Supplemental Material

Supplemental Table I. Sarcomere function and cytoplasmic calcium in freshly-isolated myocytes from WT and SKI mice.

Sarcomere	WT	SKI	p-value
Baseline (um)	1.86 ± 0.01	1.82 ± 0.01	0.07
Dep V (um/sec)	-2.77 <u>+</u> 0.33	-1.57 <u>+</u> 0.18	0.002*
Peak T (msec)	0.038 ± 0.001	0.047 ± 0.002	0.009*
Calcium	WT	SKI	p-value
Diastolic	1.64 <u>+</u> 0.05	1.58 <u>+</u> 0.04	0.32
Dep V (um/sec)	76.97 <u>+</u> 5.7	59.8 <u>+</u> 5.03	0.02*
Systolic	2.19 ± 0.06	2.04 <u>+</u> 0.06	0.08
Peak T (msec)	0.017 ± 0.00	0.019 <u>+</u> 0.001	0.13

Values are mean \pm SEM. (n=7-12; *P<0.05 vs. WT; unpaired t-test).

Supplemental Figure I.

A.



WT Sham SKI Sham WT AAC SKI AAC

B.



Supplemental Figure I. Cardiac myocyte crosssectional area. Panel A. Representative photomicrograph of myocardium stained with hematoxylin and eosin (bar = 25μ m). Panel B. Mean myocyte cross-sectional area measured 12 weeks after AAC (n = 5-7; * = P<0.001 vs. WT sham; # = P<0.01 vs. WT AAC; ANOVA with Bonferroni correction).

Supplemental Figure II.

Α.



WT Sham SKI Sham WT AAC SKI AAC



Supplemental Figure II. Interstitial fibrosis. Panel A. Representative photomicrograph of myocardium stained with Masson's trichrome to assess fibrosis (collagen stains blue; bar = 50 μ m). Panel B. Mean percentage of interstitial fibrosis as assessed with Masson's trichrome staining measured 12 weeks after AAC (n = 5-7; * = P<0.05 vs. WT Sham; #= P<0.05 vs. WT AAC; ANOVA with Bonferroni correction).

Supplemental Figure III.



WT Sham SKI Sham WT AAC SKI AAC

Supplemental Figure III. Immunohistochemical staining to identify active caspase 3. Cleaved caspase 3 stains red. Bar = $25 \mu m$. Score data are depicted in Figure 7A.

Supplemental Figure IV.



Supplemental Figure IV. TUNEL staining to identify cardiac myocyte apoptosis 12 weeks after AAC. Representative photomicrographs (40X magnification) of left ventricular myocardium illustrating technique for identification of terminal deoxynucleotidyl transferase dUTP nick end-labeling (TUNEL) of apoptotic myocytes. An apoptotic nucleus (arrow) is identified by green fluorescence; nuclei stained by Hoechst 33258 are shown in blue; cardiomyocytes identified by α -sarcomeric actin staining are shown in red. Mean data are depicted in Figure 7B.