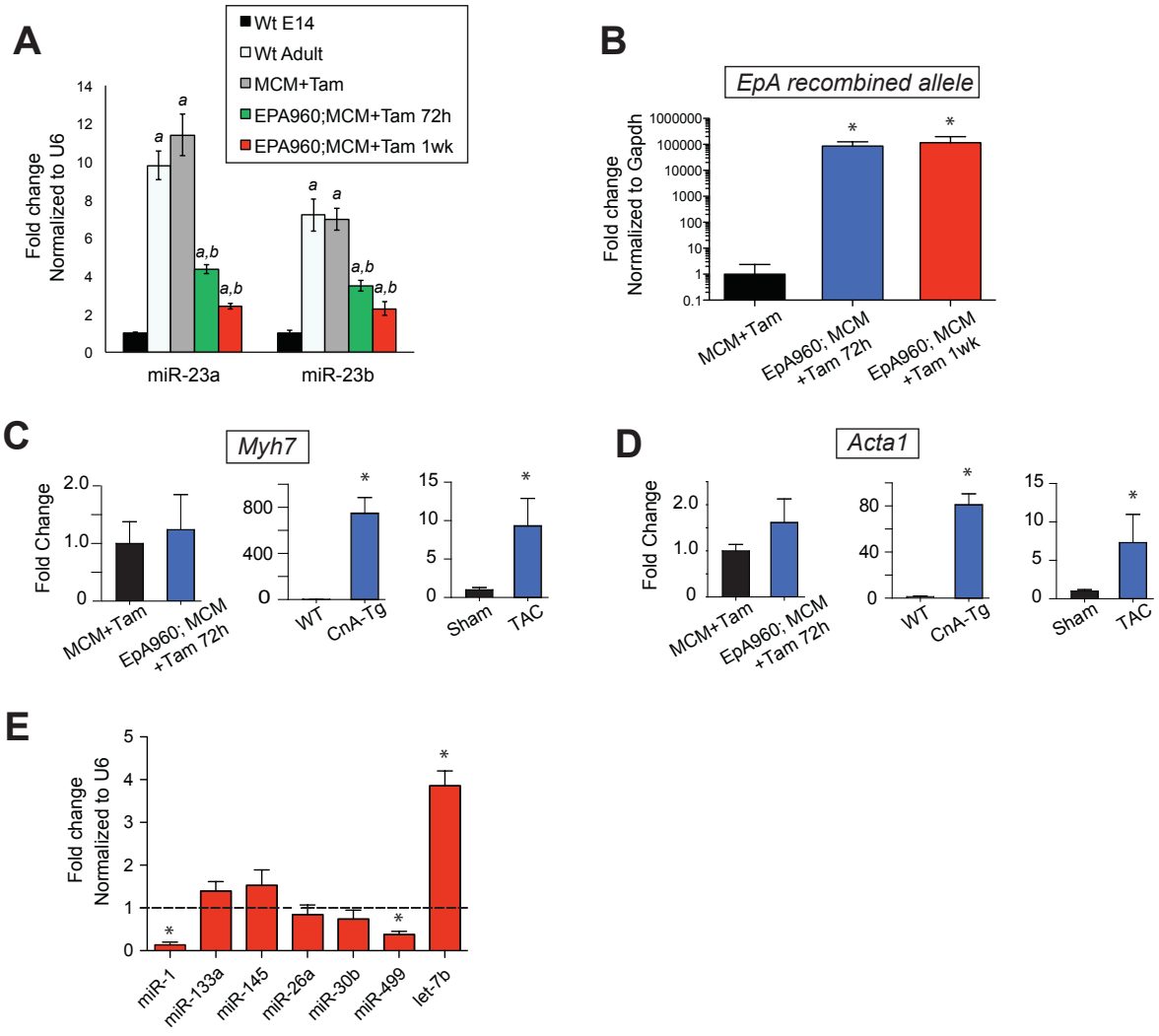

Figure S1. *miRNA*, EpA960 recombined allele, *Myh7* and *Acta1* expression in mouse and human DM1 and non-DM1 cardiomyopathies. (A) Steady state *miR-23a* and *miR-23b* levels during normal mouse heart development and in EpA960; MCM+Tam (DM1) mouse model were determined by real time quantitative PCR (qRT-PCR). Each bar represents fold change in expression (mean ± SD) relative to wild type (Wt) embryonic day (E)14. 'a' represents significantly different from Wt adult; 'b' represents significantly different from Wt E14. Relative expression of cardiac hypertrophy markers (**B**) Relative expression of the EpA960 recombined allele at 72hr and 1wk following tamoxifen

