Supplemental material

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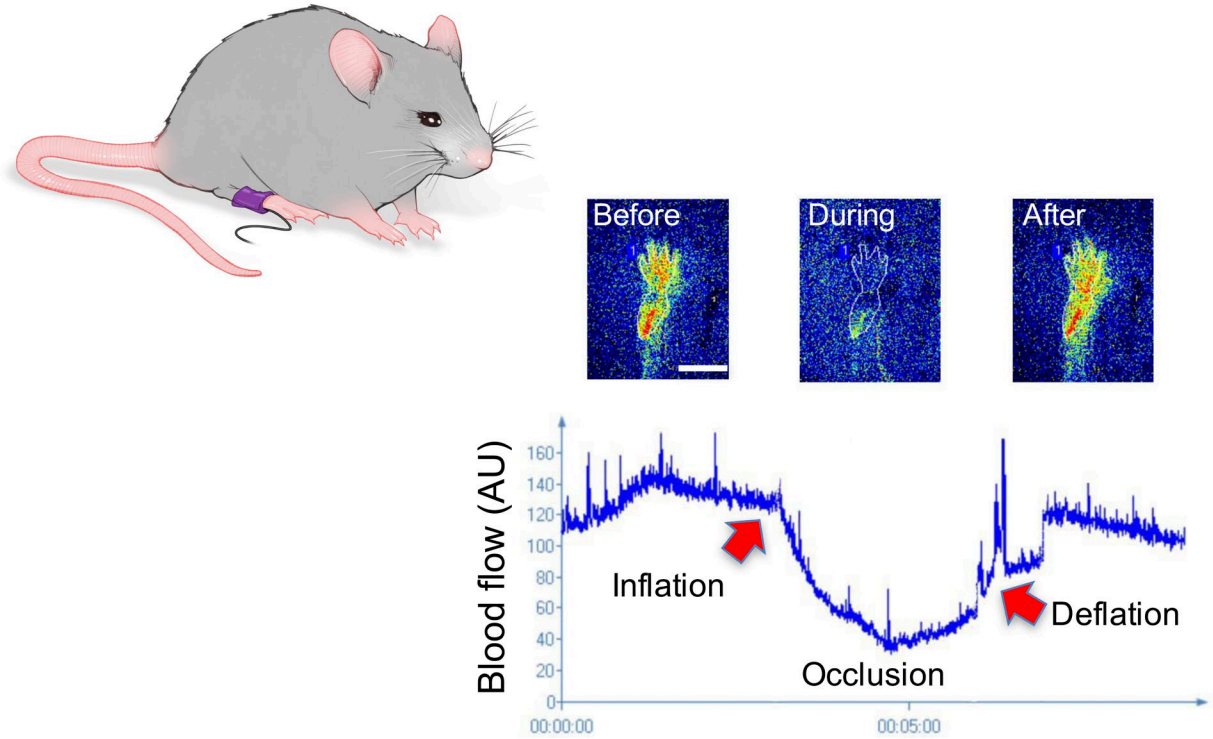

Figure S1. **Placement and validation of RIC.** Illustration depicts cuff placement on the hind limbs. RIC (four cycles × 5-min duration × 5-min interval) was bilaterally delivered via the hind limbs and the magnitude of limb ischemia was monitored using laser speckle contrast imaging. Baseline blood flow was measured in the left hind limb before cuff inflation. Representative laser speckle contrast images in the paw are shown along with a trace of blood flow before, during, and after cuff inflation. Bar, 4 mm.

