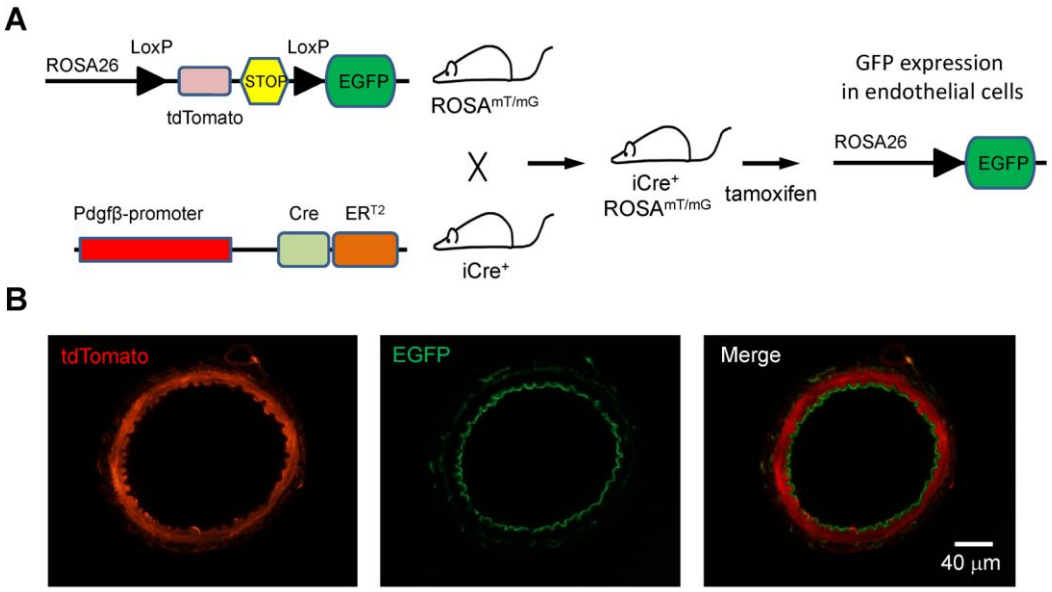
SUPPLEMENTAL MATERIAL

Table S1. primers sequences for RT-PCR.

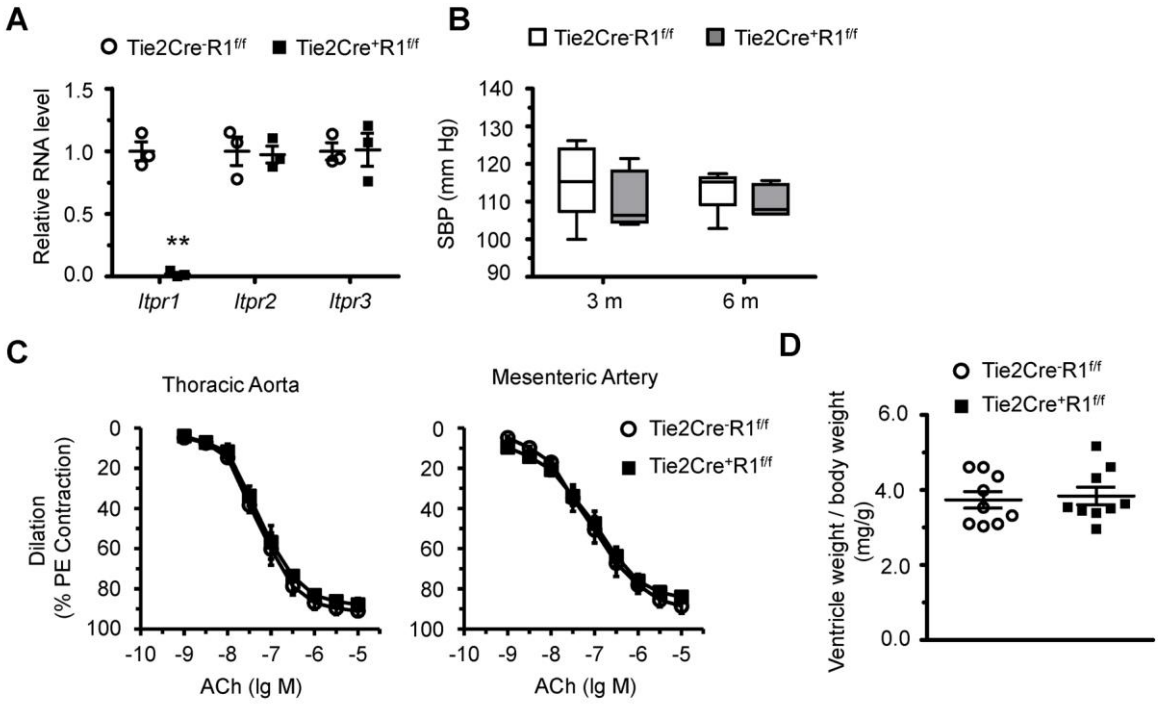
Gene	Forward primer（5'-3')	Reverse primer（5'-3')
Itpr1	CTCTGTATGCGGAGGGATCTAC	GCGGAGTATCGATTCATAGGAC
Itpr2	CTTCCTCTACATTGGGGACATC	GGCAGAGTATCGATTCATAGGG
Itpr3	AGCCAAGCAGACTAAACAGGAC	GCCGCTTGTTCACAGTTAAGTA
NOS3	TACGCACCCAGAGCTTTTCT	CTTGGTCAACCGAACGAAGT
CHRM1	TGACAGGCAACCTGCTGGTGCT	AATCATCAGAGCTGCCCTGCGG
CHRM2	CGGACCACAAAAATGGCAGGCAT	CCATCACCACCAGGCATGTTGTTGT
CHRM3	CCTCTTGAAGTGCTGCGTTCTGACC	TGCCAGGAAGCCAGTCAAGAATGC
CHRM4	TGTGGTGAGCAATGCCTCTGTCATG	GGCTTCATCAGAGGGCTCTTGAGGA
CHRM5	ACCACTGACATACCGAGCCAAGCG	TTCCCGTTGTTGAGGTGCTTCTACG
CHRNA7	GTAACCATGCGCCGTAGG	CCGAGGCTTGTGCTGAC
Gapdh	TGGCCTTCCGTGTTCCTAC	GAGTTGCTGTTGAAGTCGCA

