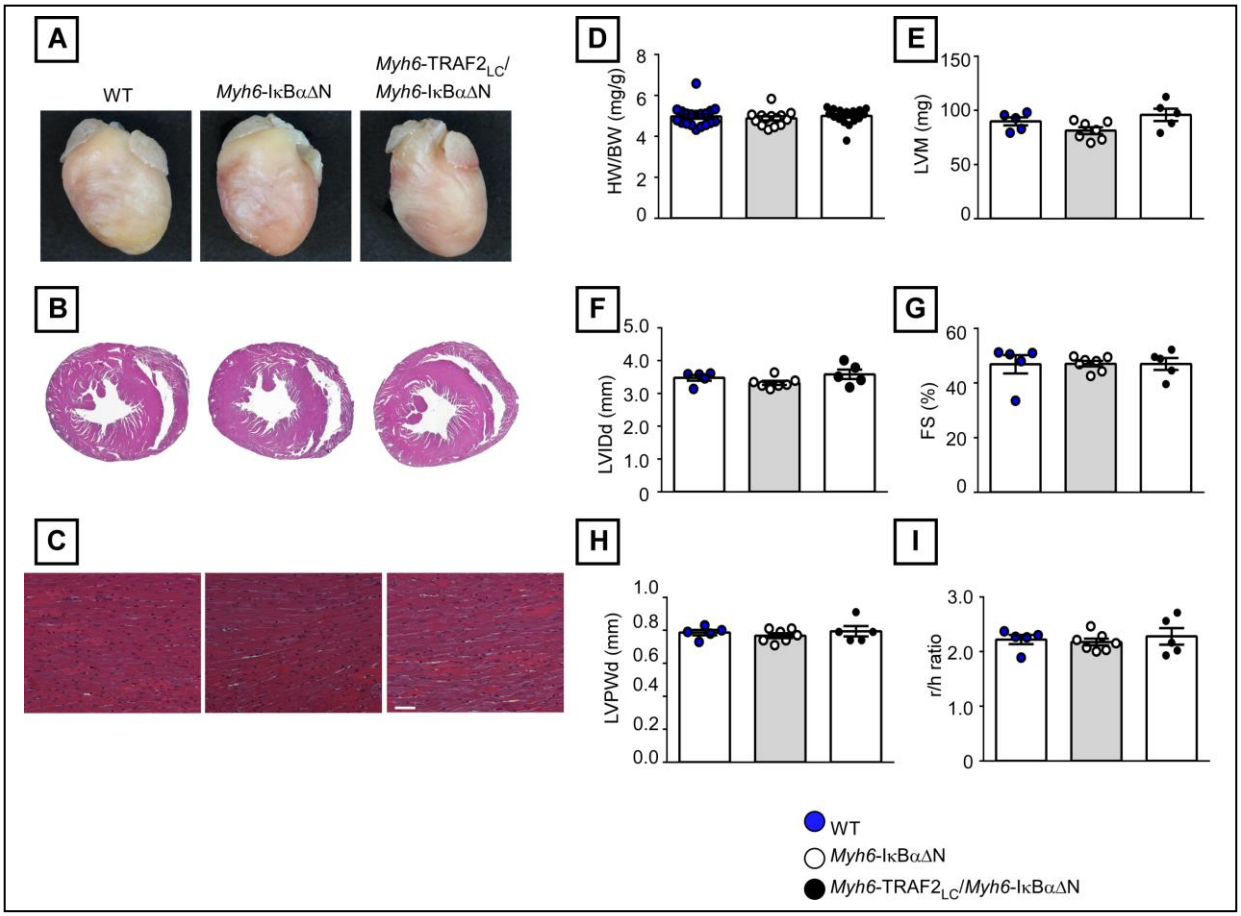
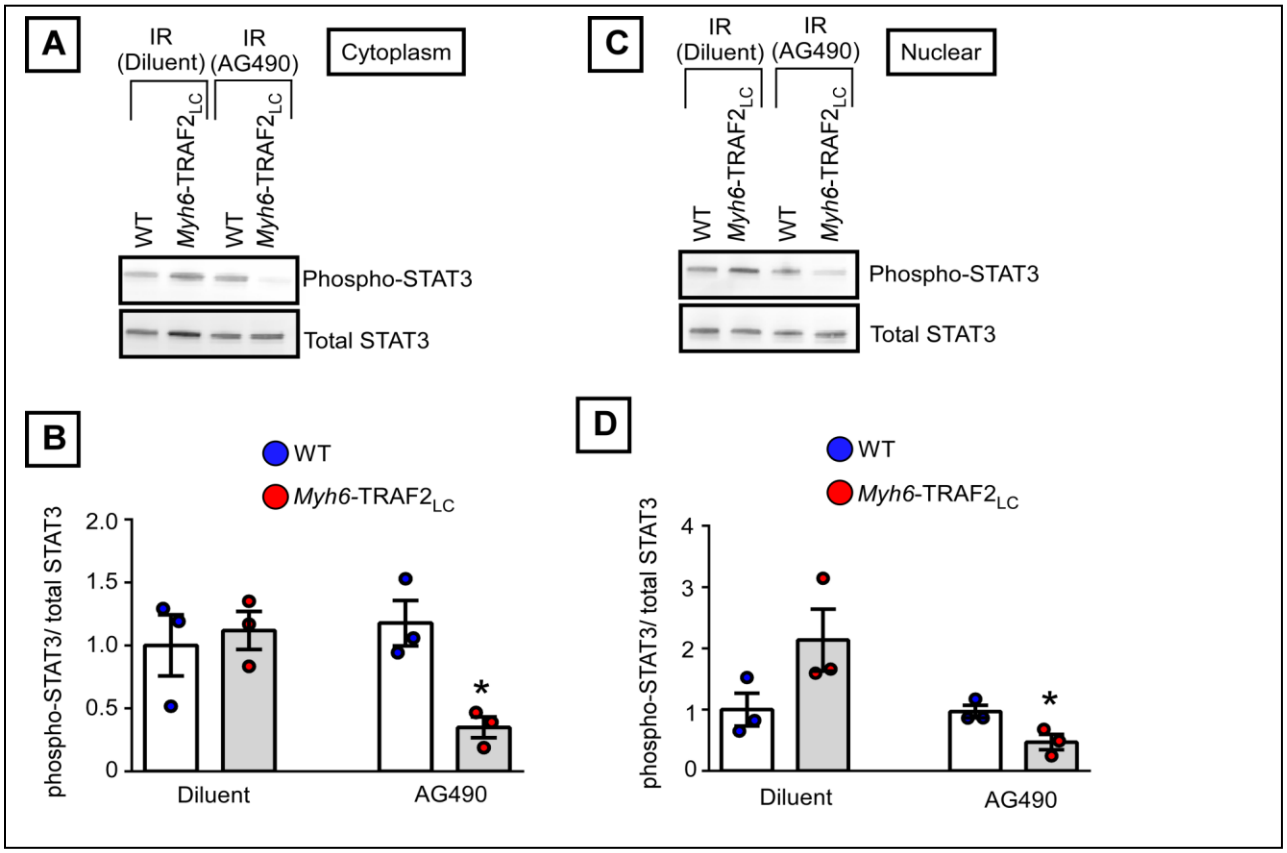
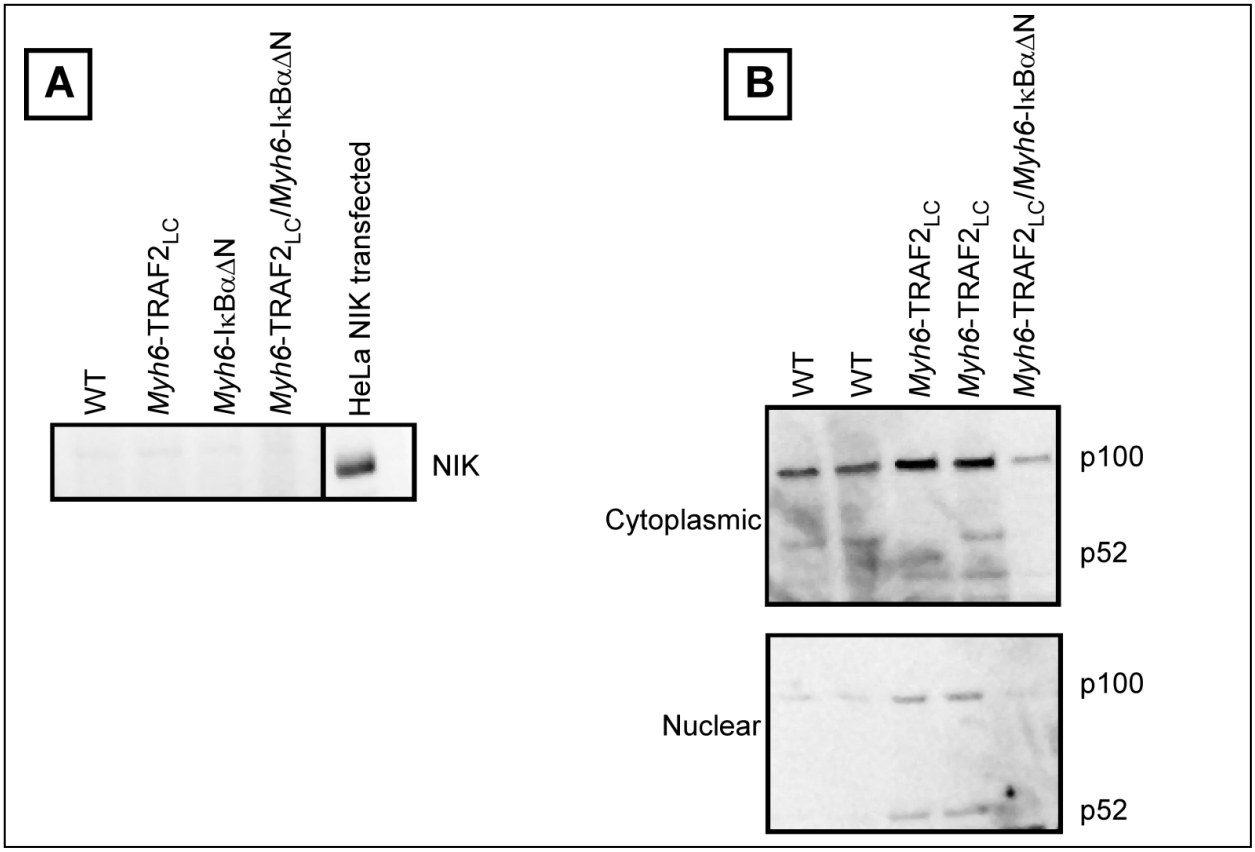


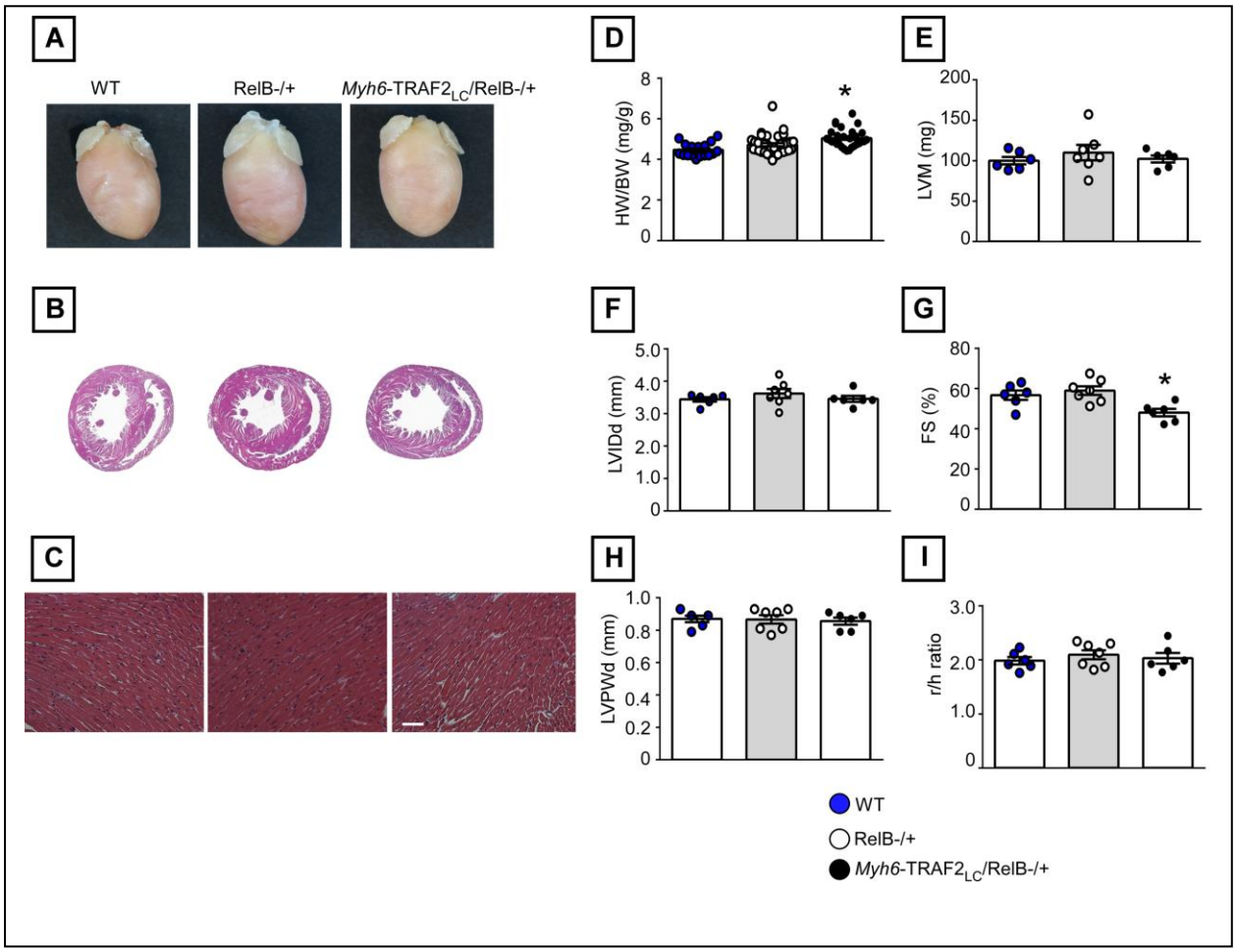
Supplemental Figure 1. Baseline characterization of *Myh6*-TRAF2$_{LC}$ x *Myh6*-IκBαΔN mice. A) Gross morphology (data representative of 5 independent experiments), B) Hematoxylin & eosin (H& E) staining (data representative of 5 independent experiments), C) H&E staining (scale bar =50μm) (data representative of 5 independent experiments), D) Heart weight-to-body weight (HW/BW) ratio (mg/g) (n=14-19/group), E) Left ventricular mass (LVM) (mg) (n=5-7/group), F) Left ventricular internal dimension- diastole (LVIDd) (mm) (n=5-7 per group), G) Percent fractional shortening (%FS) (n=5-7 per group), H) Left ventricular posterior wall-diastole (LVPWd) (mm) (n=5-7/group), I) r/h ratio (n=5-7/group). Data are presented as mean ± SEM. (*=p<0.05 by ANOVA compared to WT controls).



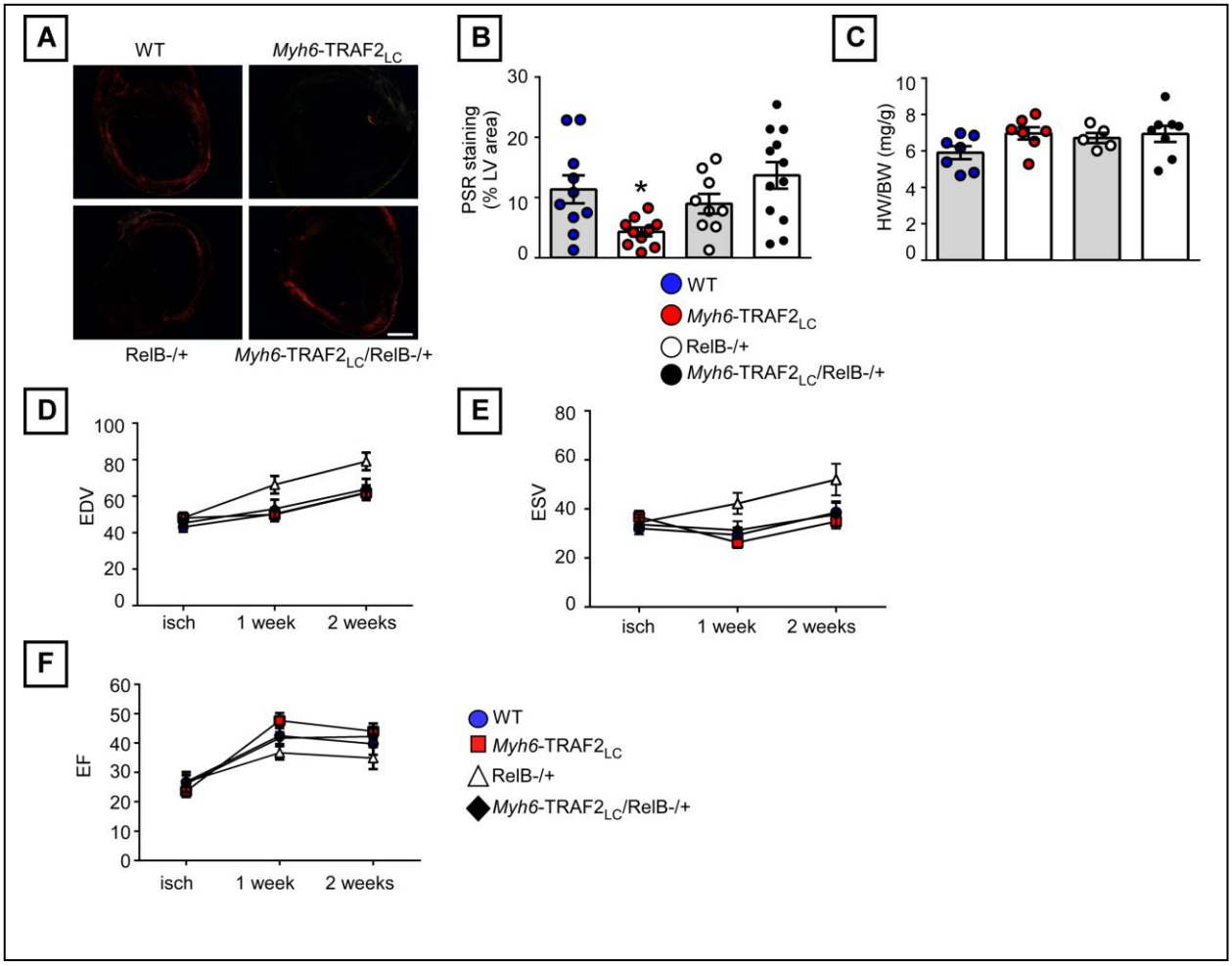
Supplemental Figure 2. Effect of TRAF2 overexpression on STAT-3 phosphorylation and