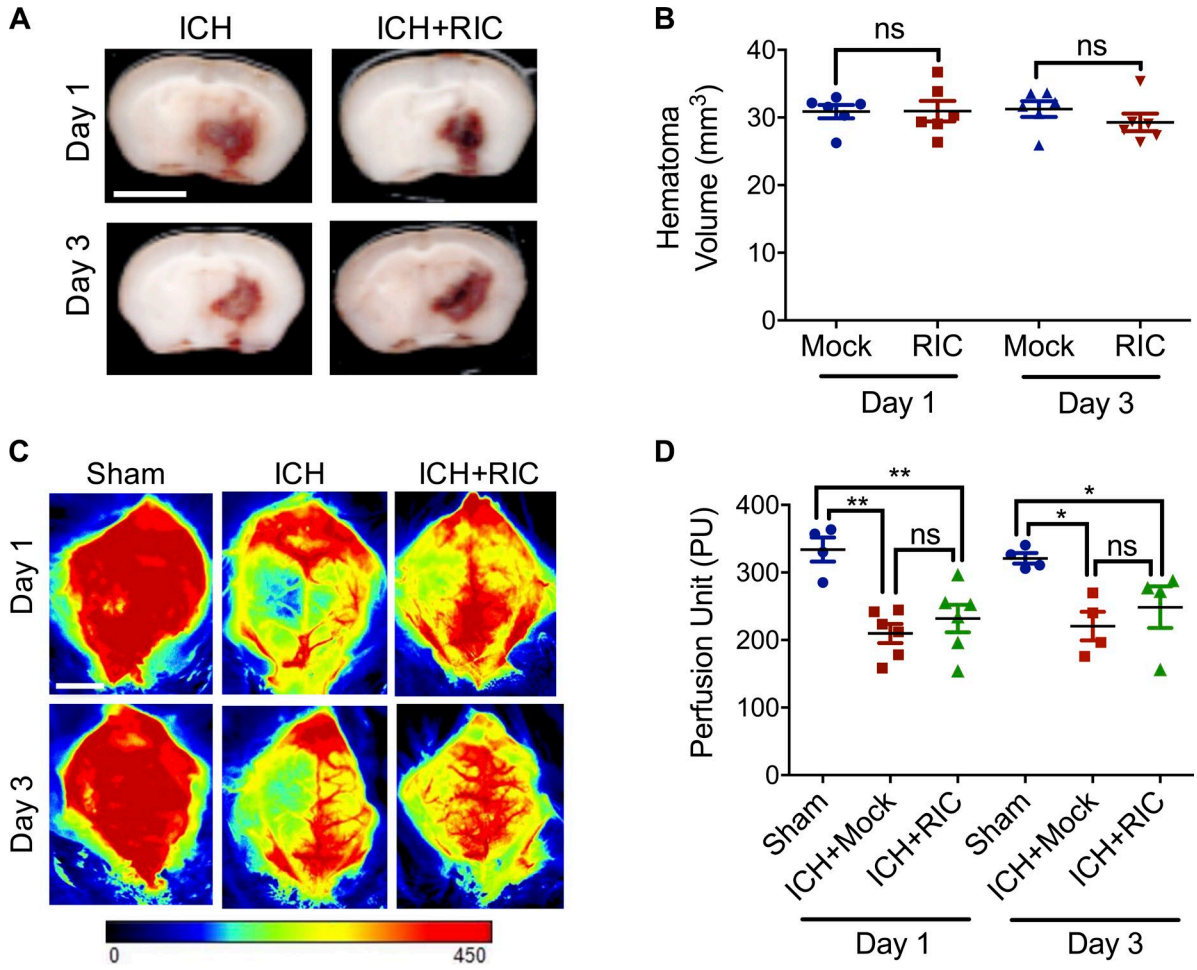

Figure S2. **RIC does not reduce initial hematoma size after ICH. (A and B)** Mixed sex C57BL/6J littermates were randomized to receive once-daily mock conditioning or bilateral RIC beginning at 2 h after sham or collagenase-induced ICH. At day 1 or 3, hematoma area was quantified in serial 2-mm coronal slices. Bar, 4 mm. Data are mean ± SEM from n = 5–6 mice/group and were analyzed by one-way ANOVA followed by Tukey's post-hoc test (ns, not statistically significant). Data are representative of two independent experiments. **(C and D)** Mixed sex C57BL/6J littermates were randomized to receive once-daily mock conditioning or bilateral RIC beginning at 2 h after sham or collagenase-induced ICH. At day 1 or 3, peri-hematoma blood flow was assessed by laser speckle contrast imaging. Bar, 4 mm. Data are mean ± SEM from n = 4–6 mice/group and were analyzed by one-way ANOVA followed by Tukey's post-hoc test (*, $P < 0.05$; **, $P < 0.01$; ns, not statistically significant). Data are representative of two independent experiments.