Figure S1. Endothelial cell-specific gene deletion in adult mice by Pdgfb-iCreER.



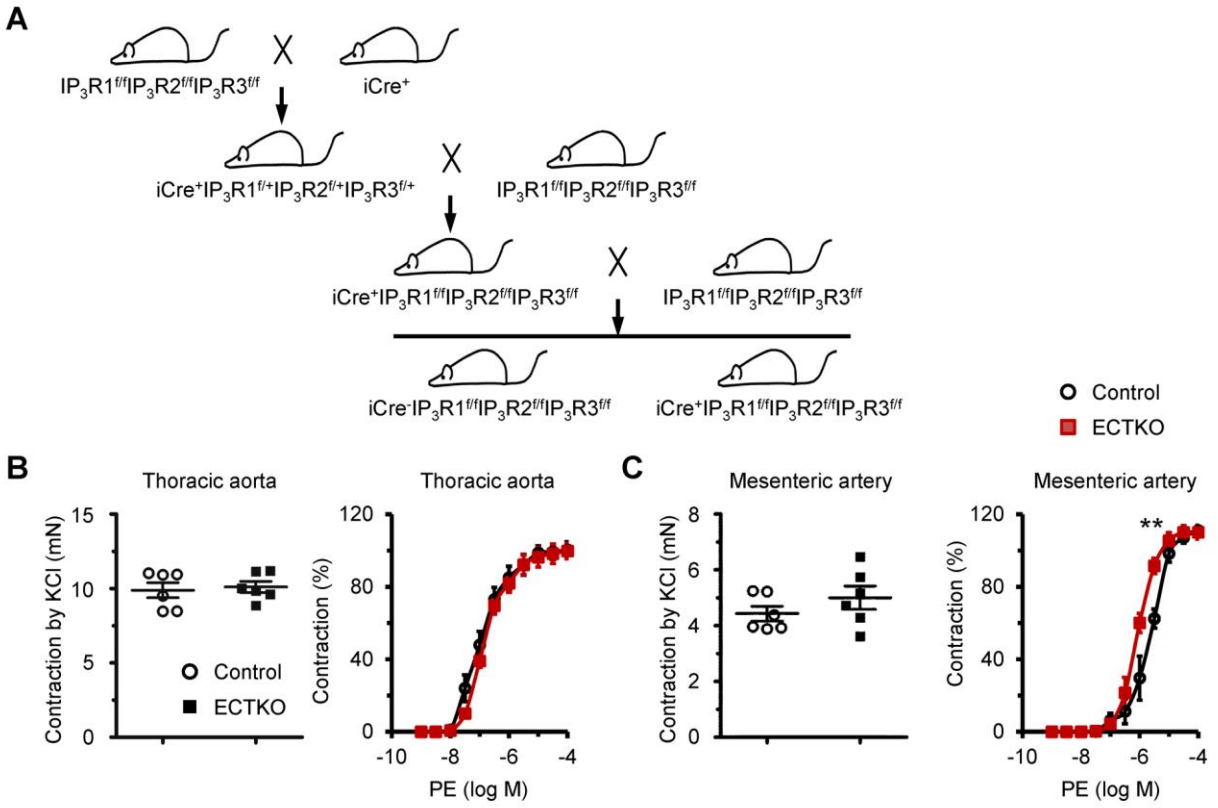
The Pdgfb-iCreER (iCre^{+}) mice were crossed with the ROSA$^{mT/mG}$ reporter mice to generate the iCre^{+}ROSA$^{mT/mG}$ mice. Administration of tamoxifen in adult iCre^{+}ROSA$^{mT/mG}$ mice led to expression of cell membrane-localized EGFP in endothelial cells, while non-endothelial cells expressed cell membrane-localized tdTomato. (**A**) Schematic diagram demonstrating the crossing strategy and the induction of EGFP expression. (**B**) Confocal fluorescent imaging showing the localization of EGFP and tdTomato in the cross-section of the mesenteric artery isolated from iCre^{+}ROSA$^{mT/mG}$ mice after tamoxifen administration. Scale bar, 40 μm.

