

#### **Additional files: Supplementary Figure legends**

##### **Supplementary Fig. S1. Sirt2 is not expressed in GFAP-positive astrocytes in mouse hippocampus.**

(A) Brain sections were stained with anti-Sirt2 (red) and anti-GFAP (green) antibodies, and cell nuclei were stained with Hoechst. A representative image of the hippocampus is shown. Scale bar: 300  $\mu\text{m}$ . (B) The enlarged view of the white boxes in (A). Scale bar: 30  $\mu\text{m}$ .

##### **Supplementary Fig. S2. Sirt2 is expressed in NeuN-positive neurons, but not in GFAP-positive astrocytes in the cortex.**

(A) Brain sections were stained with anti-Sirt2 (red) and anti-NeuN (green) antibodies, and cell nuclei were stained with Hoechst. A representative image of the cortex is shown. Scale bar: 150  $\mu\text{m}$ . The enlarged view of the white boxes is shown in the right panel. Scale bar: 15  $\mu\text{m}$ . (B) Brain sections were stained with anti-Sirt2 (red) and anti-GFAP (green) antibodies, and cell nuclei were stained with Hoechst. A representative image of the cortex is shown. Scale bar: 150  $\mu\text{m}$ . The enlarged view of the white boxes is shown in the right panel. Scale bar: 15  $\mu\text{m}$ . (C) Mean fluorescence intensity of Sirt2-positive cells in the cortex ( $n = 8$  per group). All values are presented as the mean  $\pm$  SD,  $*p < 0.05$ , as determined by Student's  $t$ -test.

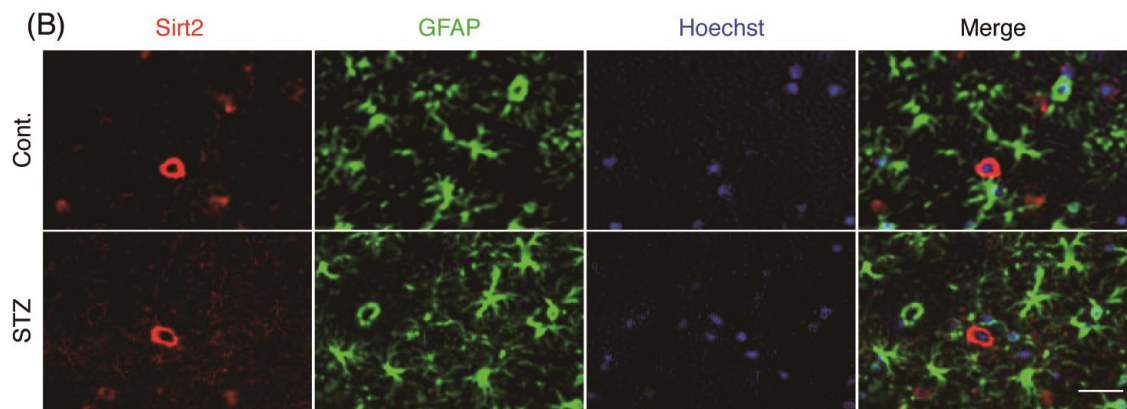
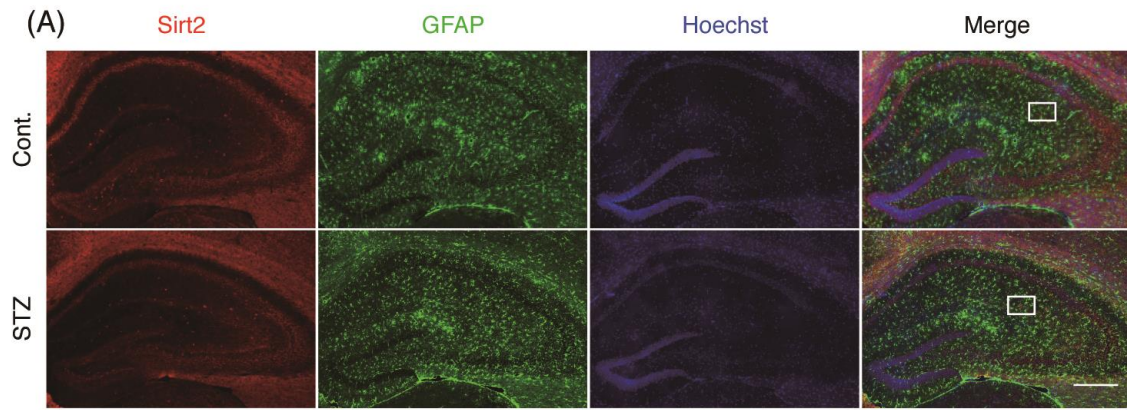
**Supplementary Fig. S3. Sirt2 regulates the phosphorylation levels of tau and ERK in Neuro2a cells.**