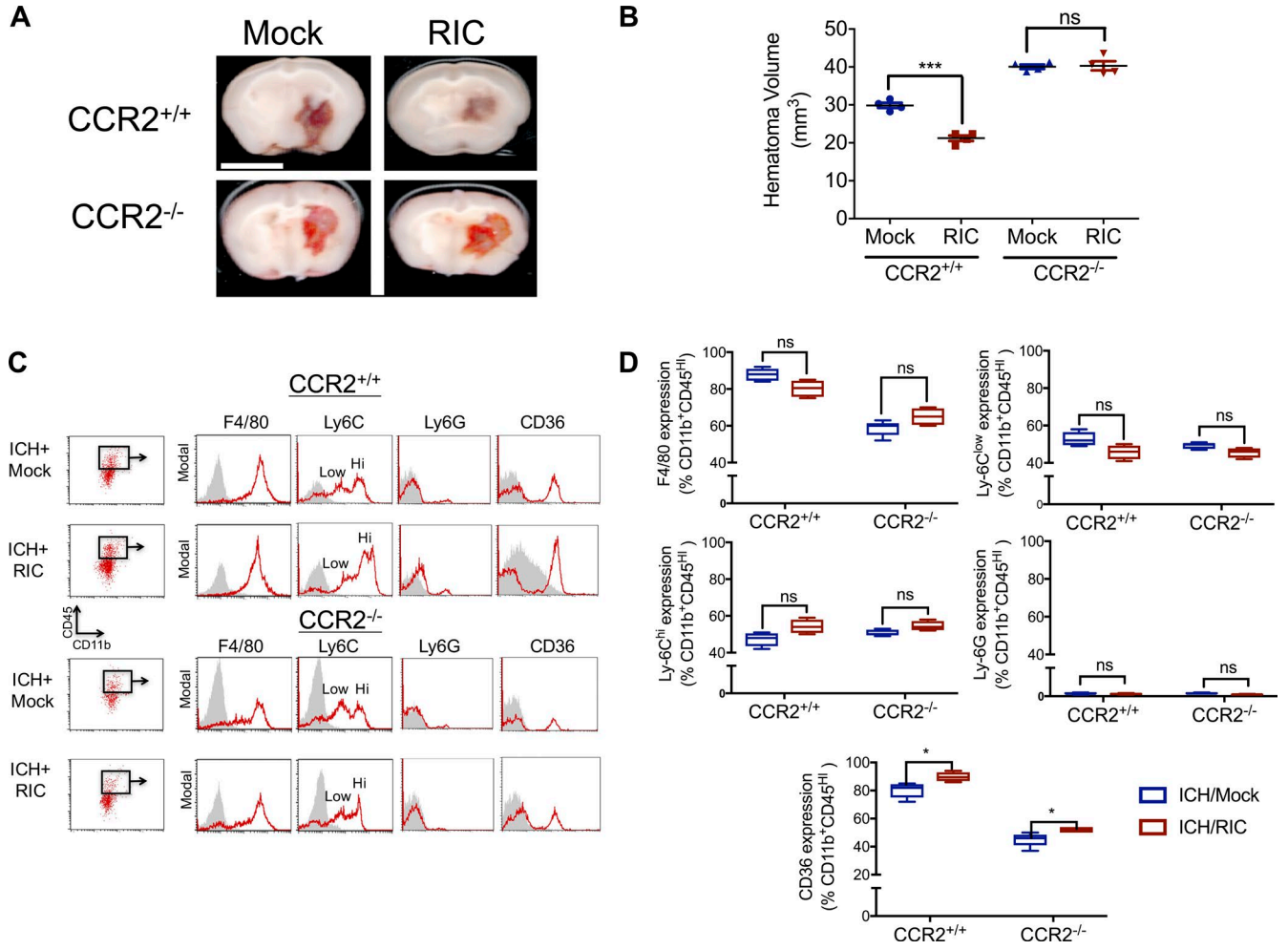

Figure S3. **RIC-induced hematoma resolution is lost in CCR2$^{-/-}$ mice.** Mixed sex CCR2$^{+/+}$ (WT; C57BL/6J) and CCR2$^{-/-}$ mice littermates were randomized to receive once-daily mock conditioning or bilateral RIC beginning at 2 h after sham or collagenase-induced ICH. **(A and B)** At day 5, hematoma area was quantified in serial 2-mm coronal slices. Bar, 4 mm. Data are mean ± SEM from *n* = 4 mice/group and were analyzed by one-way ANOVA followed by Tukey's post-hoc test (***, P < 0.001; ns, not statistically significant). Data are representative of two independent experiments. **(C and D)** Phenotypic analysis of CD11b^{+}, CD45^{hi}-infiltrated macrophages within peri-hematoma brain tissue of CCR2$^{+/+}$ or CCR2$^{-/-}$ mice. Representative histograms are provided for each marker. Gray-shaded areas indicate isotype controls. Plots depict the mean ± SEM from *n* = 4 mice/group. Data were analyzed using a one-way ANOVA followed by Tukey's post-hoc test (*, P < 0.05; ns, not statistically significant). Data are representative of two independent experiments.

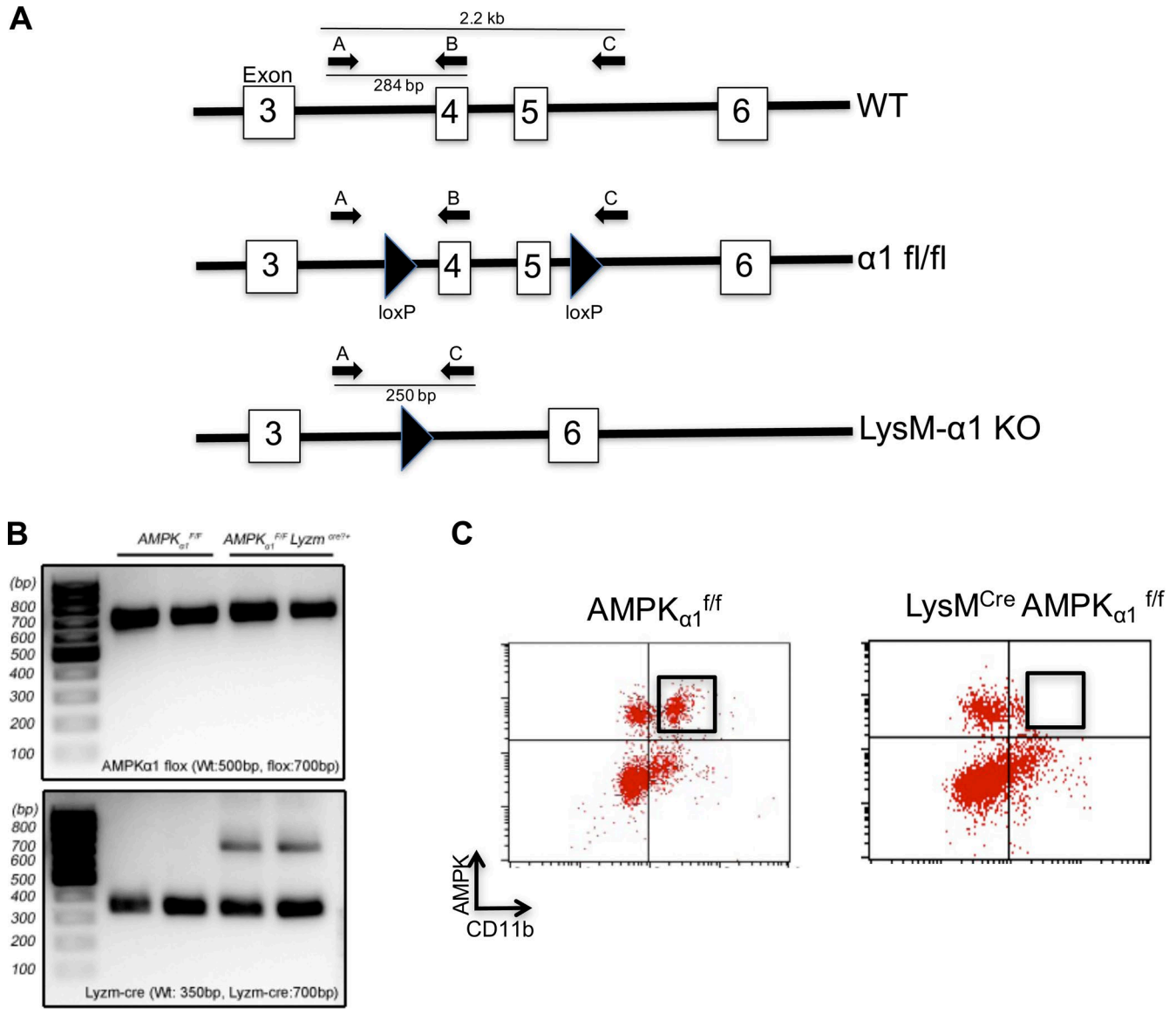

Figure S4. **Breeding strategy used to generate myeloid-specific AMPKα1 knockout mice.** Mice harboring a floxed *AMPKα1* locus were crossed with mice expressing Cre recombinase under the control of the *lysozyme 2* (LysM) promoter to generate LysM^{Cre} AMPKα1$^{f/f}$ mice. **(A and B)** PCR primer positions (A) and representative genotyping gel (B) demonstrating the