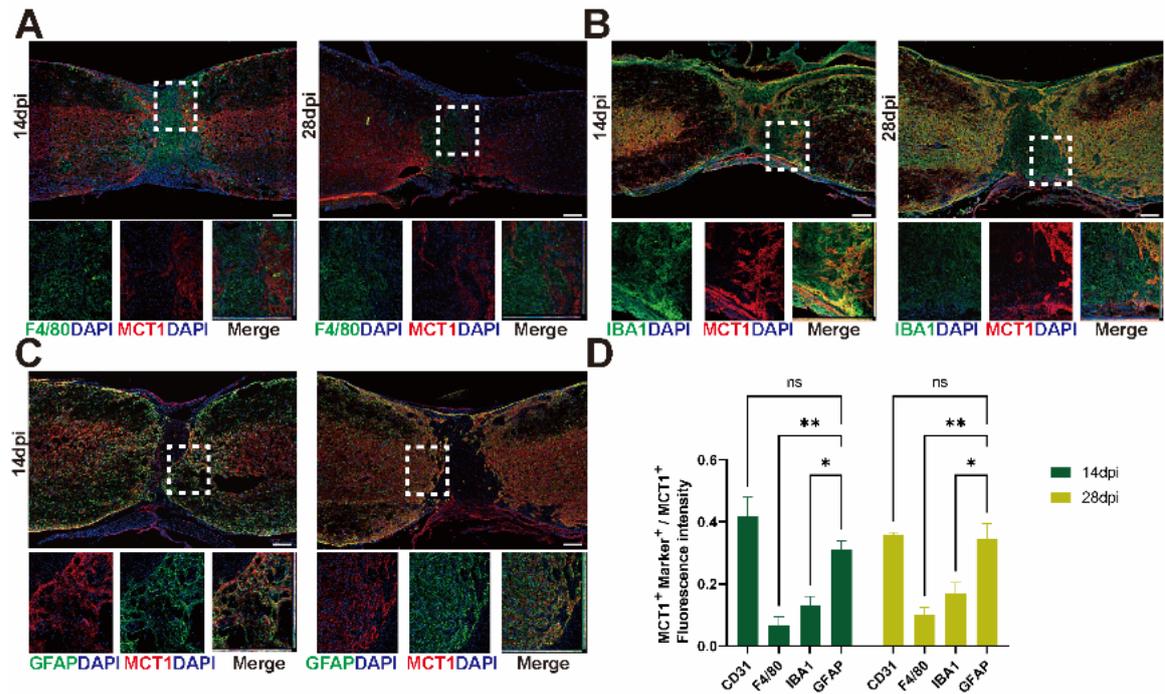
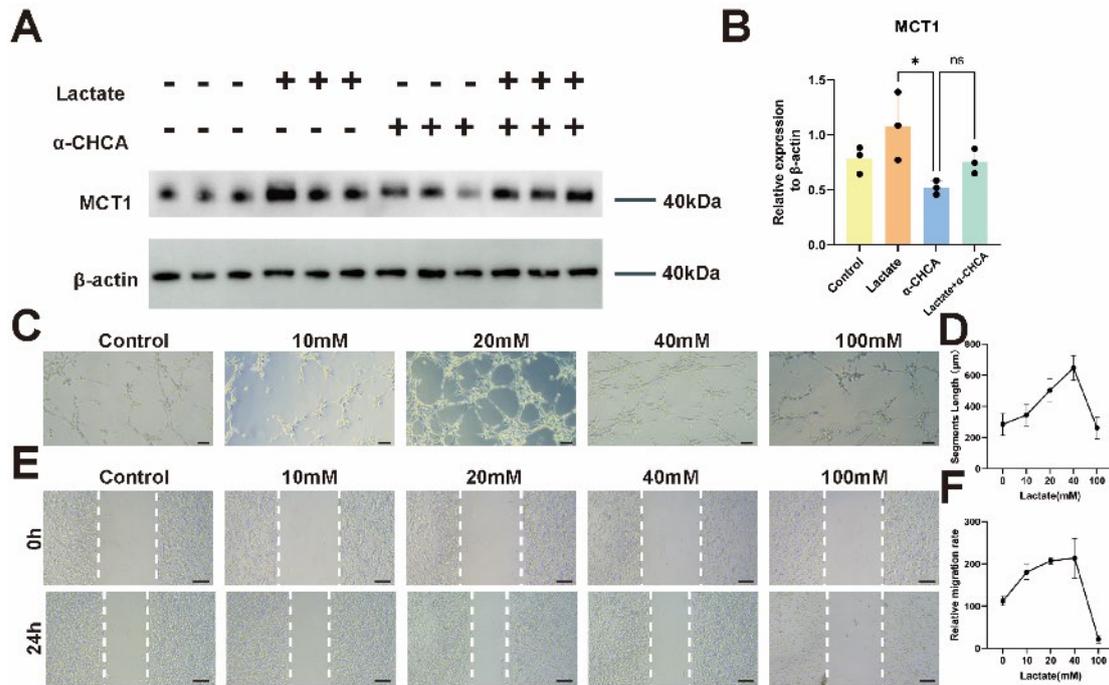


