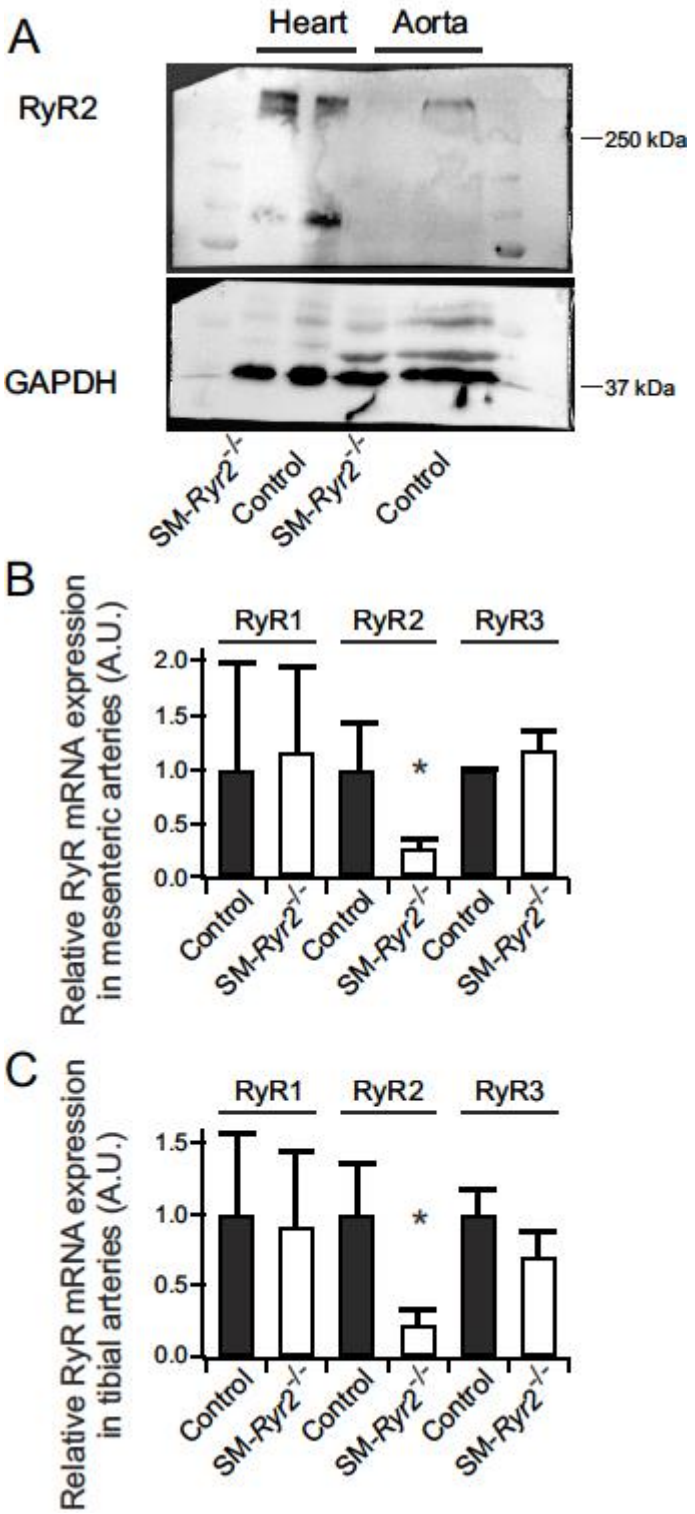
Supplemental Material

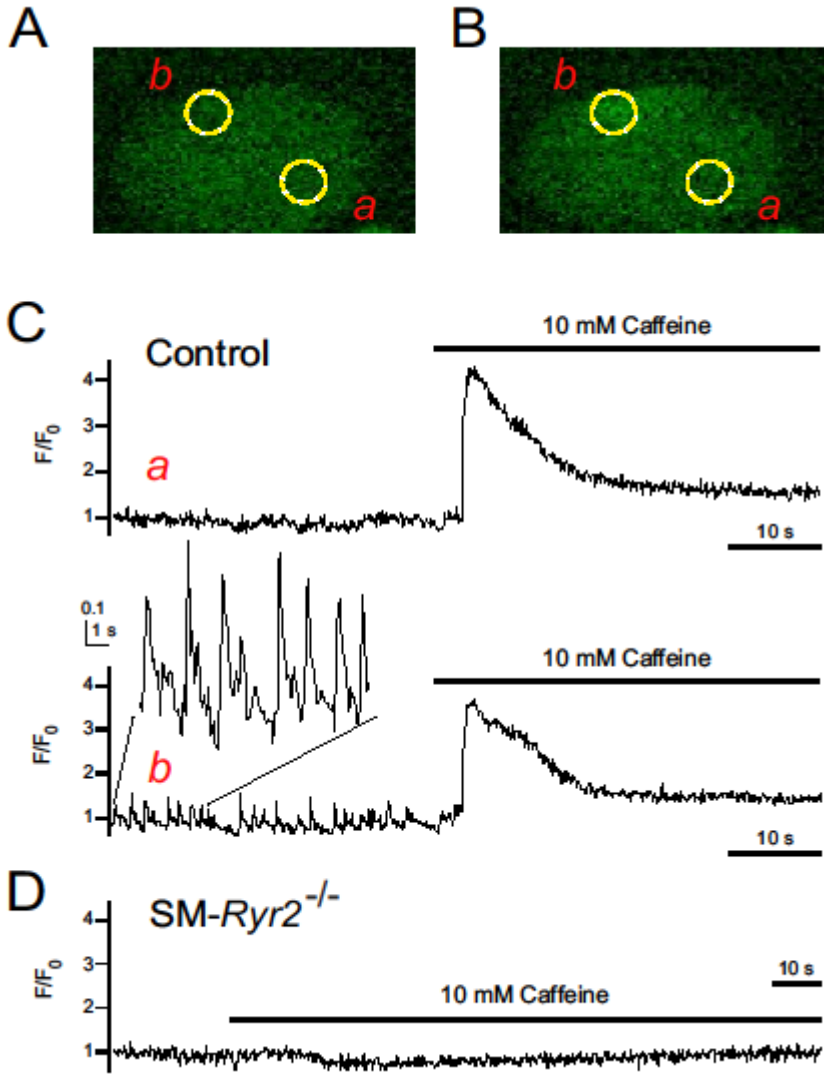
Figure S1. Detection of RyR2 in hearts and different arteries of wild-type and SM-*Ryr2*$^{-/-}$ mice.



