Expanded View Figures

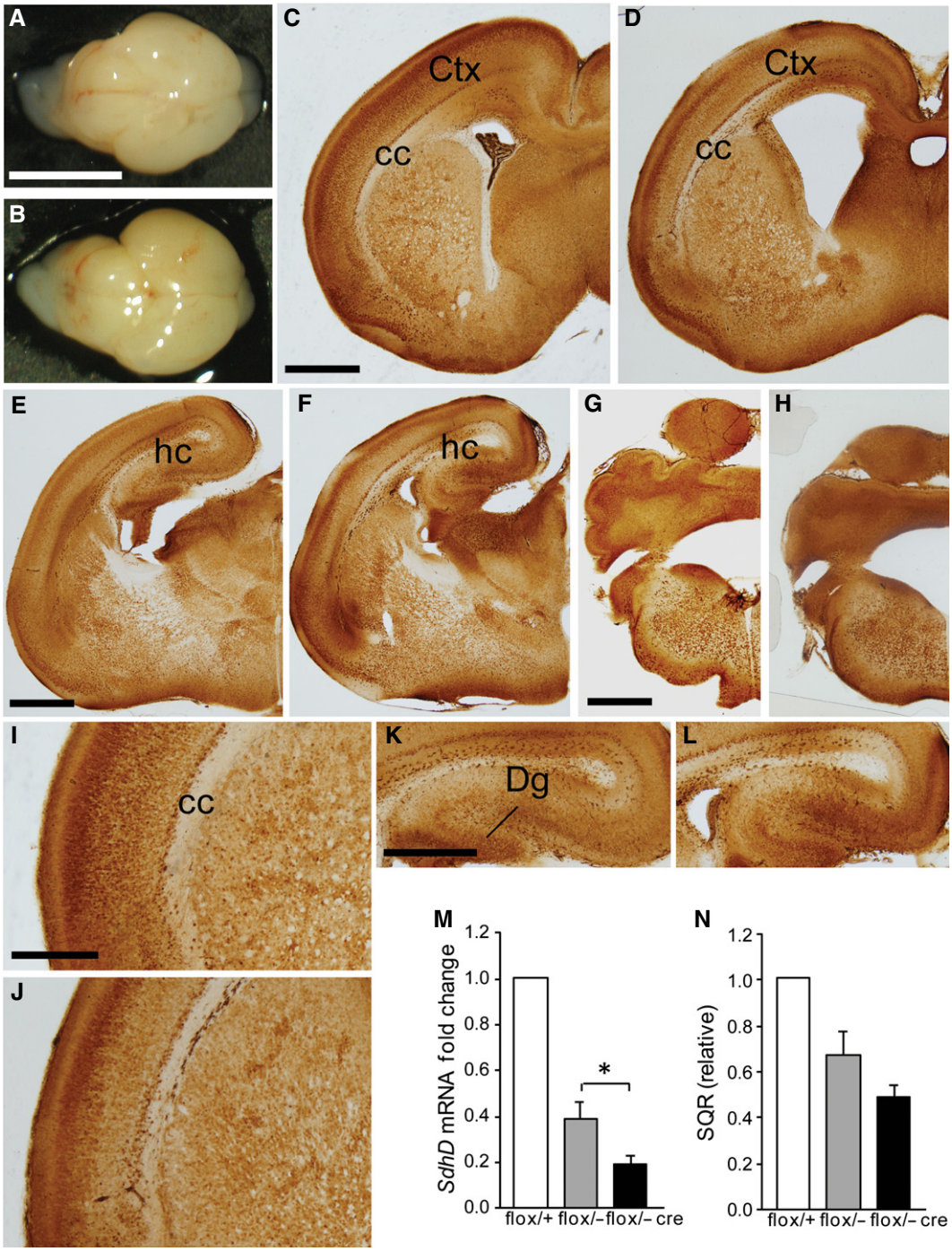

Figure EV1. Brain structures in newborn wild-type and hGFAP-SDHD mice.

A, B Whole brain of control (A) and hGFAP-SDHD (B) mice. Scale bar: 5 mm.

C–L Brain sections of newborn (P0) control (C, E, G, I, K) and hGFAP-SDHD (D, F, H, J, L) mice immunostained with NeuN antibody. Scale bars: 1 mm (C–H), 200 μm (I–L). Ctx: cortex; cc: corpus callosum; Dg: dentate gyrus; hc: hippocampus.

