#### SUPPLEMENTAL FIGURE LEGENDS

**Supplemental Figure 1.** (A-D) HDAC3 expression was analyzed in wild-type and multiple settings of cardiac dysfunction. HDAC3 expression was not significantly changed following angiotensin infusion (A), thoracic aortic constriction (B), or myocardial infarction (C). HDAC3 expression was significantly decreased following 7 days of isoproterenol infusion (D). (E) No significant difference was seen in HDAC3 protein levels between wild-type and ZDF rat hearts. \*P<0.05 versus wild-type littermates. ANG, angiotensin; TAC, thoracic aortic constriction; MI, myocardial infarction; BZ, border zone; REM, remote; ISO, isoproterenol.

**Supplemental Figure 2.** Electrocardiography (ECG) from lead II of wild-type and HDAC3cKO mice. HDAC3cKO mice show no overt abnormalities in sinus rhythm, although do show a larger QRS complex, indicative of a larger heart.

Supplemental Figure 3. Nuclear receptor expression in HDAC3cKO hearts. PPAR $\alpha$ , PPAR $\gamma$ , ERR $\alpha$ , and PGC-1 $\alpha$  were analyzed by real-time PCR. No significant changes were detected. All samples were normalized to 18S.

**Supplemental Figure 4.** MEF2 activity is moderately increased in HDAC3cKO hearts. HDAC3cKO mice were crossed to the desMEF reporter mice and stained for betagalactosidase activity. Only moderate induction of MEF2 is seen at 6 weeks of age, however, this is a timepoint where these mice are undergoing they hypertrophic program. **Supplemental Data.** Spreadsheets of all significantly up-regulated and down-regulated genes in HDAC3cKO hearts at 5-weeks-old compared to wild-type littermates.



## Supp Fig 1

### wild-type

### HDAC3cKO







# Supp Fig 3







HDAC3<sup>loxP/+</sup>;

 $\alpha$ MHC-Cre;











### Supp Fig 4

Primers for genotyping as seen in Figure 1C.

HDAC3	5'	loxP	For Primer
HDAC3	5'	loxP	Rev Primer
HDAC3	3'	loxP	Rev Primer

GCTTGGTAGCCAGCCAGCTTAG CATGTGACCCCAGACATGACTGG CAGTCCATGCCTATAATCCCAGC

Primers for RT-PCR as seen in Figure 2A.

HDAC3 exon 10 For Primer	GGCTGTGATCGATTAGGCTGC
HDAC3 exon 13 For Primer	CCGCATCGAGAATCAGAACTC
HDAC3 exon 15 Rev Primer	CCTTGTCGTTGTCATGGTCGCC

Primers for ChIP assays as seen in Figure 6A.

UCP2 For Primer	CTTGGCTTAGCTTGGTGCAGAG
UCP2 Rev Primer	TCCAGGGACCGGAACCAACC
UCP3 For Primer	GGAATCCAGTGCCTCCATGC
UCP3 Rev Primer	GAAGCCTGAGCAGGGAACAG
FACS For Primer	TTCCCACCGGGAACCTAGCA
FACS Rev Primer	GAAGTTGCTGGTGGTGGGGGTA
FATP For Primer	GAATCTCGGTCCAGGGTGCC
FATP Rev Primer	GCTCACACTTGATCACTCTTGC
PDK4 For Primer	CAGGTGCACAGCCCTTTGAG
PDK Rev Primer	CGAGCTGTTCTCCCGCTACAG
UCP3 exon 5 For	GGGTGTGGTGTCTGTCTGTG
UCP3 exon 5 Rev	TCCAGCAGCTTCTCCTTGAT

Primers for qChIP assays as seen in Figure 6C.

mUCP2 For	GTGCAACAGGCGAGGCTCT
mUCP2 Rev	ACCGGCACAAACCCGGGTG
mUCP3 For	GGAGCCACATTAAAGAGCCC
mUCP3 Rev	CACCATTCACTGTTGTCTCTGC
mFACS For	GAGGCTATGCCAAGGTGTC
mFACS Rev	GAGCATGGCTGTCAGCAAGC
mFATP For	GGGTCAAGAGCCCTAAACCTAA
mFATP Rev	TGCCTGCCCTCCTACTTGCTC
mPDK For	GAGAATCCCGAGTTCTTCGGT
mPDK Rev	CAGCTGCTGGACTTTGGTGAGA