A, Full-range Western blot of RyR2 in aortas from wild-type (control) and SM-*Ryr*2$^{-/-}$ mice; 40 µg of aortic tissue and 10 µg of heart tissue were loaded per lane. B, mRNA expression for RyR1, RyR2, and RyR3 in mouse mesenteric artery tissue and C, for mouse tibial artery tissue. mRNA levels for RyR1/2/3 were normalized against 18s mRNA. Mean mRNA expression value was arbitrarily set at 100 for wild-type control tissue, and relative expression was calculated for SM-*Ryr2*$^{-/-}$ tissue (panel B: n = 3 *vs.* 2 arterial tissues each for

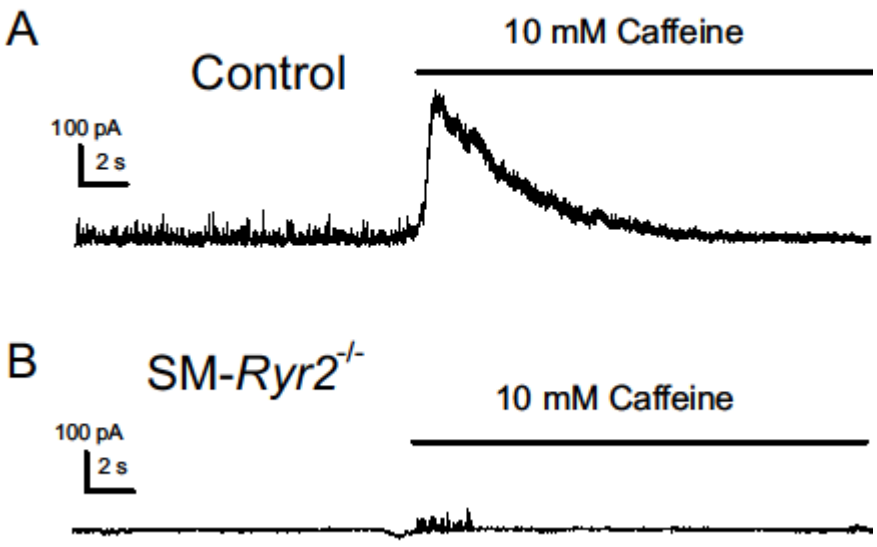
RyR1, n = 4 vs. 5 arterial tissues each for RyR2 and n = 2 *vs*. 2 arterial tissues each for RyR3 from n = 4 control mice and n = 5 SM-*Ryr2*$^{-/-}$ mice, respectively; panel C: n=4 *vs.* n=5 arterial tissues (RyR1, RyR2, RyR3) each from n = 4 control mice and n = 5 SM-*Ryr2*$^{-/-}$ mice, respectively; *, $p < 0.01$ vs. wild-type; one-sample t-test).

Figure S2. Ca^{2+} sparks in wild-type and SM-*Ryr2*$^{-/-}$ mesenteric artery SMCs.



A, Ca^{2+} fluorescence image of a Fluo-4-AM–loaded control VSMC. **B**, Ca^{2+} fluorescence image of the same cell as in A during the occurrence of a Ca^{2+} spark. Two-dimensional images were recorded at a rate of 10 s^{-1}. **C**, Time course of Ca^{2+} fluorescence changes in cellular ROIs without sparks (ROI *a,* upper panel) and with sparks (ROI *b,* lower panel). Note that ROIs *a* and *b* are also labeled in panels A and B. Presence of caffeine (10 mmol/L) is indicated in by horizontal lines. **D**, Time course of Ca^{2+} fluorescence changes in a ROI (similar size as that in panel A) of a SM-*Ryr2*$^{-/-}$ VSMC in the absence and presence of caffeine (10 mmol/L).

Figure S3. BK_{Ca} channel currents in response to caffeine in wild-type and SM-*Ryr2*$^{-/-}$ VSMCs.



A, Whole-cell outward current in a tibial artery SMC isolated from a wild-type (control) mouse. Holding potential was -40 mV. The presence of caffeine is indicated by a horizontal line. **B**, Same protocol as in A, but the VSMC was isolated from a SM-*Ryr2*$^{-/-}$ mouse. Mean values for the evoked currents were larger in control cells (203 ± 41 pA, n = 5 cells out of 3 mice) compared to SM-*Ryr2*$^{-/-}$ cells (16 ± 11 pA, n = 11 cells out of 2 mice; $p < 0.05$).