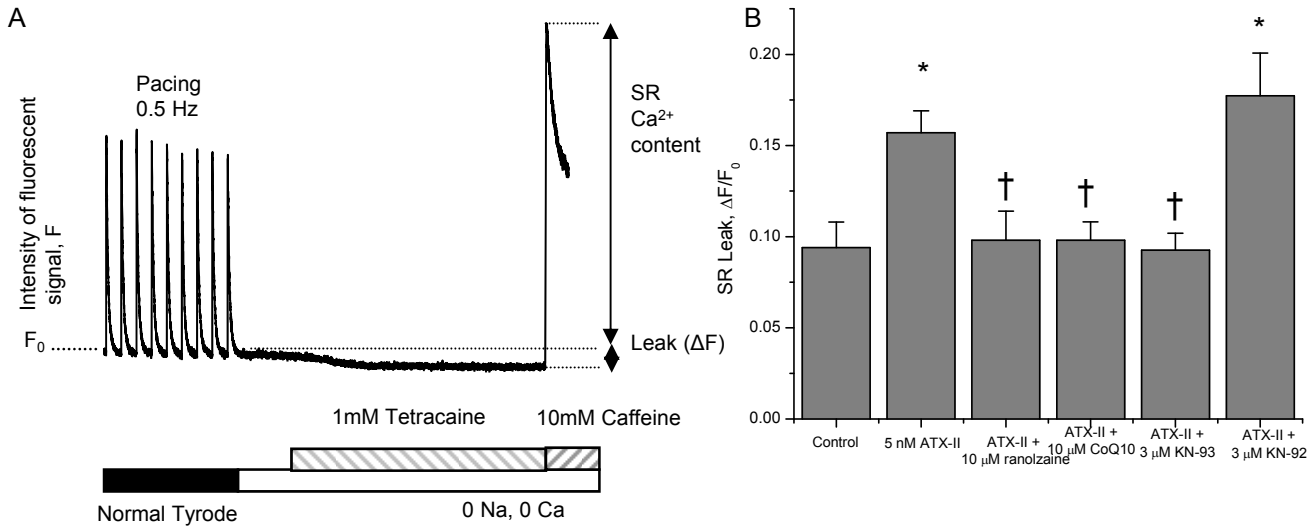
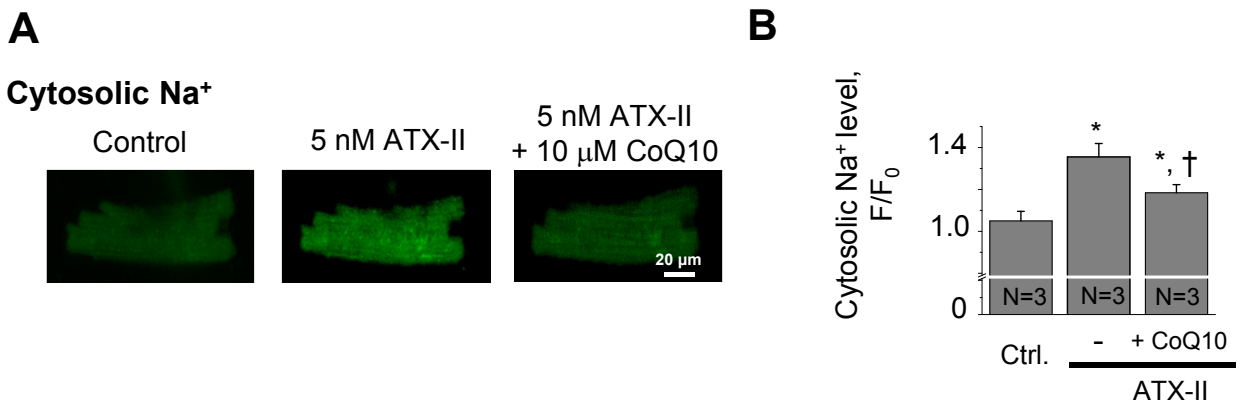
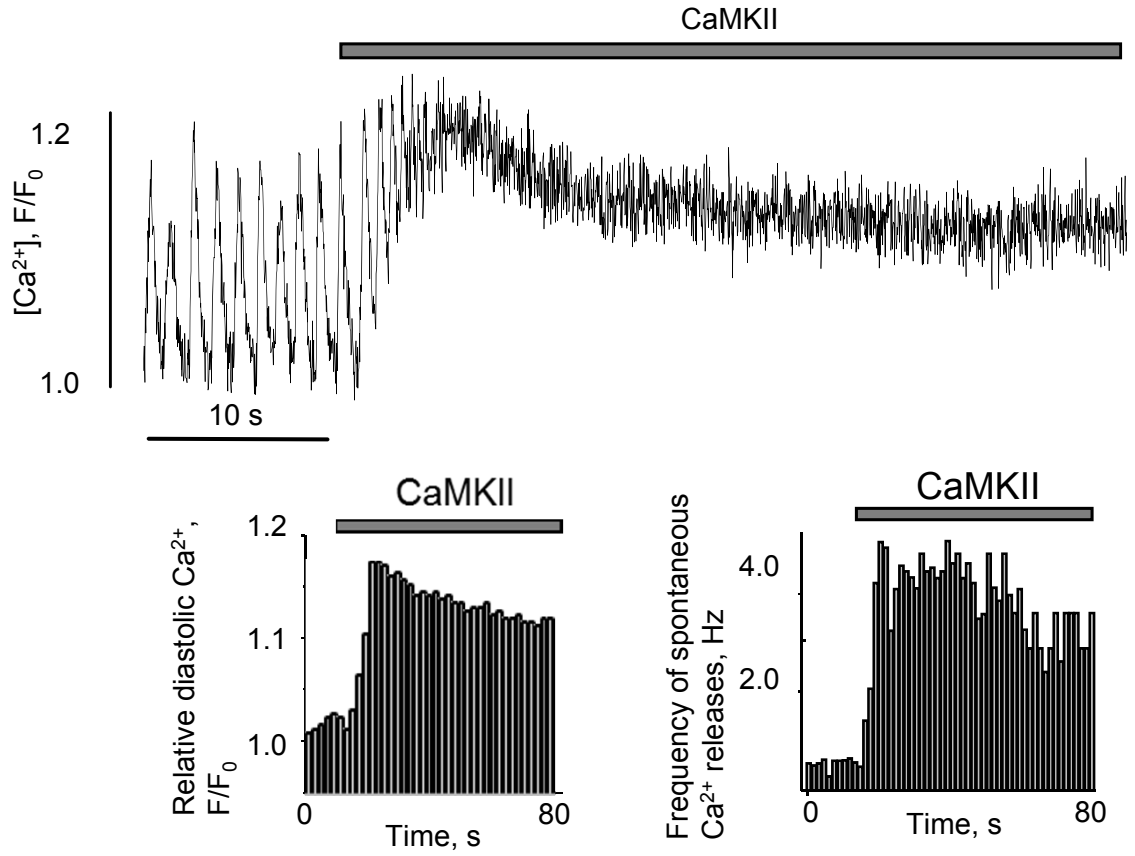
Supplemental Figures and Table