M Relative levels of *SdhD* mRNA in the entire brain (P0) as determined by RT–qPCR of total RNA. Data are presented as mean ± SEM (n = 3–5). Statistical significance: *$P \leq 0.05$. The Mann–Whitney U-test was applied.

N Succinate-ubiquinone oxidoreductase (SQR) activity of mitochondria isolated from the entire brain (P0). Data are presented as mean ± SEM (n = 4–8).

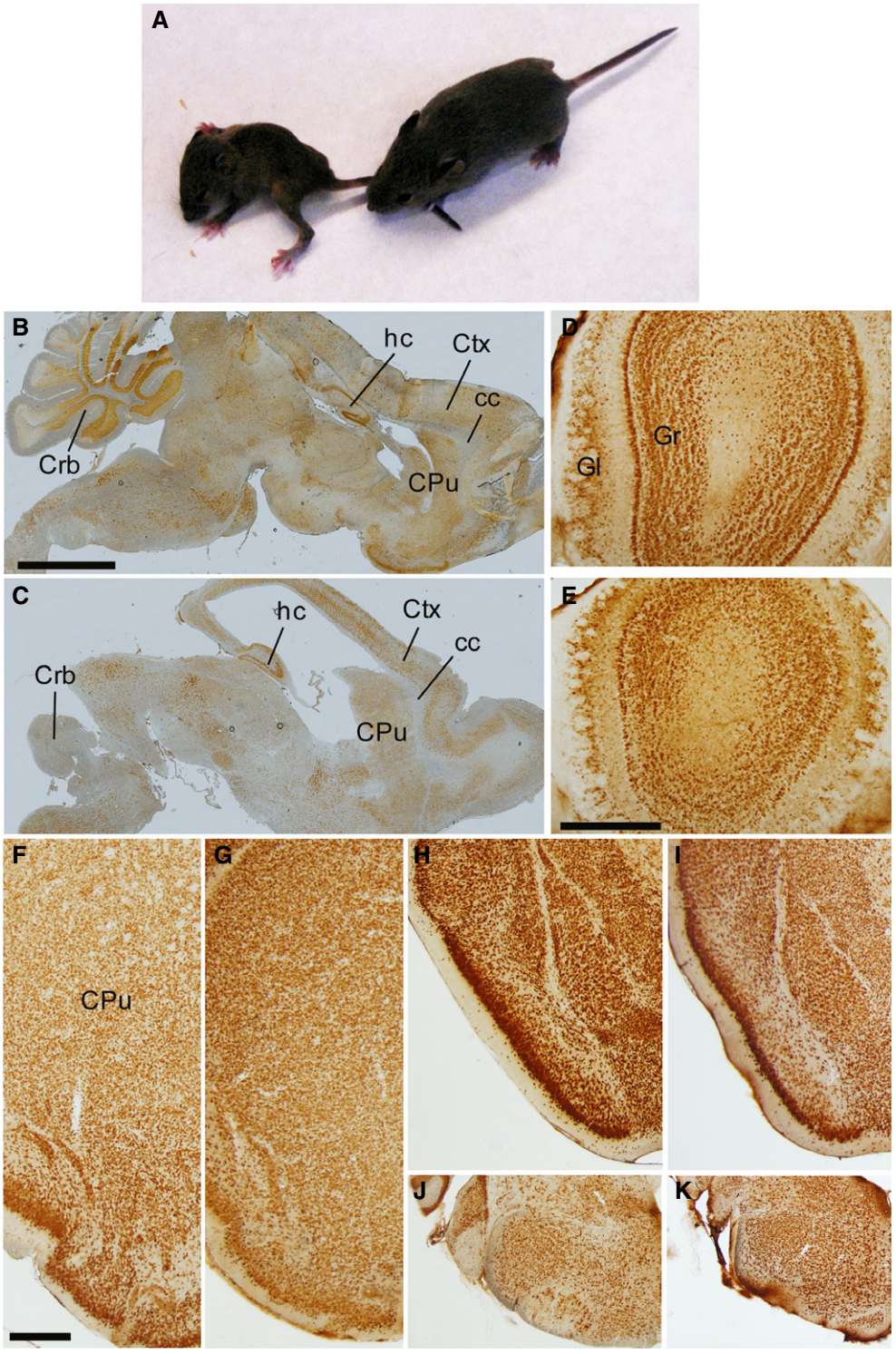

Figure EV2. Differences in body size and brain structures between postnatal wild-type and hGFAP-SDHD mice.