(A) Neuro2a cells were transfected with mock control or Sirt2 vector for 48 h before lysis. (B) Neuro2a cells were transfected with the control or Sirt2 siRNA for 72 h before lysis. Protein levels were determined by western blotting and quantified by densitometry. Quantification of phosphorylated (p-) protein levels normalized to total (t-) protein levels and expressed as values relative to the control. All values are presented as the mean  $\pm$  SEM, \* $p < 0.05$ , \*\*\* $p < 0.001$ , as determined by Student's *t*-test; n = 3 per group.

**Supplementary Fig. S4. Sirt2 knockdown reduces the phosphorylation levels of tau and ERK in primary cultured neurons.**

Primary cultured neurons were transfected with control or Sirt2 siRNA for 72 h before lysis. Protein levels were determined by western blotting and quantified by densitometry. Quantification of Sirt2 protein levels normalized to Actin. Quantification of phosphorylated (p-) protein levels normalized to total (t-) protein levels and expressed as values relative to the control siRNA. All values are presented as the mean  $\pm$  SEM, \* $p < 0.05$ , \*\*\* $p < 0.001$ , N.S., no significant difference, as determined by Student's *t*-test; n = 3 per group.

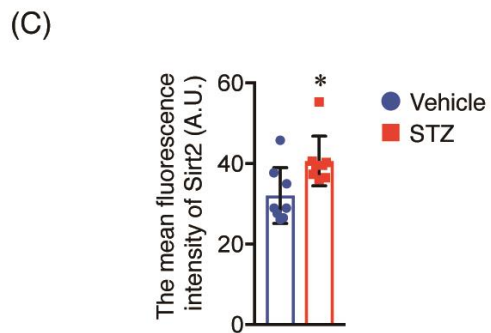
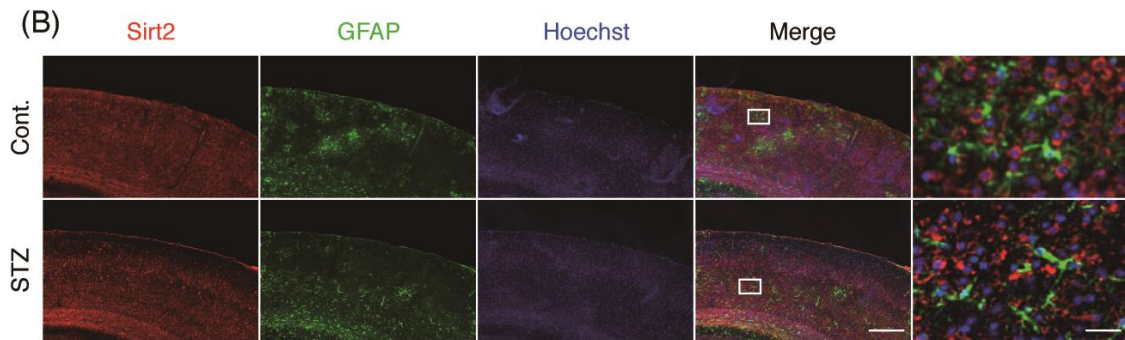
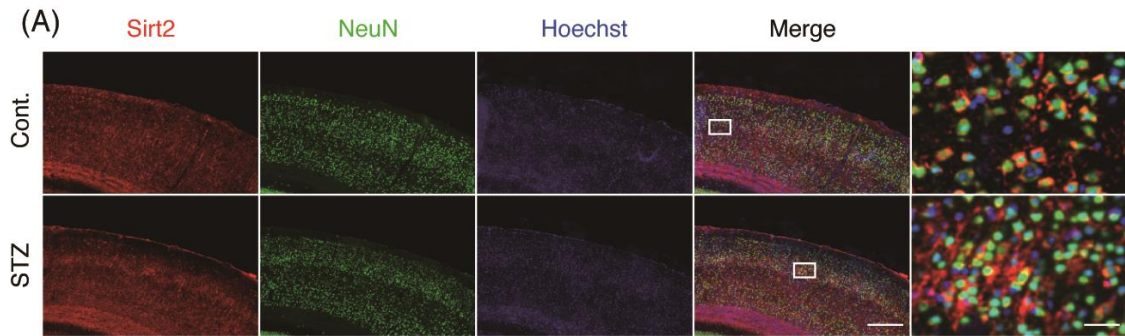
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Supplementary Fig. S1.