Figure S2. Deletion of IP3R1 by Tie2-Cre in mice did not alter blood pressure and vasodilation.



The constitutively active Tie2-Cre instead of the inducible Pdgfb-iCreER was used to delete IP_3R1 in endothelial cells from as early as the embryonic stage. (**A**) Quantitative RT-PCR analysis of the expression of 3 IP_3R subtypes in isolated endothelial cells from Tie2-Cre$^-$R1$^{f/f}$ and Tie2-Cre$^+$R1$^{f/f}$ mice. n = 3 (with endothelial cells from 3 mice pooled as one sample) per group. Significance was determined by the 2-tailed, unpaired Student's t test. $^{**}P < 0.01$ versus Tie2-Cre$^-$R1$^{f/f}$ mice. Data are presented as mean ± SEM. (**B**) Systolic blood pressure (SBP) were measured at the ages of 3 months and 6 months using the tail cuff system, respectively. n = 5-8 mice per group. Significance was determined by 2-way ANOVA analysis with Bonferroni post-hoc test. (**C**) Vascular reactivity in response to ACh in aortas and mesenteric arteries. The vessels were pre-constricted by 10 μM phenylephrine (PE) and the vasorelaxing effects of ACh were presented as a percentage of PE-induced contraction. n = 6 mice per group. Significance was determined by 2-way ANOVA analysis with Bonferroni post-hoc test. (**D**) The ratio of ventricle weight to body weight was comparable between Tie2-Cre$^-$R1$^{f/f}$ and Tie2-Cre$^+$R1$^{f/f}$ mice at the age of 6 months. n = 9 mice per group. Significance was determined by 2-tailed, unpaired Student's t test.

Figure S3. Mouse breeding strategy and measurement of vascular contractility in control and ECTKO mice.



(**A**) Schematic diagram showing the mouse breeding strategy to generate $iCre^{+}IP_3R1^{f/f}$ $IP_3R2^{f/f}$ $IP_3R3^{f/f}$ mice. (**B**) Reference contraction induced by high potassium (100mM) and the dose-dependent contractile response to phenylephrine (PE) in control and ECTKO aortas. n = 6 per group. (**C**) Reference contraction induced by high potassium (100mM) and the dose-dependent contractile response to phenylephrine (PE) in control and ECTKO mesenteric arteries. n = 6 per group. For all dose-response curves, data were expressed as a percentage of the peak of K^{+}-induced contraction, and significance was determined by 2-tailed, unpaired Student's t test or 2-way ANOVA analysis with Bonferroni post-hoc test. **P < 0.01 versus control. Error bars represent mean ± SEM.