A GFAP-SDHD mutant (left) and control (right) littermates at P15.

B–K Brain sections from postnatal (P15) control (B, D, F, H, J) and GFAP-SDHD (C, E, G, I, K) mice immunostained with NeuN antibody. The images in (B, C) represent sagittal sections of different areas of the brain. The images in (D, E) correspond to sections of the olfactory bulb. The images in (F–K) present brain regions shown in Fig 1 at higher magnification. (F, G) Ventrolateral brain as in Fig 1B and C. (H, I) Ventrolateral brain as in Fig 1F and G. (J, K) Ventrolateral brain stem as in Fig 1J and K. Scale bars: 2 mm (B, C), 500 μm (D–K). CPu: caudate putamen; Crb: cerebellum; Ctx: cortex; cc: corpus callosum; Gl: glomerular layer; Gr: granular layer; hc: hippocampus.

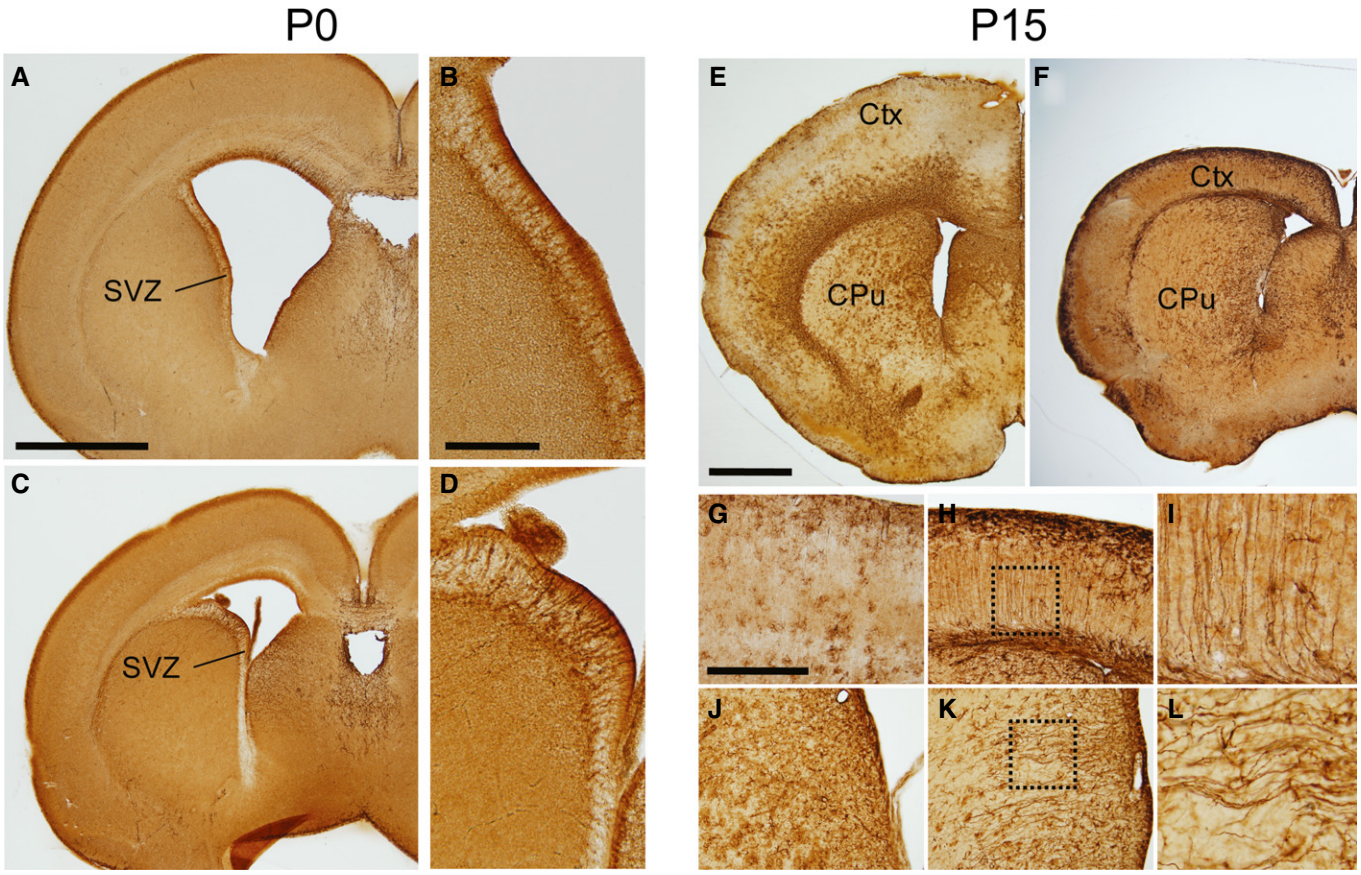

Figure EV3. GFAP$^+$ glial cells in wild-type and hGFAP-SDHD mice.

A–L Brain sections of newborn (P0; A–D) and postnatal (P15; E–L) control (A, B, E, G, J) and hGFAP-SDHD littermates (C, D, F, H, K, I, L) immunostained with GFAP antibody. The images in (B) and (D) are higher magnifications of the subventricular zone in (A) and (C), respectively. Images in (G, H) are higher magnifications of the cortex, and images in (J, K) of caudate-putamen areas shown in (E, F), respectively. Insets in (H) and (K) are higher magnified in (I) and (L), respectively. Scale bars: 1 mm (A, C, E, F), 200 μm (B, D), 500 μm (G, H, J, K). Ctx: cortex; CPu: caudate putamen; SVZ: subventricular zone.