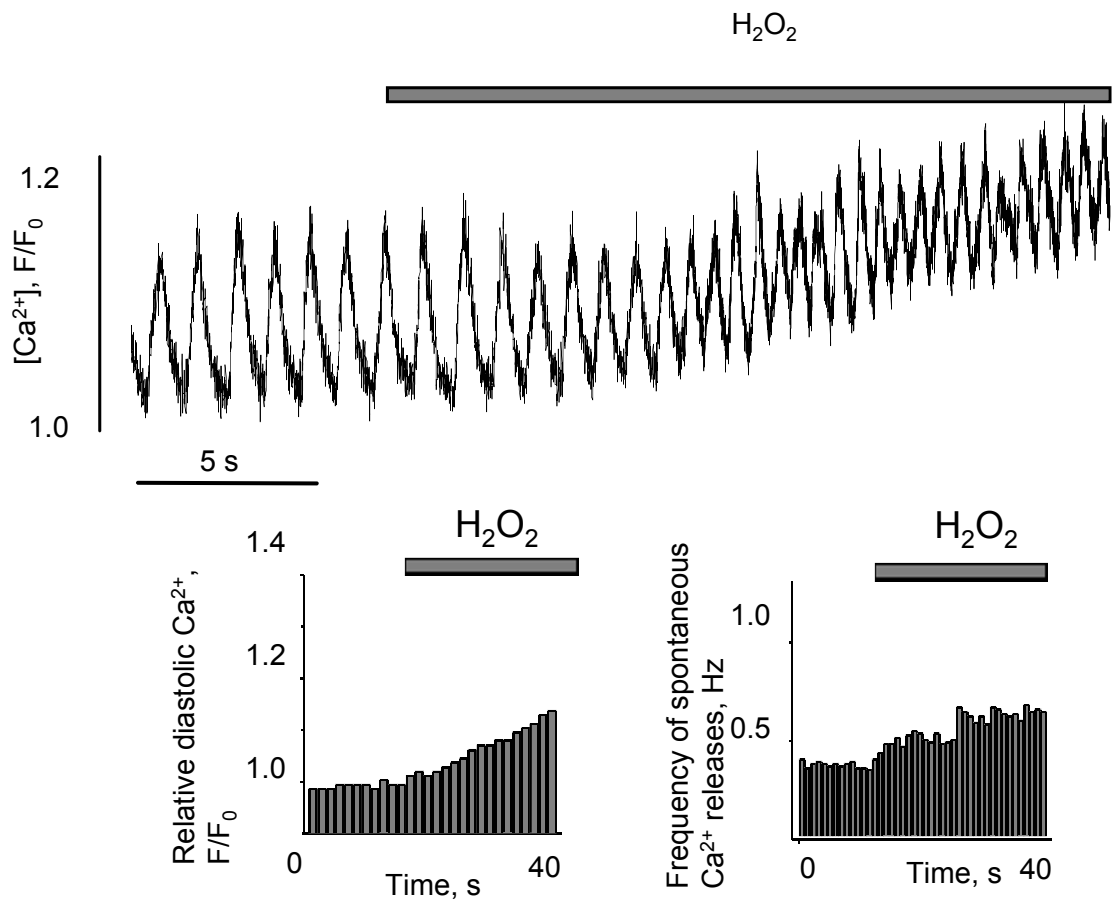
Supplementary Figure 1. ATX-II induced diastolic Ca^{2+} leak in rabbit ventricular myocytes. A:. Scheme of protocol used to estimate diastolic SR Ca^{2+} leak. B. Pooled data on SR Ca^{2+} leak in control cells, after AXT-II application alone and after application of ATX-II + CoQ10, ATX-II + KN-93 and ATX-II + KN-92. N=5-13, * $P<0.05$ vs control; †$P<0.05$ vs ATX-II.