inhibition with AG490. A) Western blot of phospho-STAT3 and total STAT3 in cytoplasmic extracts from WT and *Myh6*-TRAF2$_{LC}$ hearts following 30 minutes of ischemia and 15 min of reperfusion ex vivo in the presence of 10μM AG490 or diluent control (representative images of 3 independent experiments), B) Group data for cytoplasmic phospho-STAT3 levels (n=3 per group), C) Western blot of phospho-STAT3 and total STAT3 in nuclear extracts following 30 minutes of ischemia and 15 min of reperfusion ex vivo in the presence of 10μM AG490 or diluent control (representative images of 3 independent experiments), D) Group data for nuclear phospho-STAT3 levels (n=3 per group), (*= $p < 0.05$ by 2-tailed t-test compared with diluent controls). Data are presented as mean ± SEM.



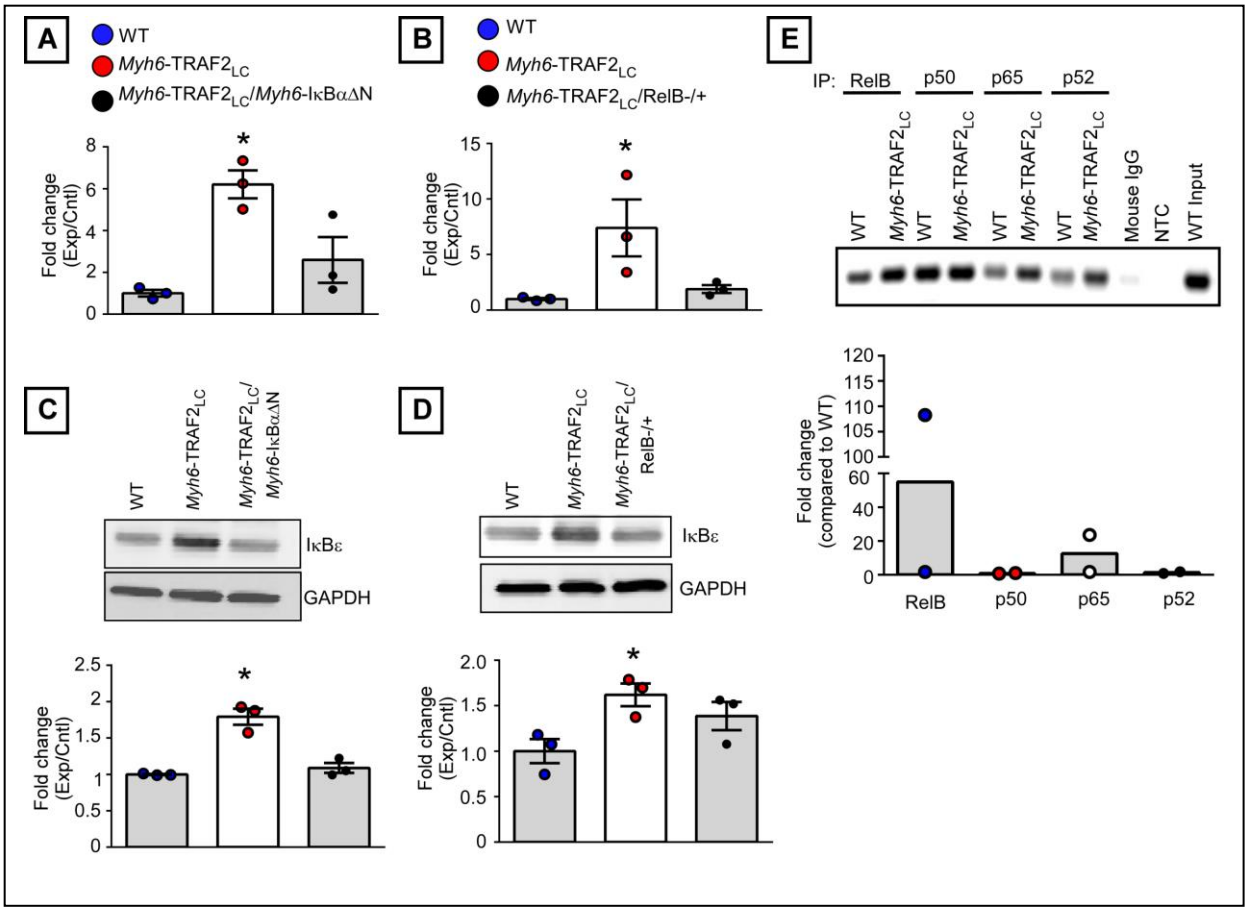
Supplemental Figure 3. Noncanonical NFκB pathway activation. A) Western blot of NIK expression in wild-type (WT), *Myh6*-TRAF2$_{LC}$, *Myh6*-IκBαΔN, *Myh6*-TRAF2$_{LC}$/*Myh6*-IκBαΔN mice at baseline (NIK-transfected HeLa cell extract as positive control) (Lanes were run on the same gel but were noncontiguous) (data are representative of 3 independent experiments), B) Western blot of p100 and p52 in cytoplasmic and nuclear extracts from WT, *Myh6*-TRAF2$_{LC}$, *MYH6*-TRAF2$_{LC}$/*Myh6*-IκBαΔN hearts (data are representative of 3 independent experiments).



Supplemental Figure 4. Baseline characterization of *Myh6*-TRAF2$_{LC}$ x RelB$^{-/+}$ mice. A) Gross morphology (representative of 6 independent experiments), B) Hematoxylin & eosin (H& E) staining (representative of 6 independent experiments), C) H&E staining (scale bar =50μm) (representative of 6 independent experiments), D) Heart weight-to-body weight (HW/BW) ratio (mg/g) (n=6/group), E) Left ventricular mass (LVM) (mg) (n=6-7/group), F) Left ventricular internal dimension- diastole (LVIDd) (mm) (n=6-7 per group), G) Percent fractional shortening (%FS) (n=6-7 per group), H) Left ventricular posterior wall-diastole (LVPWd) (mm) (n=6-7/group), I) r/h ratio (n=6-7/group), (*= $p < 0.05$ by ANOVA compared with WT controls). Data are presented as mean ± SEM.



