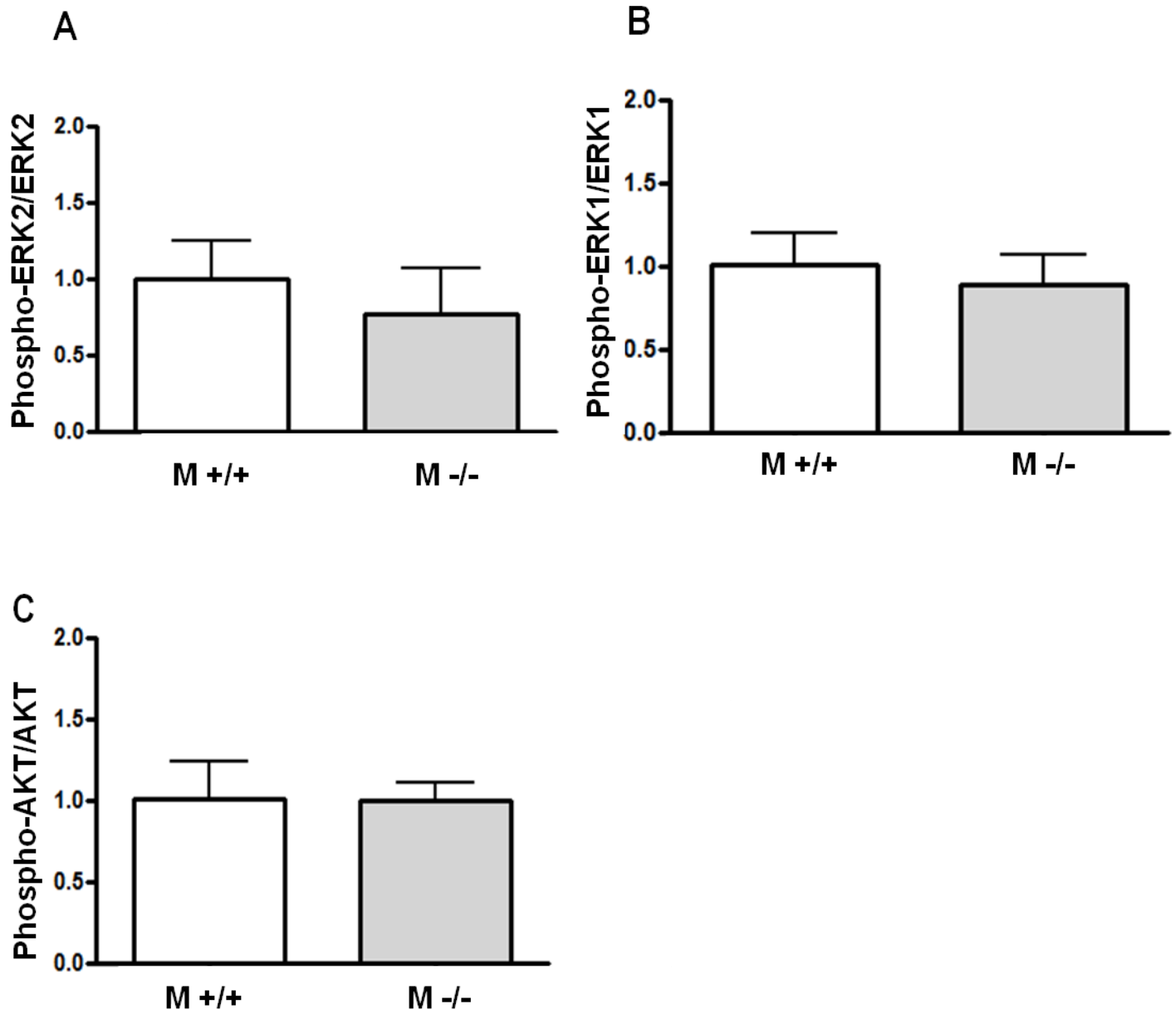


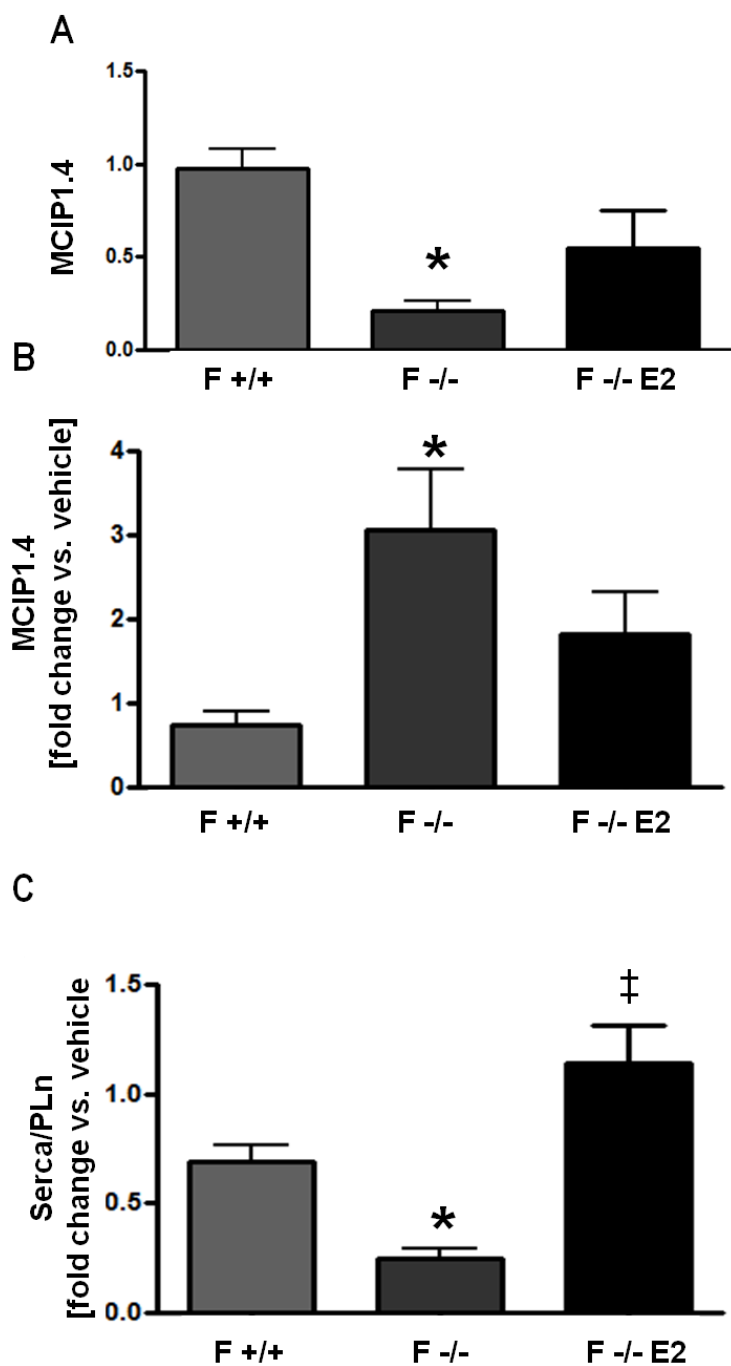
C

	1	2	3	4	5	6	7	8	9
A	Positive Control	p38 α	ERK1/2	JNK	GSK-3 α/β	Blank	p53 (S392)	Blank	Positive Control
B	Blank	MEK 1/2	MSK 1/2	AMPK α 1	AKT (S473)	Akt (T308)	p53 (S46)	Blank	Blank
C	TOR	CREB	HSP27	AMPK α 2	B-catenin	p70 S6 K (T389)	p53 (S15)	P27 (T198)	Paxillin
D	Src	Lyn	Lck	STAT2	STAT5a	p70 S6 Ki (T421)	RSK 1/2/3 (S380)	P27 (T157)	PLC γ -1
E	Fyn	Yes	Fgr	STAT3	STAT5b	p70 S6 Ki (T229)	RSK 1/2 (S221)	c-jun	Pyk2
F	Hck	Chk-2	FAK	STAT6	STAT5a/b	Stat1	Stat4	eNOS	Blank
G	Positive Control	Blank	Blank	Blank	Blank	Blank	Blank	Blank	Blank

