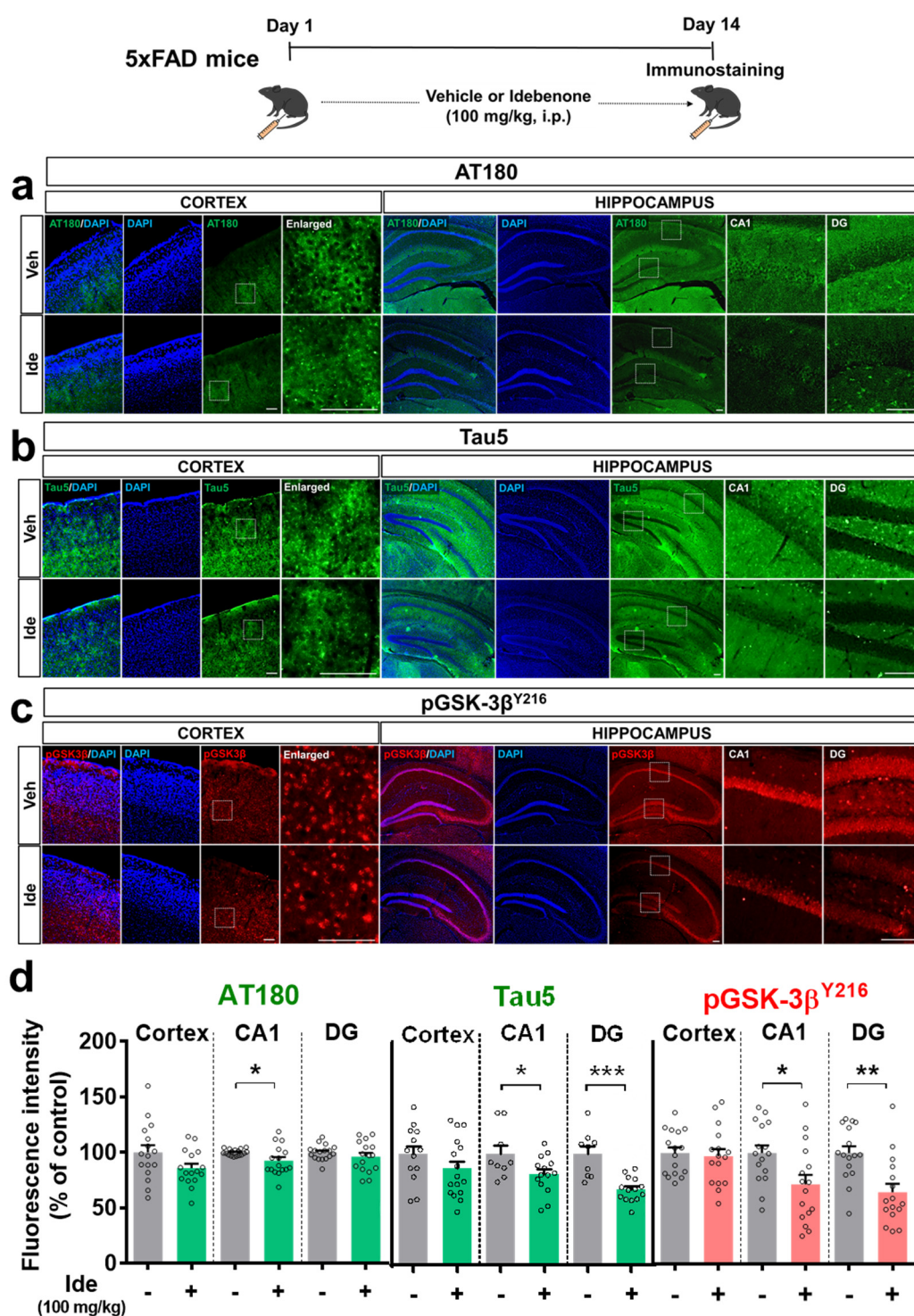
