Supplemental Figure 1

Supplemental Figure 1 Effect of EMD (3 µM) on ventricular action potential, L-type Ca\(^{2+}\) currents and outward K\(^{+}\)-currents

(A) Membrane potential recording using the perforated patch technique from a mouse ventricular myocyte paced at 4 Hz at baseline (CON) and in presence of EMD.

(B) Mean APD90, APD70, APD50 and APD30 before and after application of EMD. *p<0.05 by paired t-test. N=7 myocytes

(C) Strong cytosolic buffering with EGTA (14 mM) that prevents myofilament activation and myocyte contraction completely abolishes the effect of EMD on mean APD90, APD70, APD50 and APD30. N=12 myocytes

(D) L-type Ca\(^{2+}\) currents recorded in response to step-wise membrane depolarizations. EMD has no significant effect. N=8 myocytes

(E) Voltage-gated outward K\(^{+}\) currents recorded in response to step-wise membrane depolarizations. EMD has no significant effect. N=9 myocytes

Supplemental Figure 2

Supplemental Figure 2 Ca\(^{2+}\) sensitized transgenic hearts exhibit APD70 shortening at all pacing rates.

(A-D) Average AP durations measured at 90% (APD90, panel A), 70% (APD70, panel B) 50% (APD50, panel C), and 30% repolarization (APD30, panel D) plotted as function of pacing cycle length (PCL). Note that Ca\(^{2+}\) sensitized transgenic hearts (I79N and ssTNI) exhibited significantly shortened APD70 at all pacing rates. APD90, APD50 and APD30 were not significantly different from NTG or WT hearts. NTG n=6 hearts, WT n=12, R278C n=6, I79N n=11, ssTNI n=6. **p<0.01 by 2-way ANOVA with repeated measures compared to WT or NTG.
Supplemental Figure 3 Beat-to-beat APD instability is significantly increased in Ca^{2+}-sensitized mouse and cat hearts.

(A) Example of a prominent APD alternans in an I79N heart. Pacing cycle length (PCL) = 100 ms.

(B-C) Average beat-to-beat instability in APD90 of mouse (B) and cat (C) hearts at two different pacing rates. APD instability increased with faster pacing predominantly in the Ca^{2+} sensitized hearts. To quantify APD instability, the absolute difference in the APD90 between two consecutive beats was measured and expressed as % of APD90. For each heart and each pacing rate, 7-10 consecutive beats were analyzed and averaged. N = 6-7 mouse hearts per group, n = 7-9 recordings from 4 cat hearts per group, *p<0.05, **p<0.01 compared to NTG and WT for mouse hearts and compared to CON and WASH for cat hearts by Mann-Whitney Test.