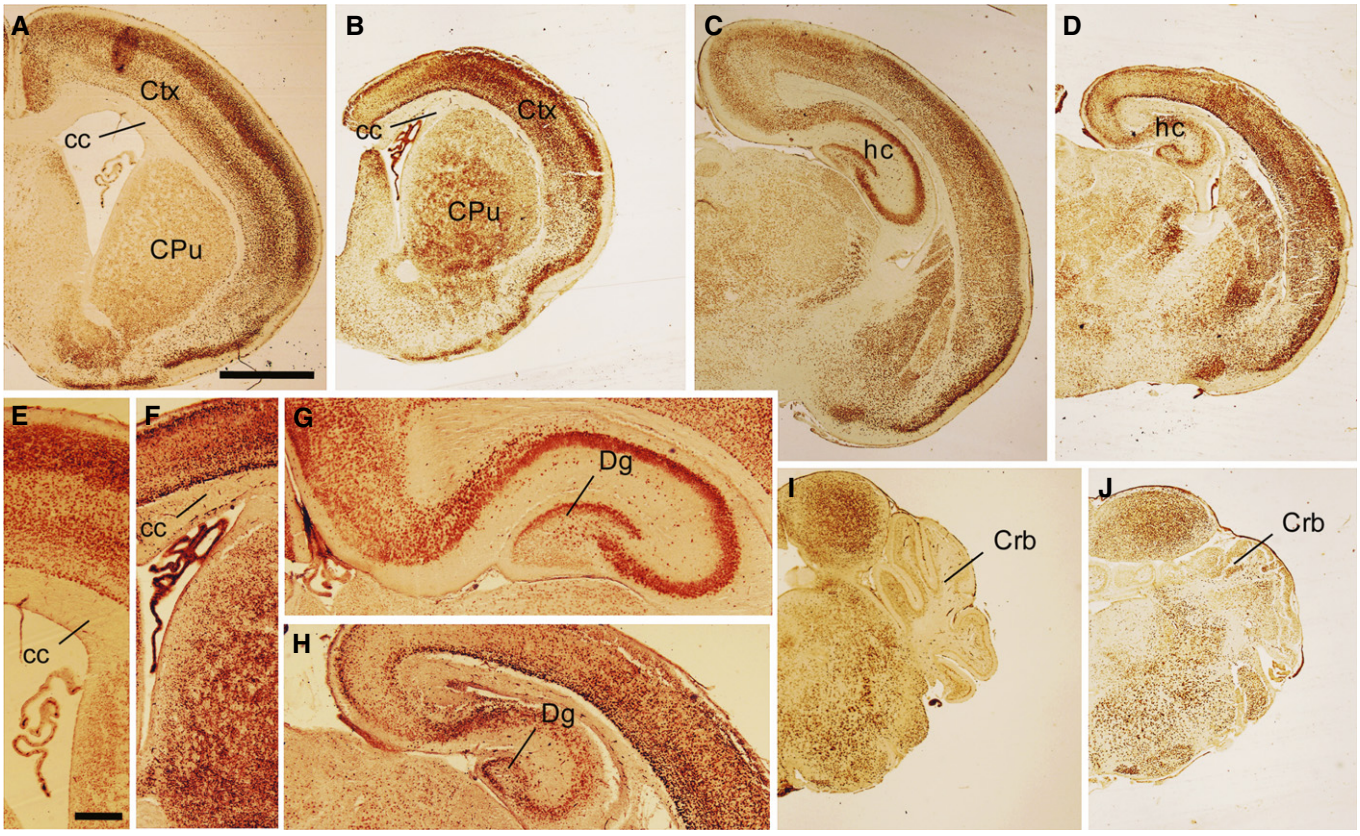

Figure EV4. Brain structures in postnatal (P5) wild-type and hGFAP-SDHD mice.

A–J Brain sections of postnatal (P5) control (A, C, E, G, I) and GFAP-SDHD (B, D, F, H, J) mice immunostained with NeuN antibody. Scale bar: 2 mm (A–D, I, J), 500 μm (E–H). CPu: caudate putamen, Crb: cerebellum; cc: corpus callosum; Ctx: cortex; Dg: dentate gyrus; hc: hippocampus.

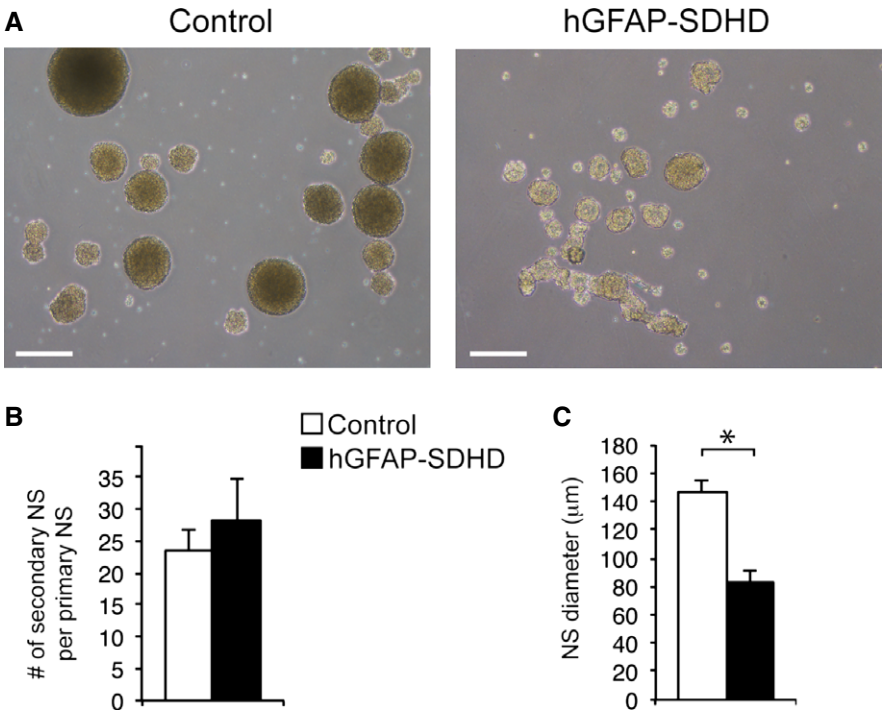

Figure EV5. Self-renewal of SVZ stem cells from wild-type and hGFAP-SDHD mice.

A Bright-field pictures of secondary neurospheres obtained after dispersion and re-plating of SVZ primary neurospheres from wild-type or hGFAP-SDHD mice. Scale bar: 200 µm.

B Quantification of the number of secondary neurospheres obtained per primary neurosphere. Data are presented as mean ± SEM (n = 3 cultures/mice per genotype).