generation of LysM^{Cre} AMPKα1$^{f/f}$ knockout mice. **(C)** Representative scatterplot demonstrating the functional and complete deletion of AMPKα1 in CD11b^{+} myeloid cells in LysM^{Cre} AMPKα1$^{f/f}$ mice, as compared with WT AMPKα1$^{f/f}$ mice.

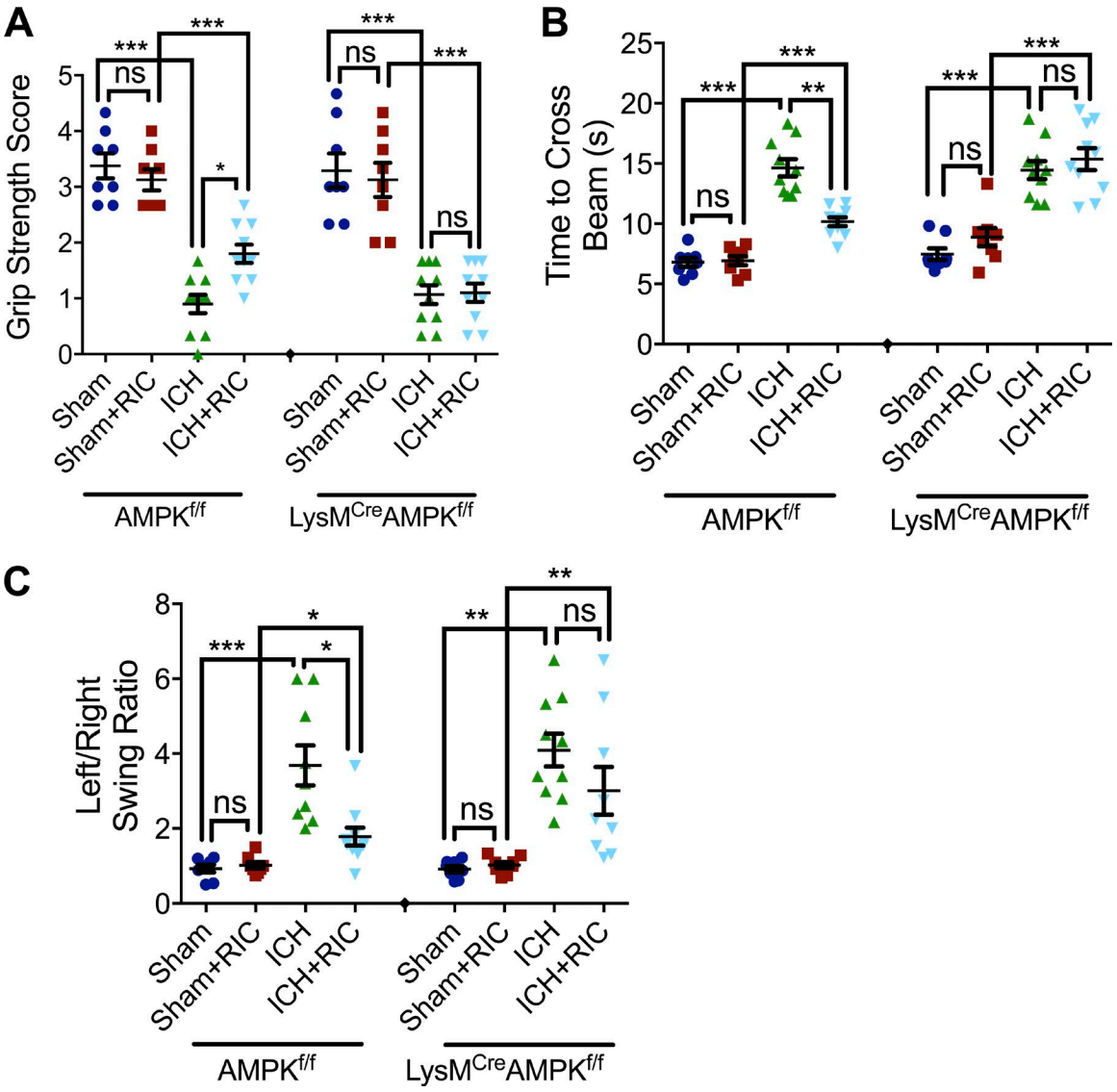

Figure S5. **AMPKα1-dependent motor improvements by RIC after collagenase-induced ICH.** WT (AMPKα1$^{f/f}$) or myeloid-specific AMPKα1 knockout mice (LysM^{Cre}AMPKα1$^{f/f}$) were randomized to sham/collagenase-induced ICH groups and littermate received either mock conditioning or once-daily RIC beginning at 2 h after injury. **(A)** RIC improved grip strength at day 4 after collagenase-induced ICH in AMPKα1$^{f/f}$ mice, whereas this benefit was lost in LysM-^{Cre}AMPKα1$^{f/f}$. **(B)** RIC improved motor balance and coordination, as assessed by a reduced time to traverse a narrow beam, following ICH in AMPKα1$^{f/f}$ mice. In contrast, RIC was ineffective at improving motor outcomes in LysM^{Cre}AMPKα1$^{f/f}$ mice. **(C)** RIC normalized asymmetric motor behavior, as assessed by the left/right swing ratio task, in AMPKα1$^{f/f}$ mice. The beneficial effects of RIC were not observed in LysM^{Cre}AMPKα1$^{f/f}$ mice. For all tasks, scatter plots depict individual values along with the mean ± SEM from *n* = 7–10 mice/group. Data were analyzed by One-Way ANOVA followed by Tukey's post-hoc test (*, P < 0.05; **, P < 0.01; ***, P < 0.001; ns, not statistically significant). Data are representative of two independent experiments.