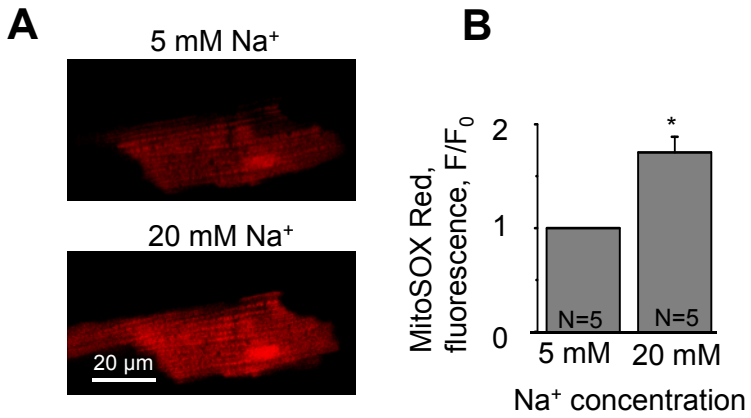
Supplementary Figure 2. Antioxidant CoQ10 reduced Na^+_i overload induces by ATX-II.
A. Confocal images of a rabbit ventricular myocyte paced at 1 Hz and loaded with Na^+ dye Asante NaTRIUM Green AM. Application of ATX-II (5 nM) for 2 min increased cytosolic Na^+ compared to control (Ctrl), which was reduced by CoQ10 (10 μM). **B.** Quantification of results for ATX-II-induced changes cytosolic Na^+, in the absence and presence of CoQ10 (10 μM). Data are normalized to F_0 - the baseline fluorescence signal at the beginning of an experiment. N=3, * $p<0.05$ vs control; † $P<0.05$ vs ATX-II.