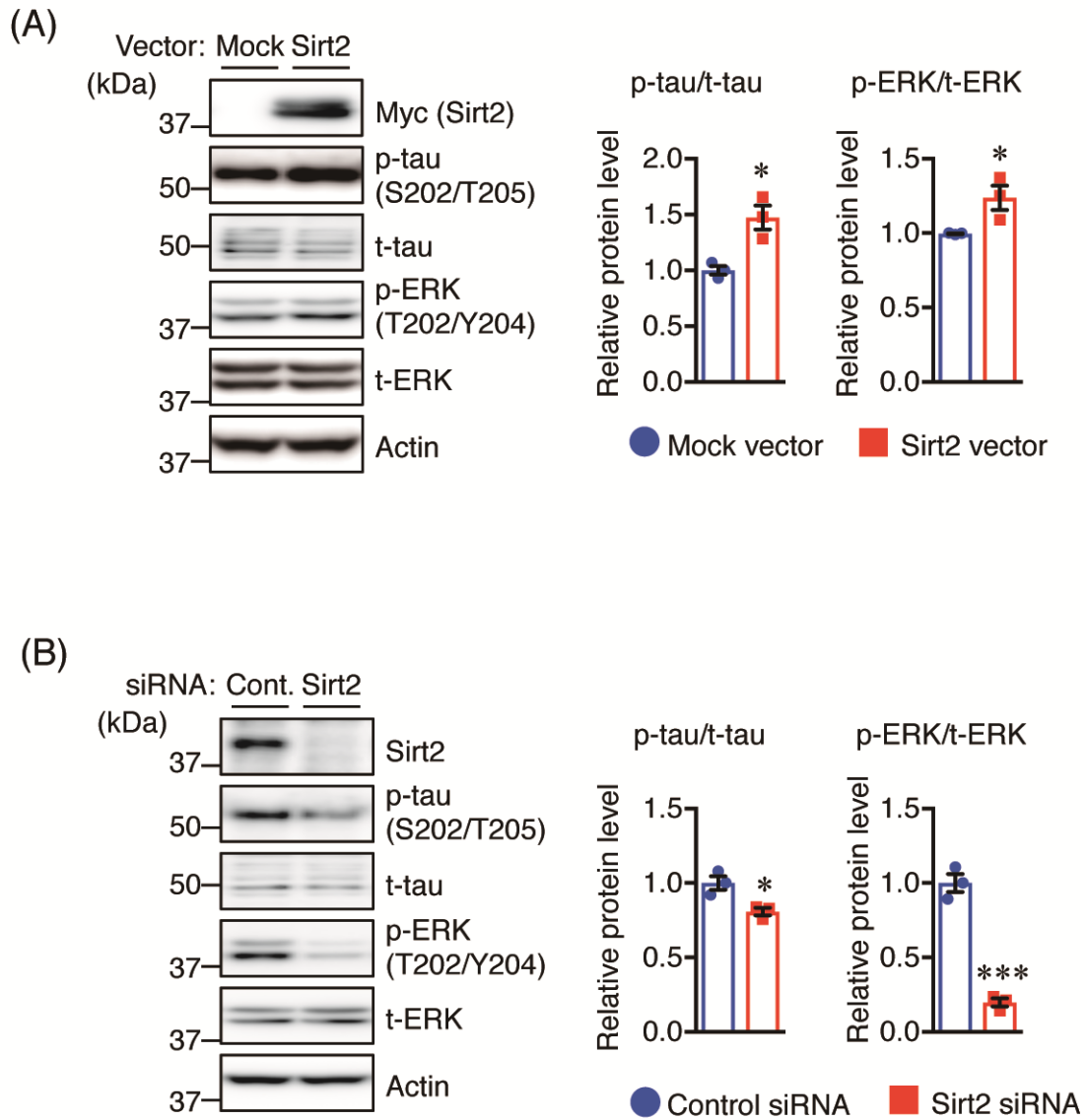
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Supplementary Fig. S2.