**Supplementary Figure 1. Endothelium-derived lactate feeds nerve cells. (A)** Immunofluorescence of Laconic lentivirus-infected cortical neurons treated with different concentrations of lactate. **(B)** Representative images showing CFP (blue) and YFP (yellow) fluorescence in control and lactate (100 mM) -treated CATH.a. (scale bar = 10 $\mu$ m). **(C)** Quantification of the CFP/YFP fluorescence ratio of laconic (lactate sensor) showing concentration-dependent lactate uptake in CATH.a. (n = 6 from 3 independent experiments. Error bars indicate the standard error of the mean (SEM)). **(D)** Representative confocal image showing CFP (blue) and YFP (yellow), Bright field (white) fluorescence from bEnd.3 and laconic-infected CATH.a on a 2-well

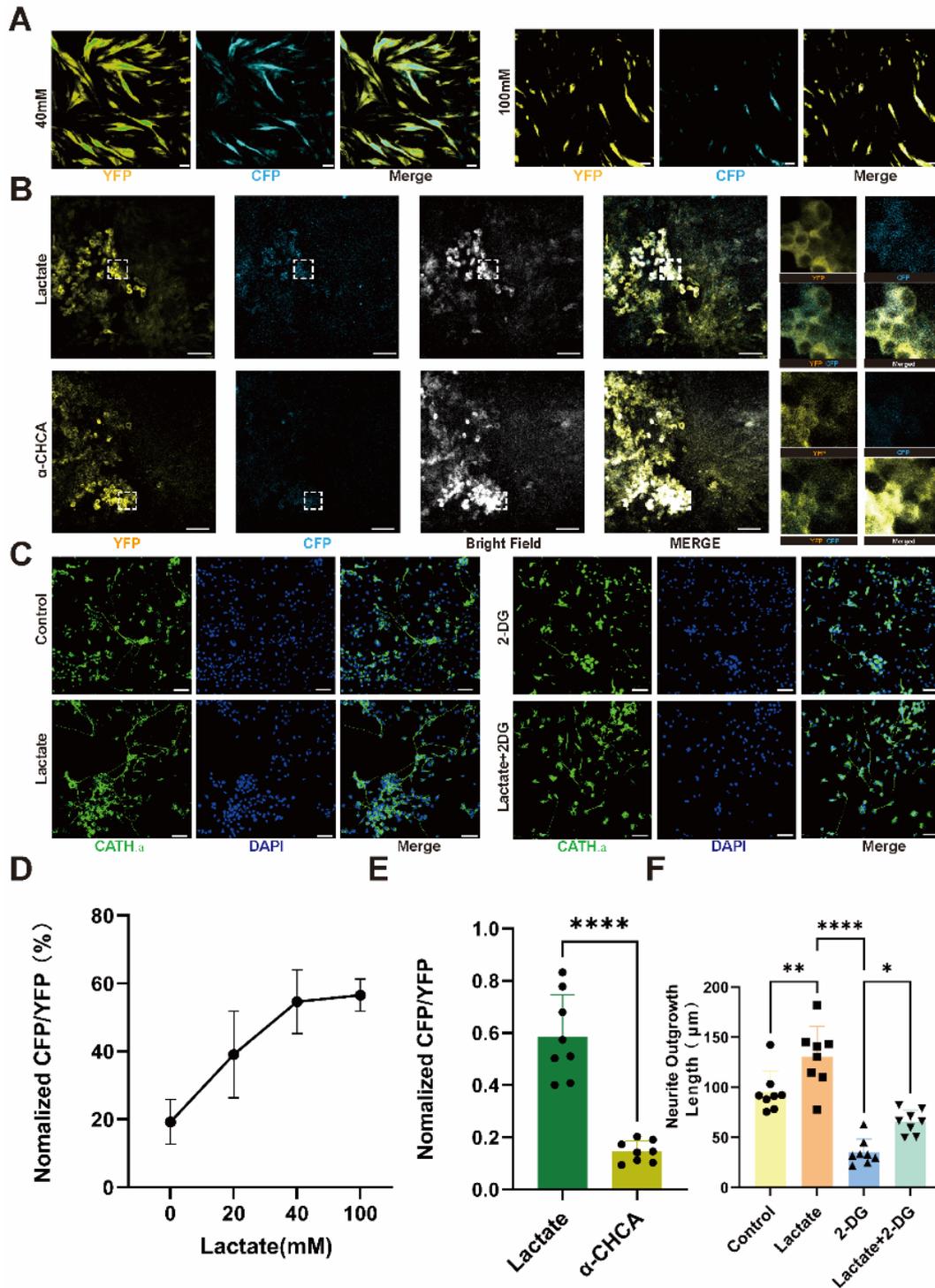
chamber. (scale bar = 100  $\mu\text{m}$ ). **(E)** Localized enlargements showing CFP (blue) and YFP (yellow), Bright field (white) fluorescence from bEnd.3 and laconic-infected CATH.a on a 2-well chamber. The upper panel shows CATH.a with endothelial contact and the lower panel shows CATH.a without endothelial contact (scale bar = 10  $\mu\text{m}$ ). **(F)** Quantification of the CFP/YFP fluorescence ratio of laconic in CATH.a with endothelial contact (EC-NEU contact) or CATH.a alone (NEU only) ( $n = 8$  from 3 independent experiments. Error bars indicate the standard error of the mean (SEM) from unpaired Student's t-test, \*\*\*\*  $p < 0.0001$ ). **(G)** Representative time-lapse imaging at 0, 10, 20, and 30 min, along with CFP (blue), bright field (white) fluorescence from laconic-infected cortical neurons alone on a 2-well chamber. (scale bar = 20  $\mu\text{m}$ ). **(H)** Quantification of the CFP fluorescence ratio of laconic showing time-dependent lactate transport from bEnd.3 to cortical neurons.