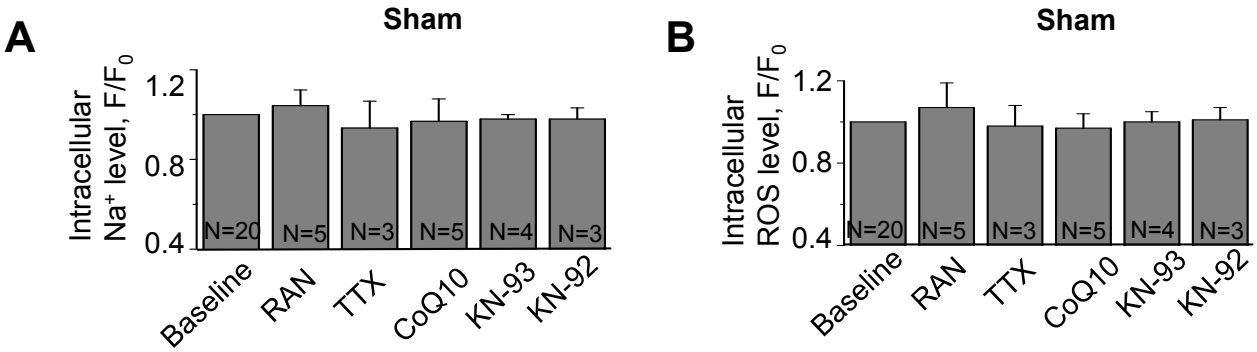
Supplementary Figure 3. Effect of exogenous pre-activated CaMKII (2 units activity/L) on spontaneous Ca^{2+} waves in membrane-permeabilized rabbit ventricular myocytes. Cytosolic Na^{+} concentration was 5 mM.



Supplementary Figure 4. Effect of H_2O_2 (100 μM) on spontaneous Ca^{2+} waves in membrane-permeabilized rabbit ventricular myocytes. Cytosolic Na^+ concentration was 5 mM.



Supplementary Figure 5. Elevated $[Na^+]_i$ increases mitochondrial ROS in membrane-permeabilized cardiomyocytes. A. Mitochondrial ROS level was assessed using MitoSOX Red in permeabilized rabbit ventricular myocytes subjected to 5 mM and 20 mM Na^+. B. High $[Na^+]_i$ resulted in an increase in mitochondrial ROS generation. N=5, * $p<0.05$ (20 mM Na^+ vs. 5mM Na^+).



Supplementary Figure 6. Effects of ranolazine (10 μM), TTX (1 μM), CoQ10 (10 μM), KN-93 (3 μM), and KN-92 (3 μM) on levels of intracellular Na^+ (A) and ROS (B) in myocytes isolated from sham mice and paced at a rate of 1 Hz (N = 3-20, $p<0.05$ compared to baseline).

	Ca^{2+} signal amplitude, F_{max}/F_0	Rise time of Ca^{2+} transients (ms)	τ decay Ca^{2+} transients (ms)	Number of experiments, N
Sham	2.6 ± 0.3	28 ± 5	183 ± 11	7
TAC	2.5 ± 0.5	39 ± 4 *	201± 17	6
TAC + 3 μmol/L KN93	2.4 ± 0.4	27 ± 7	188 ± 11	3

Supplementary Table 1. Parameters of pacing-induced Ca^{2+} transients in TAC ventricular myocytes. F_0 – baseline fluorescence, F_{max} – level of fluorescence at the peak of Ca^{2+} transient.* $p<0.05$ vs sham.