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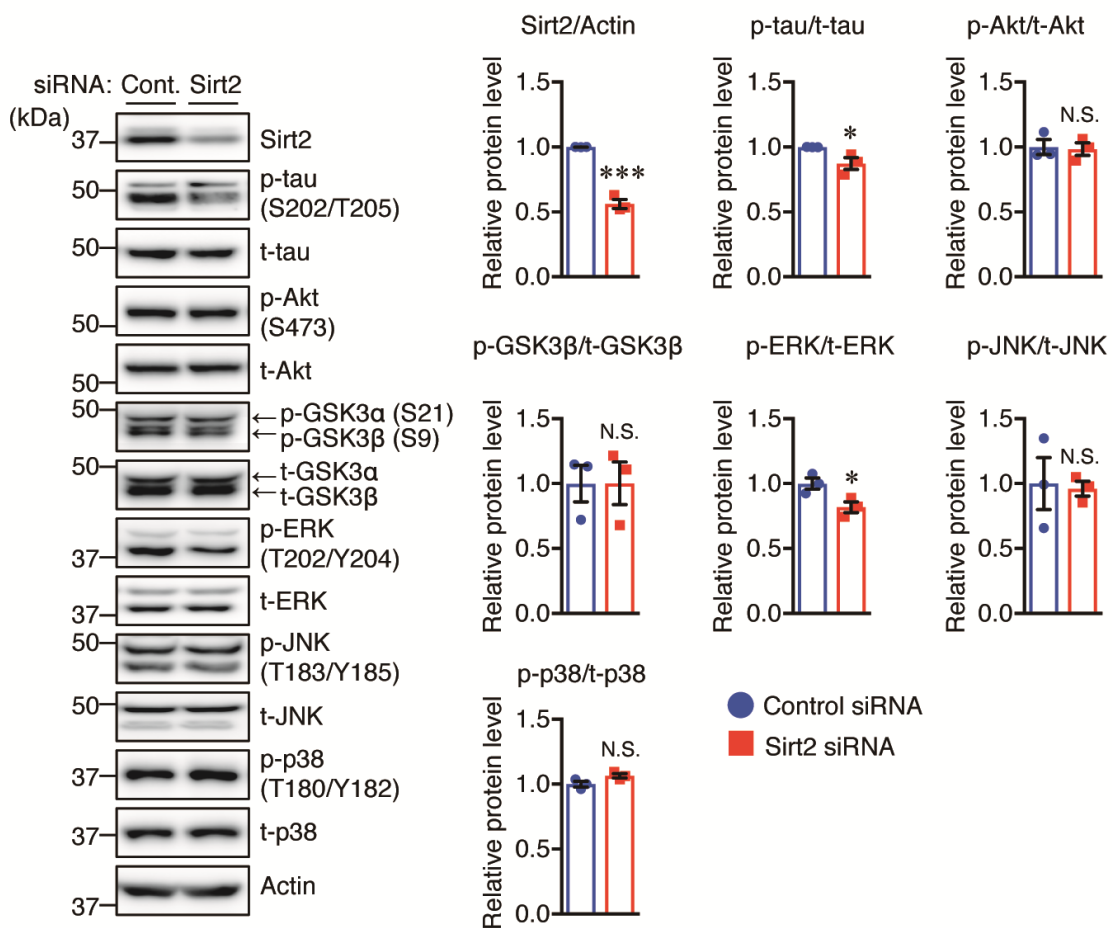
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Supplementary Fig. S3.

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Supplementary Fig. S4.