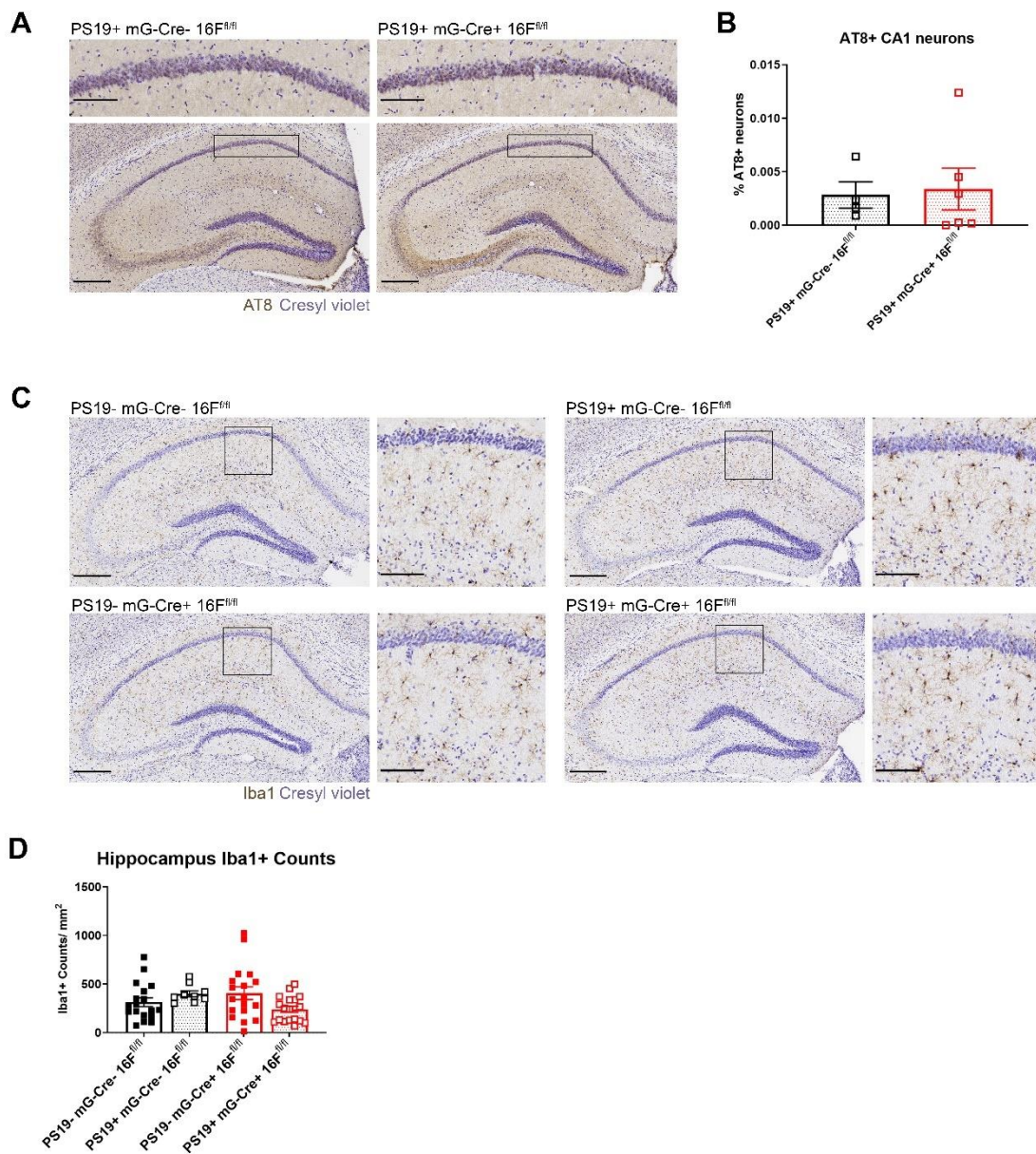
Figures S1 to S2



**Figure S1. Hyperphosphorylated tau pathology was not detectable in 3-month-old TMEM16F knockout mice.**

(A) Representative images of AT8 immunostaining of hyperphosphorylated tau in the hippocampus and CA1 (*Inset*) in 3-mo-old PS19+ TMEM16F WT (16F WT) and TMEM16F KO (16F KO) mice. Cresyl violet, neuronal counterstain. (Scale bar, 300  $\mu$ m for hippocampus and 100  $\mu$ m for *Inset*.)

(B) Quantification of AT8+ neurons within CA1 pyramidal layer in PS19+ WT, n = 7 and PS19+ KO mice, n = 5; 1 hippocampal section/mouse.



**Figure S2. 6-month-old microglial conditional TMEM16F knockout mice without detectable pathology.**

(A) Representative images of AT8 immunostaining of hyperphosphorylated tau in the hippocampus and CA1 (*Inset*) in 6-mo-old PS19+ microglial TMEM16F WT (mG-Cre- 16F<sup>fl/fl</sup>) and microglial TMEM16F conditional knockout mice (mG-Cre+ 16F<sup>fl/fl</sup>). Cresyl violet, neuronal counterstain. (Scale bar, 300  $\mu$ m for hippocampus and 100  $\mu$ m for *Inset*.)

(B) Quantification of AT8+ neurons within CA1 pyramidal layer in PS19+ mG-Cre- 16F<sup>fl/fl</sup>, n = 3 and PS19+ mG-Cre+ 16F<sup>fl/fl</sup> mice, n = 3; 3 to 4 hippocampal sections/mouse. ( $P = 0.7619$ , Mann-Whitney test). Error bars in SEM.

(C) Representative images of Iba1 immunostaining of microglia in the hippocampus and CA1 (*Inset*) of 6-mo-old PS19- mG-Cre- 16F<sup>fl/fl</sup>, PS19- mG-Cre+ 16F<sup>fl/fl</sup>, PS19+ mG-Cre- 16F<sup>fl/fl</sup>, and PS19+ mG-Cre+ 16F<sup>fl/fl</sup> mice. Cresyl violet, neuronal counterstain. (Scale bar, 300  $\mu$ m for hippocampus and 100  $\mu$ m for *Inset*.)

(D) Quantification of number of microglia per area (count/mm<sup>2</sup>) in the hippocampus of 6-mo-old PS19- mG-Cre- 16F<sup>fl/fl</sup>, PS19- mG-Cre+ 16F<sup>fl/fl</sup>, PS19+ mG-Cre- 16F<sup>fl/fl</sup>, and PS19+ mG-Cre+ 16F<sup>fl/fl</sup> mice, n = 4 – 5 per genotype, 3 regions of interest per mouse. (ns =  $P > 0.05$ , two-way ANOVA, Tukey's multiple comparisons test). Error bars in SEM.