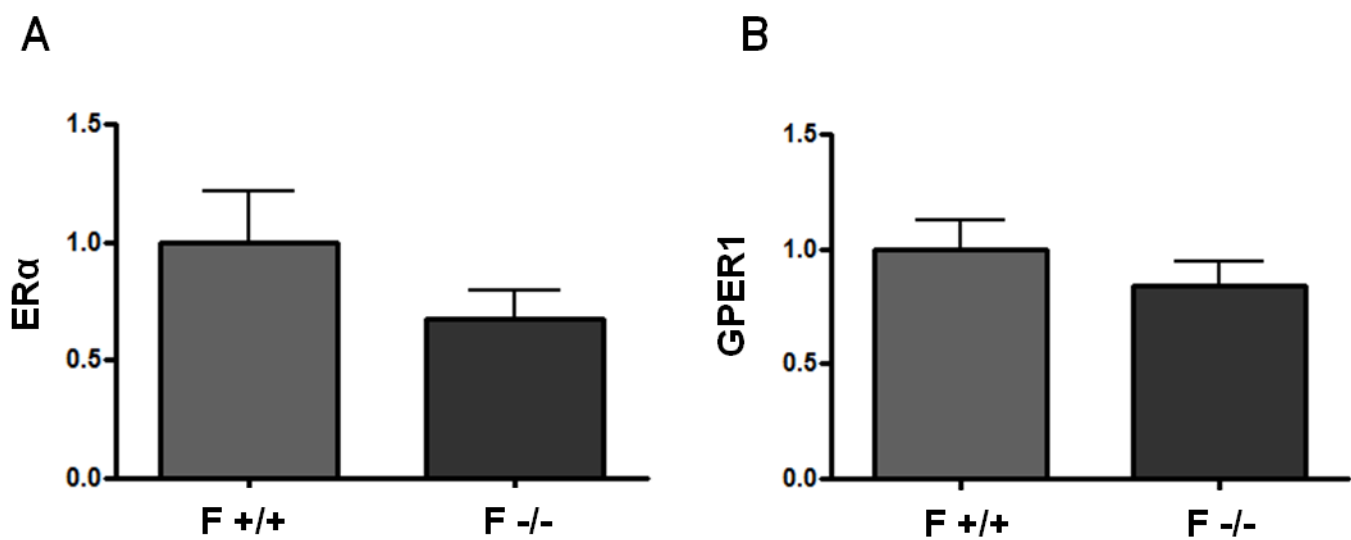
Supplemental Figure 1. *Phospho-kinase array of selected kinases in female ArKO and WT hearts.* The phosphorylation level of 46 intracellular kinases in female WT (A) vs. female ArKO (B) was measured using a phospho-kinase array. Cardiac lysates from three animals per group were pooled for each array. (C) The location of specific kinases on the phospho-kinase array.



Supplemental Figure 2. *Phosphorylation of selected kinases in male ArKO mouse hearts.* Quantification of western blot analyses of pERK2/ERK2 (A), pERK1/ERK1 (B), and pAKT/AKT (C) in male WT and ArKO hearts.



Supplemental Figure 3. Transcriptional analyses of the selected genes. (A) MCIP1.4 mRNA levels in vehicle-treated animals. (B) Fold change of MCIP1.4 after 7 days of Iso treatment compared to vehicle controls. (C) Fold change of the ratio of SERCA to PLN after 7 days of Iso treatment compared to vehicle controls. All genes were measured using qRT-PCR and normalized to 18s.. *, $p < 0.05$ relative to F +/+, ‡, $p < 0.05$ relative to F -/-, n=4-5 animals per group



Supplemental Figure 3. *Transcriptional analyses of the selected genes.* (A) ER α mRNA levels in WT and ArKO females (B) GPER1 mRNA levels in WT and ArKO mice. All genes were measured using qRT-PCR and normalized to GAPDH, n=4-5 animals per group