injection. **(C)** *Myh7* and (**D**) *Acta1* in DM1 mice, Calcineurin transgenic (CnA-Tg) mice and wild type mice after 8 weeks of Transverse Aortic Constriction (TAC). Individual bars represent fold change in *Myh7* or *Acta1* mRNA steady state levels (mean ± SD) from heart samples of EpA960;MCM+Tam mice relative to MCM+Tam controls, CnA-Tg mice relative to littermate controls (n=3) or from mice that underwent TAC surgery relative to shams. **(E)** Relative expression of miRNAs in failing human heart samples in comparison to non-disease controls based on qRT-PCR analysis. **P* < 0.05.

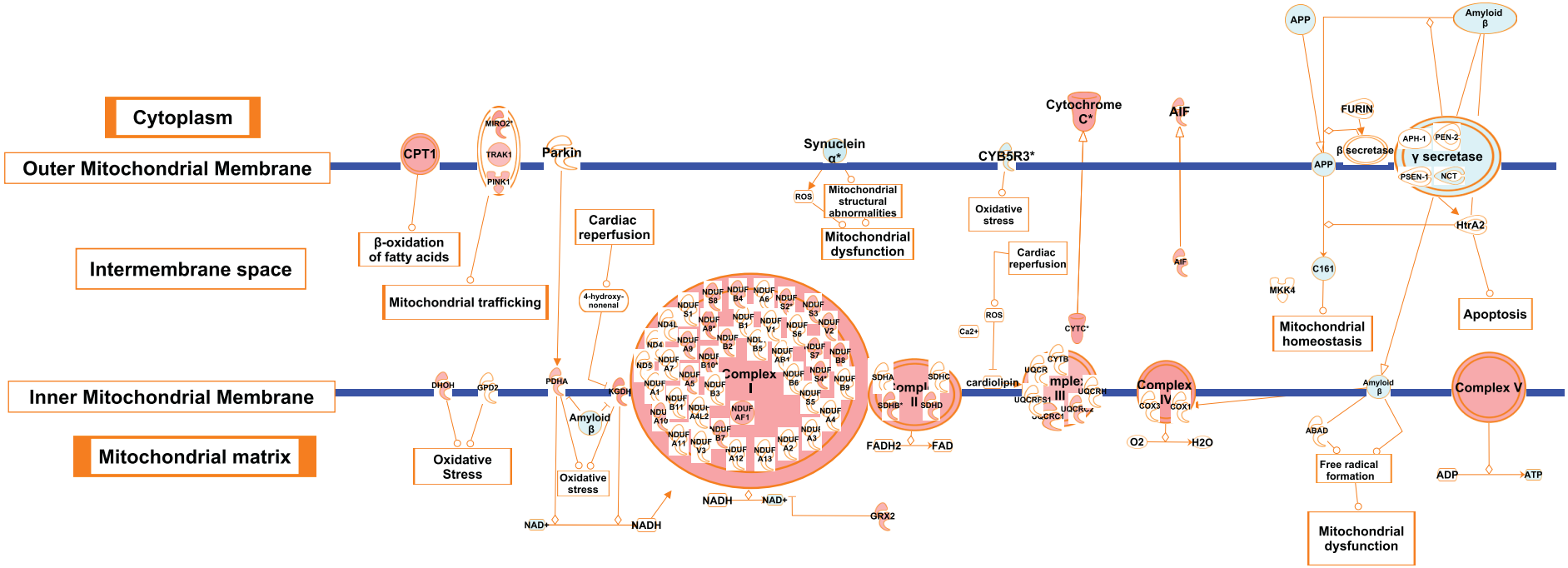

Figure S2. Ingenuity Pathway Analysis showing genes affected in DM1 mouse hearts regulate mitochondrial function.

