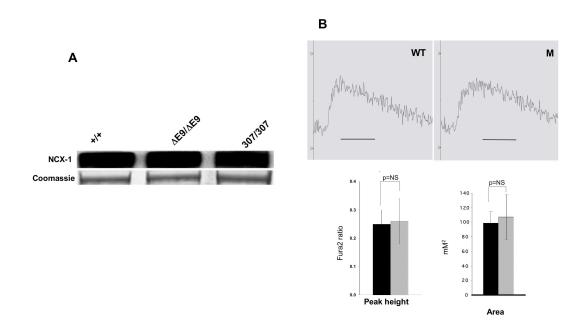
	WT (n=6)	M (n=9)	P value
Baseline (F2 ratio)	0.66±0.13	0.659±0.07	ns
Peak height (F2 ratio)	0.25±0.05	0.26±0.8	ns
Time to peak 50% (msec)	17±6	26±12	ns
Tau (msec)	389±57	425±73	ns
Area (mm²)	99±16	107±31	ns

**Supplement Table 1.** Ca<sup>2+</sup> transients of electrically paced wild-type and CASQ2 deficient cardiomyocytes during constant Caffeine (10mM) perfusion

	WT	WT+ Mg <sup>2+</sup>	P value
Baseline (F2 ratio)	0.5±0.14	0.47±0.10	ns
Peak height (F2 ratio)	0.39±0.009	0.25±0.03	0.001
Time to peak 50% (msec)	9±1	10±3	ns
Tau (msec)	119±19	123±21	ns
Area (mm²)	55±17	36±6	0.014
Rest Sarcomere length (µm)	1.71±6	1.7±5	ns
% Sarcomere shortening	6.6±2.5	2.7±1.6	0.001

**Supplement Table 2.** Ca<sup>2+</sup> transients and sarcomere lengths of wild-type Cells with and without Mg. Analysis of 14 cells from 3 mice.

## Supplement Figure 1



**Figure 1.** Assessment of Na<sup>+</sup>/Ca<sup>2+</sup> exchanger (NCX) levels and activity. (**A**) Western blot analyses of NCX protein in cardiac extracts from mutant and wildtype mice. Note unchanged protein levels in CASQ2-deficient hearts. (**B**) Ca<sup>2+</sup> transients produced by electrical stimulation (60 Hz) of wildtype (WT) and CASQ2-deficient (M = CASQ<sup> $\Delta$ E9/ $\Delta$ E9</sup> and CASQ<sup>307/307</sup>) myocytes in 10mM caffeine Ca<sup>2+</sup> Tyrode solution. Traces represent the average of 15 contraction-relaxation cycles from one representative cell of each genotype. (Bar = 0.2 second). Graphs denote pooled data from 6 WT (black) and 9 mutant cells (striped). \* p=ns.