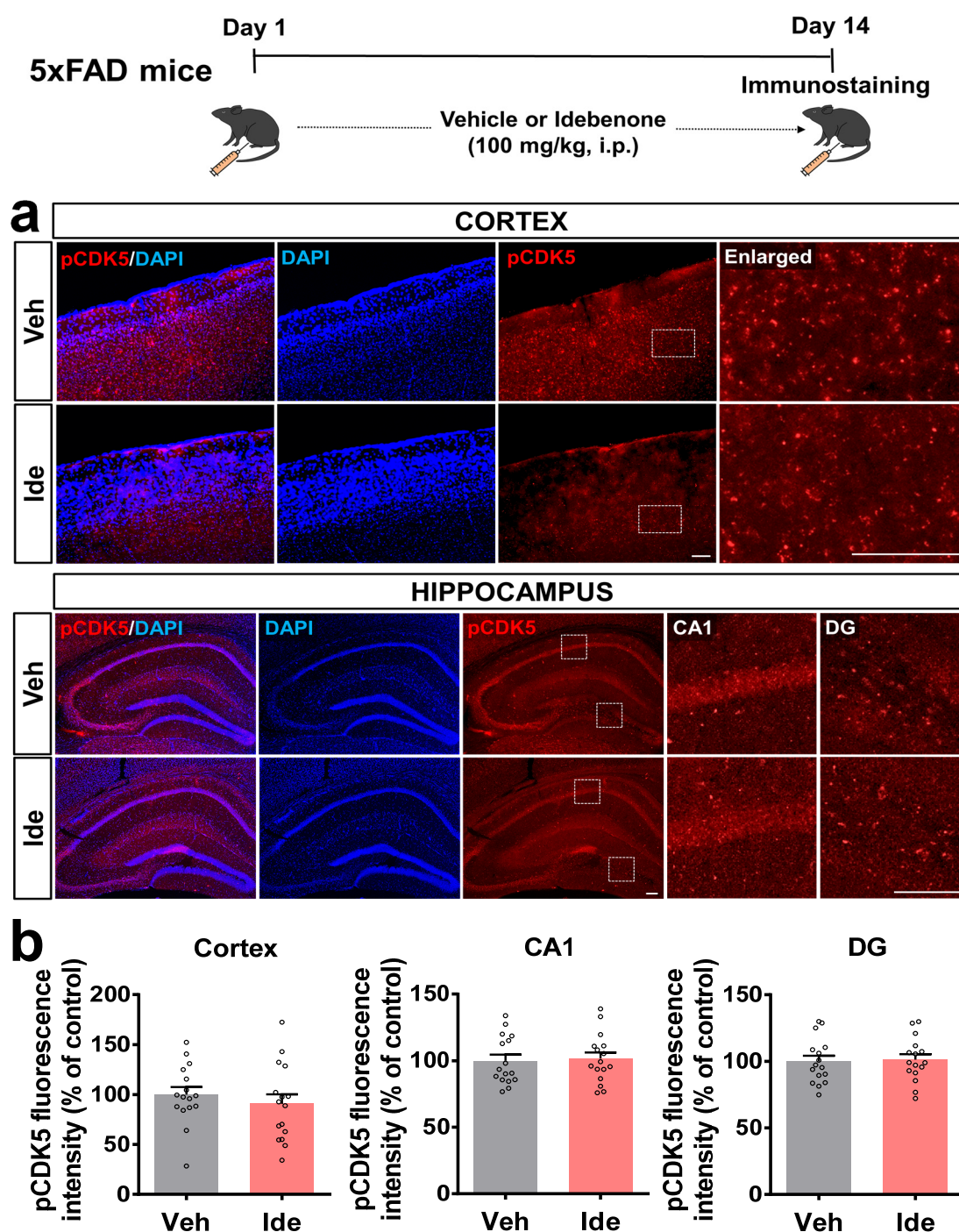