Supplemental Figure 5. Additional data for in vivo closed-chest ischemia reperfusion on *Myh6*-TRAF2$_{LC}$ x RelB$^{-/+}$ mice. A) Picrosirius Red staining (representative images of 6 independent experiments) (scale bar=1mm), B) Group data for picrosirius red staining (n=10-12/group), C) HW/BW ratio (mg/g) (n=5-8/group) (*= $p < 0.05$ by ANOVA compared with WT controls), D) End diastolic volume (EDV) (μl) (n=6-11/group), E) End systolic volume (ESV) (μl) (n=6-11/group), F) Ejection Fraction (EF) (%) (n=6-11/group), (*= $p < 0.05$ compared to WT controls by repeated measures analysis using mixed models methodology). Data are presented as mean ± SEM.



Supplemental Figure 6. Upregulation of IκBε by TRAF2. A) Real-time qPCR quantification of *Nfkbie* expression in WT, *Myh6*-TRAF2$_{LC}$, *Myh6*-TRAF2$_{LC}$/*Myh6*-IκBαΔN mice (n=3/group), B) Real-time qPCR quantification of *Nfkbie* in WT, *Myh6*-TRAF2$_{LC}$, *Myh6*-TRAF2$_{LC}$ /RelB$^{-/+}$ mice (n=3/group), C) Western blot analysis of IκBε in WT, *Myh6*-TRAF2$_{LC}$, *Myh6*-TRAF2$_{LC}$/*Myh6*-IκBαΔN hearts (n=3/group), D) Western blot analysis of IκBε in WT, *Myh6*-TRAF2$_{LC}$, *Myh6*-TRAF2$_{LC}$ /RelB$^{-/+}$ hearts (n=3/group), E) Chromatin IP of *Nfkbie* promoter using antibodies to members of the NFκB family (n=3/group), (*= $p < 0.05$ by ANOVA compared with WT controls). Data are presented as mean ± SEM.

Supplemental Table 1

Probeset ID	SYMBOL	Fold-Change (FDR <0.05) (*Myh6* -TRAF2$_{LC}$ vs WT)	Fold-Change (FDR <0.05) (*Myh6* -TRAF2$_{LC}$/*Myh6* -IκBαΔN vs *Myh6* -TRAF2$_{LC}$)
ILMN_2889832	Serpina3h	6.22	-4.80
ILMN_2638061	Tsc22d4	4.92	-4.86
ILMN_2945491	Myh7	4.83	-7.48
ILMN_3159156	Strn4	3.28	-2.94
ILMN_2735350	Gdf15	2.97	-2.51
ILMN_1224034	Pde1b	2.52	-2.26
ILMN_2417863	Tnip1	2.38	-2.99
ILMN_2625451	Ankrd1	2.28	-3.31
ILMN_3144289	Traf3	2.25	-2.37
ILMN_2887065	Mvp	2.21	-2.75
ILMN_2601833	Plcg2	2.08	-2.09
ILMN_2439638	Traf3	2.08	-2.39
ILMN_2690506	Vac14	1.92	-2.42
ILMN_2748966	Tgfb3	1.88	-1.81
ILMN_2741629	Tmem130	1.87	-1.92
ILMN_2799361	Tnip1	1.80	-2.18
ILMN_1246841	Relb	1.80	-2.17
ILMN_1250075	Dpysl3	1.78	-1.63
ILMN_1259470	Tmem176b	1.75	-1.93
ILMN_1220763	Rnase1	1.70	-2.01
ILMN_1259180	Rcan1	1.63	-1.57
ILMN_1215972	Syn2	1.62	-2.18
ILMN_2702547	4930519N16Rik	1.61	-1.48
ILMN_1254016	Adora1	1.61	-1.50
ILMN_2841328	Vac14	1.57	-1.69
ILMN_1240069	LOC212390	1.56	-1.95
ILMN_1249234	9530096D07Rik	1.55	-1.52
ILMN_2758562	Stap2	1.50	-1.73
ILMN_1256676	Ddah1	1.49	-1.89
ILMN_3139253	Btbd11	1.43	-1.23
ILMN_2974021	Rpl3	1.42	-1.48
ILMN_2713898	Ddr1	1.40	-1.37
ILMN_1243507	Spsb4	1.35	-1.68
ILMN_2877443	Abhd2	1.35	-1.44
ILMN_2782061	Slc4a3	1.33	-1.45
ILMN_2682046	2900073G15Rik	1.33	-1.41
ILMN_2654624	AI593442	-1.27	1.18
ILMN_1249046	Cmtm8	-1.75	2.21
ILMN_3139875	Acot1	-1.87	1.56