		BW (g)	HW (mg)	LVW (mg)	HW/BW (mg/g)
Female					
	WT Vehicle	25.9 ± 0.6	137 ± 3.3	100 ± 3.1	5.3 ± 0.17
	WT Iso	25.3 ± 0.6	153 ± 3.45	115 ± 4.5	6.1 ± 0.10
	ArKO Vehicle	26.9 ± 0.8	119 ± 5.7	83 ± 5.4	4.4 ± 0.15
	ArKO Iso	26.7 ± 0.9	151 ± 4.5	109 ± 5.1	5.7 ± 0.12
	ArKO E2 Vehicle	23.7 ± 1.1	118 ± 8.9	88 ± 7.6	4.9 ± 0.26
	ArKO E2 Iso	21.8 ± 3.9	136 ± 23.4	102 ± 18	6.3 ± 0.98
Male					
	WT Vehicle	31.8 ± 1.0	151 ± 6.4	107 ± 6.4	4.8 ± 0.16
	WT Iso	31.9 ± 1.0	181 ± 6.9	135 ± 5.9	5.7 ± 0.17
	ArKO Vehicle	31.4 ± 1.1	146 ± 5.8	108 ± 2.3	4.7 ± 0.30
	ArKO Iso	28.5 ± 0.6	173 ± 3.0	126 ± 2.4	6.1 ± 0.14

Supplemental Table 1 – *Morphometric parameters of mice treated for seven days with vehicle or Isoproterenol.*

		BW (g)	HW (mg)	LVW (mg)	HW/BW (mg/g)
Female					
	WT Sedentary	24.5 ± 1.0	124 ± 4.3	95 ± 1.3	5.1 ± 0.22
	WT Exercise	23.3 ± 0.5	138 ± 5.3	110 ± 2.6	5.9 ± 0.16
	ArKO Sedentary	30.0 ± 1.3	127 ± 3.4	97 ± 2.0	4.3 ± .15
	ArKO Exercise	25.0 ± 1.6	138 ± 7.3	105 ± 3.2	5.6 ± 0.26
Male					
	WT Sedentary	36.3 ± 1.7	153 ± 3.5	114 ± 4.0	4.3 ± 0.17
	WT Exercise	28.2 ± 1.1	156 ± 6.7	126 ± 2.0	5.6 ± 0.11
	ArKO Sedentary	32.7 ± 1.8	146.4 ± 6.7	103 ± 7.1	4.5 ± 0.22
	ArKO Exercise	28.5 ± 0.6	159 ± 5.3	120 ± 5.7	5.6 ± 0.16

Supplemental Table 2 – *Morphometric parameters of sedentary mice or mice exercised for twenty-one days.*

		BW (g)	HW (mg)	LVW (mg)	HW/BW (mg/g)
Female					
	WT Sedentary	24.5 ± 1.0	124 ± 4.3	95 ± 1.3	5.1 ± 0.22
	WT Exercise	22.8 ± 0.6	136 ± 4.6	102 ± 3.0	5.9 ± 0.19
	ArKO Sedentary	30.0 ± 1.3	127 ± 3.4	97 ± 2.0	4.3 ± .15
	ArKO Exercise	25.5 ± 0.9	132 ± 3.5	98 ± 1.6	5.2 ± 0.23

Supplemental Table 3 – *Morphometric parameters of sedentary mice or mice exercised for seven days.*

Gene	Forward Primer	Reverse Primer
GATA-4	5'-CCCTACCCAGCCTACATGG-3'	5'-ACATATCGAGATTGGGGTGTCT-3'
NKX2.5	5'-CAAGTGCTCTCCTGCTTTCC-3'	5'-CTTTGTCCAGCTCCACTGC-3'
ANF	5'-CCAGGCCATATTGGAGCAA-3'	5'-GAAGCTGTTGCAGCCTAGTC-3'
MCIP1.4	5'-AGCTCCCTGATTGCTTGTGT-3'	5'-TGGAAGGTGGTGTCTTGT-3'
SERCA	5'-TGTAAGTGCCAGATTGCTC-3'	5'-CCTAAACAACCTGAAGTTAGG-3'
PLN	5'-GTTGTGCCCTTTTTCTACAC-3'	5'-AGAGAGAGCAGATTTGTGG-3'
ERα	5'-GATCATGGAGTCTGCCAAGGA-3'	5'-AGCCAGAGGCATAGTCATTGC-3'
GPER1	5'-TCTAGGGAGAAAGCCATCCA-3'	5'-TGTCTGATGTCTGGGCTGGT-3'
18s	5'-GCCGCTAGAGGTGAAATTCTT-3'	5'-CTTTCGCTCTGGTCCGTCTT-3'
GAPDH	5'-AGGTCGGTGTGAACGGATTTG-3'	5'-TGTAGACCATGTAGTTGAGGTCA-3'

Supplemental Table 4 – Primer sequences used for Quantitative PCR