Ingenuity analyses indicated a canonical pathway involving mitochondrial dysfunction as over-represented categories (*P* value = 5.36E-08) in DM1 mouse hearts as compared to controls. Pink/red color of molecules indicates down regulation of genes analyzed in our study, with darker shades of pink represents levels of gene down regulation. Green color indicates up regulated genes. Grey color indicates no change. Forty-five of 174 genes in the pathway were affected in heart tissue from the DM1 mouse model.

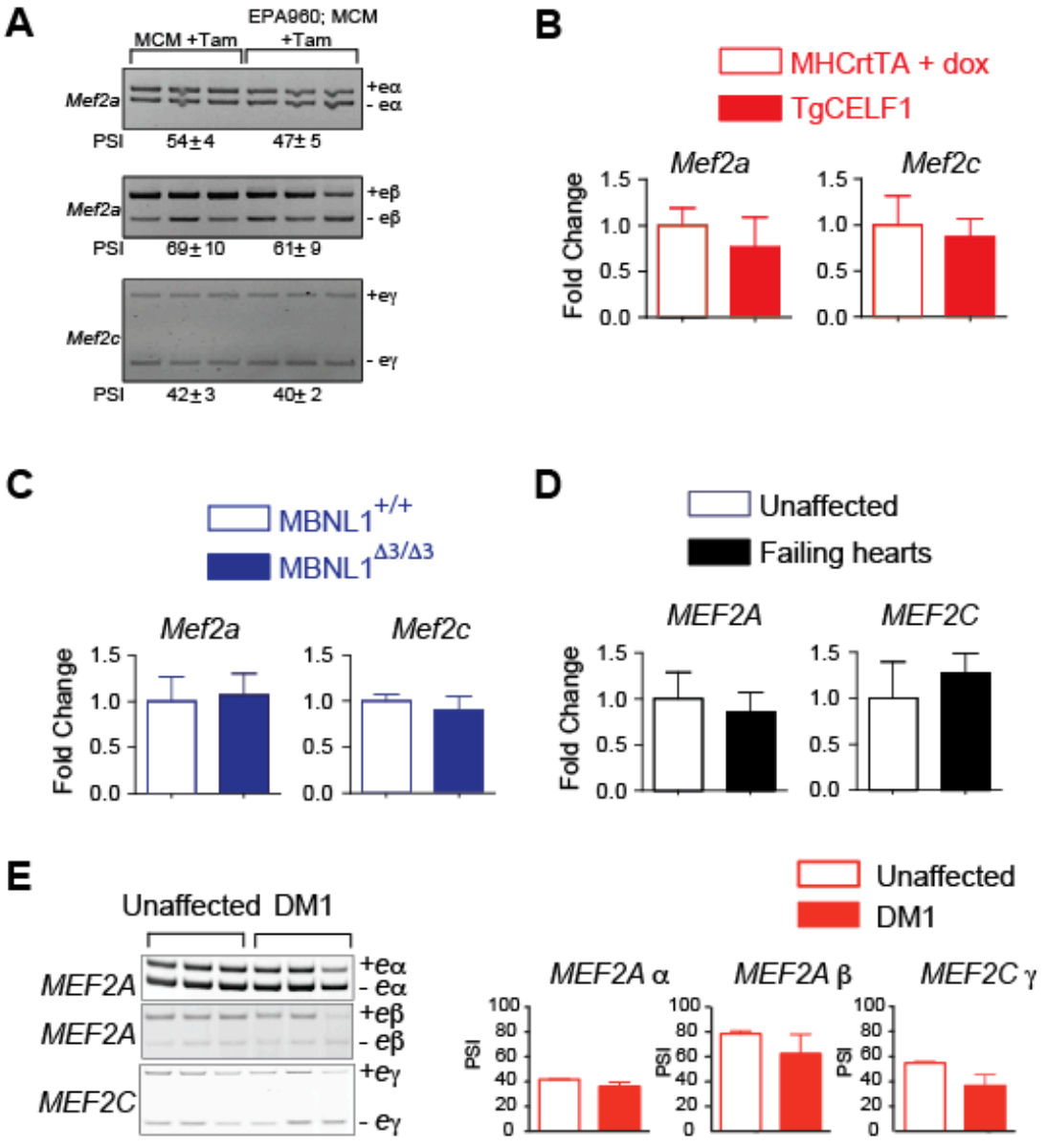

Figure S3. Mef2A and Mef2c splicing and steady state level expression analysis. (A) Alternative exons in *Mef2a (α & β* exons*)* and *Mef2c (γ* exon*)* show no significant change in PSI values after 1wk of CUG^{exp} RNA expression compared to MCM controls. qRT-PCR analysis of *Mef2a* and *Mef2c* mRNA steady state levels in, (**B**) TgCELF1 mice relative to MHCrtTA mice given doxycycline (dox), (**C**) $Mbnl1^{+/+}$ mice relative to $Mbnl1^{\Delta E3/\Delta E3}$ mice and **(D)** Unaffected human control and failing hearts. Each bar represents fold change in

expression (mean ± SD). Data is normalized relative to ribosomal protein L30 (*Rpl30*). n=3. (E) Alternative splicing of MEF2A and MEF2C in unaffected or DM1 hearts.

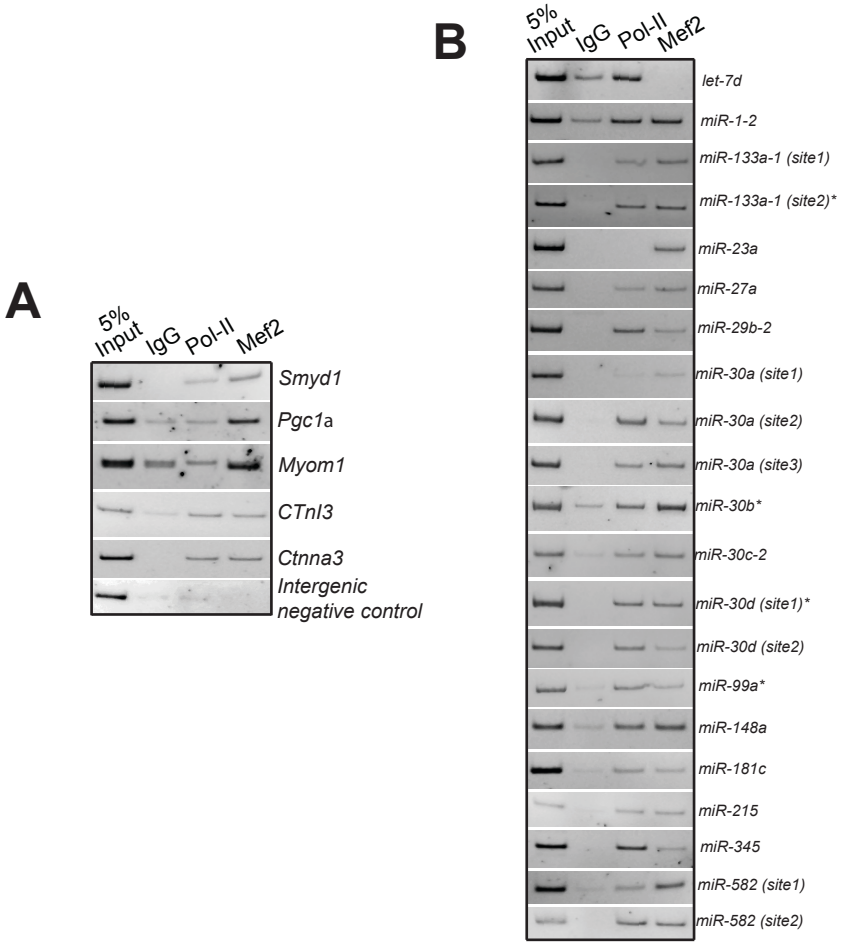

Figure S4. Mef2 proteins bind to genomic regions surrounding several miRNAs in heart. Chromatin Immunoprecipitation (ChIP) was performed using a RNA Pol II, Mef2 or control IgG on wild type adult mouse hearts as described in the Methods section. PCR of the DNA input, RNA Pol II or Mef2 immunoprecipitate, and IgG control precipitate was performed using primers flanking Mef2 consensus sites on each of the miRNAs. The primers used for PCR assays span the Mef2 binding sites in target (**A**) mRNAs or (**B**) primary miRNAs.

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