C Diameter of secondary neurospheres. Mean ± SEM (n = 3 cultures/mice per genotype). Statistical significance: *$P \leq 0.05$. The two-tailed Student's t-test was applied.

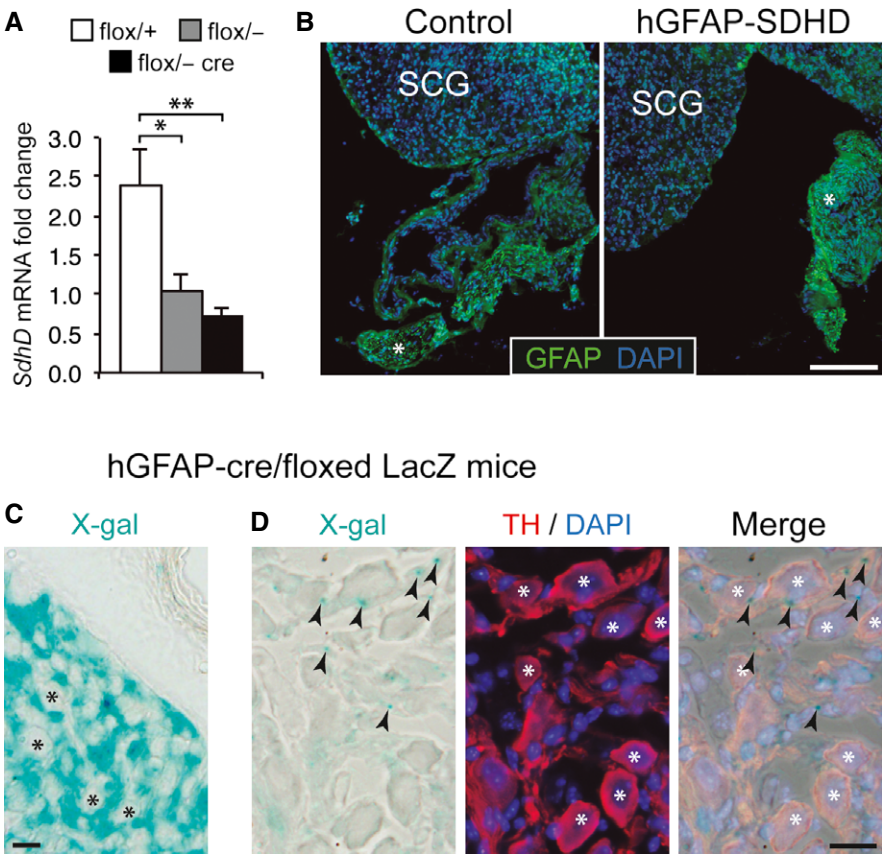

Figure EV6. GFAP expression and *SdhD* deletion in superior cervical ganglion.

A Results of quantitative RT–PCR to detect *SdhD* expression in the superior cervical ganglia of wild-type (flox/+) and mutant (flox/–, and flox/– cre) mice. Note the non-significant difference between flox/– (heterozygous) and flox/– cre mice, suggesting no major increase in deletion after GFAP-cre expression. Data are presented as mean ± SEM (n = 3–5 mice). Statistical significance: *$P \leq 0.05$; **$P \leq 0.01$. The ANOVA test with appropriate *post hoc* analysis was applied.

B Superior cervical ganglion (SCG) sections from control or hGFAP-SDHD P15 mice, immunostained with GFAP antibody. Note the relatively low expression of GFAP in the adult SCG as compared to Schwann cells of nearby nerves (asterisk).

C Intense X-gal staining (24 h) of an SCG section from an hGFAP-cre/floxed LacZ mouse, to label derivatives of GFAP$^+$ cells. Note the absence of staining in the large sympathetic neurons of the organ (asterisks), indicating that they do not derive from hGFAP$^+$ neural stem cells. Scale bar: 20 µm.

D Mild X-gal staining (12 h) of an SCG section from an hGFAP-cre/floxed LacZ mouse, to label derivatives of GFAP$^+$ cells. Large sympathetic neurons are stained with TH antibody (asterisks). Note that X-gal$^+$ precipitates (arrowheads) are always outside the neuronal somas, confirming that these neurons do not derive from hGFAP$^+$ neural stem cells. Scale bar: 20 µm.