**Supplementary Figure 2. Spatial and temporal expression of MCT1 after SCI.** (A) Representative fluorescence images showing the expression of MCT1 in the spinal cord of the 14, 28 dpi groups (red: MCT1, green: F4/80, blue: DAPI, scale bar: 200  $\mu$ m). (B) Representative fluorescence images showing the expression of MCT1 in the spinal cord of the 14, 28 dpi groups (red: MCT1, green: IBA1, blue: DAPI, scale bar: 200  $\mu$ m). (C) Representative fluorescence images showing the expression of MCT1 in the spinal cord of the 14, 28 dpi groups (red: MCT1, green: GFAP, blue: DAPI, scale bar: 200  $\mu$ m). (D) Quantification of the Colocalization of MCT1<sup>+</sup> Marker<sup>+</sup> cells with MCT1<sup>+</sup> cells in (A-C) of the 14, 28 dpi groups. (n = 8 from 6 independent experiments, mean  $\pm$  SD, two-way ANOVA, Tukey's multiple comparisons, ns no significant, \*p < 0.05, \*\*p < 0.01).



**Supplementary Figure 3. Inhibition of ECs MCT1 Expression Leads to Decreased Biological and Metabolic Functions.** (A) Western blotting analysis of the levels of MCT1, and  $\beta$ -actin in bEnd.3 Cells with different concentrations of lactate. (B) Quantification of the relative expression of MCT1 to  $\beta$ -actin in (A) (n = 3 from 3 independent experiments, mean  $\pm$  SD, one-way ANOVA, ns not significant, \* $p < 0.05$ ). (C) Representative images showing the tube-forming ability of bEnd.3 Cells with different concentrations of lactate (scale bar = 100  $\mu$ m). (D) Quantification of tube-forming ability in (C). (n = 6 from 3 independent experiments, mean  $\pm$  SD, one-way ANOVA). (E) Representative images showing the lateral migration ability of bEnd.3 Cells with different concentrations of lactate (scale bar = 100  $\mu$ m). (F) Quantification of tube-forming ability in (E) (n = 3 from 3 independent experiments, mean  $\pm$  SD, one-way ANOVA).



**Supplementary Figure 4.** (A) Immunofluorescence of Laconic lentivirus-infected bEnd.3 treated with different concentrations of lactate. (B) Representative confocal image showing CFP (blue) and YFP (yellow), Bright field (white) fluorescence from lactate or  $\alpha$ -CHCA treated bEnd.3 and laconic-infected CATH.a on a 2-well chamber. (scale bar = 100  $\mu$ m). (C) Representative immunofluorescent images of the regenerative axons under lactate or 2-DG treatment in four groups (green: TuJ1, blue:

DAPI, scale bar = 100  $\mu\text{m}$ ). **(D)** Quantification of the CFP/YFP fluorescence ratio of laconic (lactate sensor) showing concentration-dependent lactate uptake in bEnd.3. (n = 6 from 3 independent experiments. Error bars indicate the SEM). **(E)** Quantification of the CFP/YFP fluorescence ratio of laconic in CATH.a with bEnd.3 under lactate treatment or under  $\alpha$ -CHCA treatment in (B) (n = 8 from 3 independent experiments, mean  $\pm$  SD, unpaired t-test, \*\*\*\*p < 0.0001). **(F)** Quantification of total axon length in (C) (n = 8 from 3 independent experiments, mean  $\pm$  SD, one-way ANOVA, \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001).