Supplementary

# Idebenone Decreases A $\beta$ Pathology by Modulating RAGE/Caspase-3 Signaling and the A $\beta$ Degradation Enzyme NEP in a Mouse Model of AD



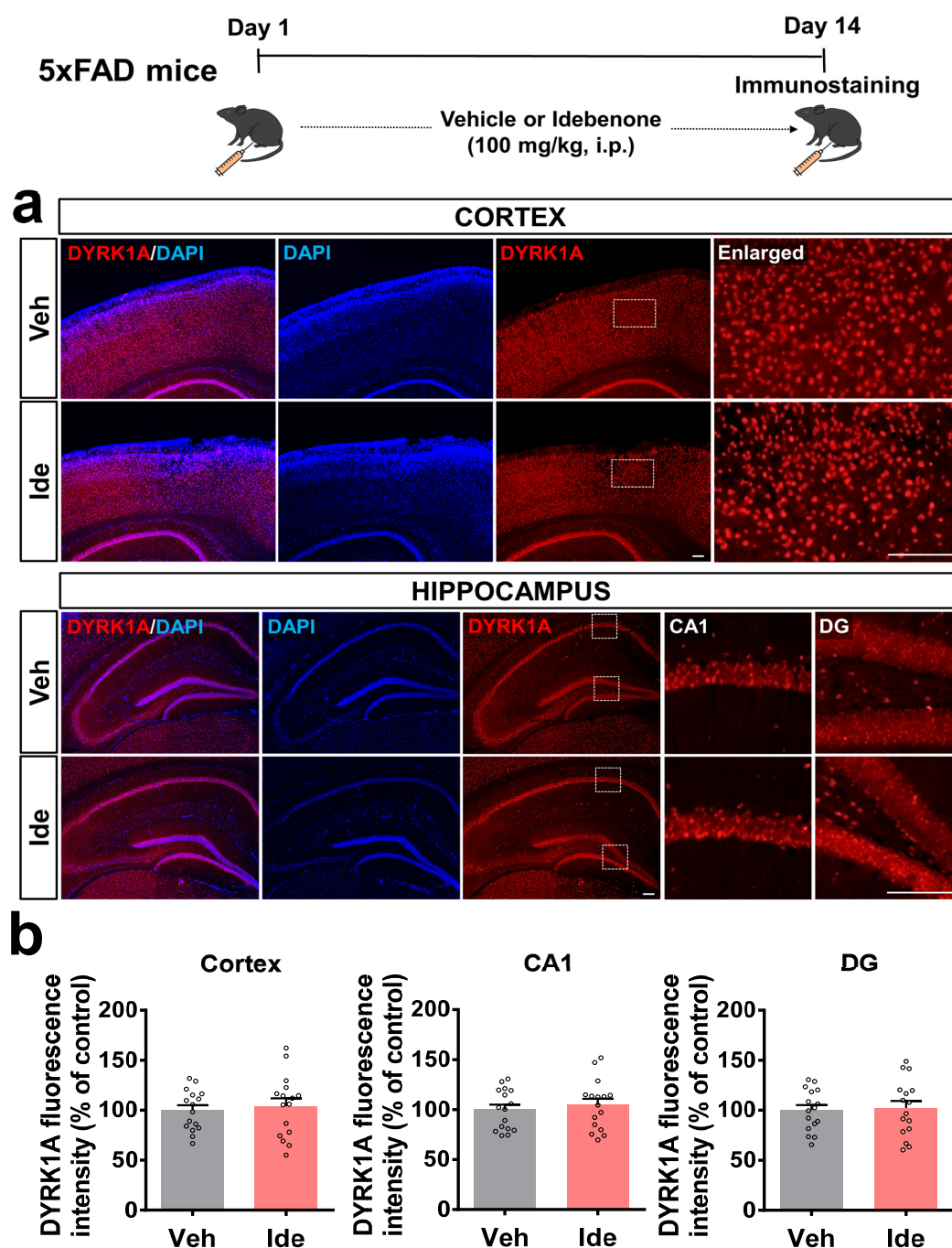
**Supplementary Figure S1.** Idebenone reduces tau phosphorylation at Thr231 (AT180) and tau kinase p-GSK3 $\beta$ <sup>Y216</sup> levels in a mouse model of AD. (a, b, c) Representative images of cortical and hippocampal AT180, Tau-5, and p-GSK3 $\beta$ <sup>Y216</sup> immunofluorescence staining. Idebenone or vehicle was administered daily to 3-month-old 5xFAD mice for 14 consecutive days as shown at the top of the figure. Immunostaining of brain sections with anti-AT180, anti-Tau-5, and anti-p-GSK3 $\beta$  were then performed. (d) Quantification of data from a-c (n = 16–17 brain slices from 4 mice/group for a, c; n = 9–16 brain slices from 3–4 mice/group for b). \*p < 0.05, \*\*p < 0.01 and \*\*\*p < 0.001 vs. vehicle-treated control. Scale bar = 100  $\mu$ m for cortex and 200  $\mu$ m for hippocampus.



**Supplementary Figure S2.** Idebenone does not alter tau kinase p-CDK5 levels in a mouse model of AD. (a) Representative images of cortical and hippocampal p-CDK5 immunofluorescent staining. Idebenone or



vehicle was administered daily to 3-month-old 5xFAD mice for 14 consecutive days as shown at the top of the figure. Immunostaining of brain sections with anti-p-CDK5 was then performed. (b) Quantification of data from a (n = 16 brain slices from 4 mice/group). Scale bar = 100  $\mu$ m for cortex and 200  $\mu$ m for hippocampus.



**Supplementary Figure S3. Idebenone does not affect tau kinase DYRK1A levels in a mouse model of AD.** (a) Representative images of cortical and hippocampal DYRK1A immunofluorescent staining. Idebenone or vehicle was administered daily to 3-month-old 5xFAD mice for 14 consecutive days as shown at the top of the figure. Immunostaining of brain sections with anti-DYRK1A was then performed. (b) Quantification of data from a (n = 16 brain slices from 4 mice/group). Scale bar = 100  $\mu$ m for cortex and 200  $\mu$ m for hippocampus.