

Supplemental Material

Table S1. Echocardiographic analysis of cardiac function of the Ctrl and cKO mice at 15 weeks age.

Groups	Ctrl (n=5)	cKO (n=5)
EF(%)	61.85 ± 5.633	64.24 ± 6.11
FS(%)	33.52 ± 4.181	35.43 ± 4.716
LVAW;d(mm)	0.8815 ± 0.01271	0.842 ± 0.05287
LVAW;s(mm)	1.262 ± 0.08974	1.377 ± 0.04749
LVPW;d(mm)	0.7654 ± 0.06403	0.8728 ± 0.05736
LVPW;s(mm)	1.132 ± 0.09744	1.209 ± 0.05877
LVID;d(mm)	3.984 ± 0.07778	3.912 ± 0.05916
LVID;s(mm)	2.66 ± 0.211	2.53 ± 0.2012
LV Vol;d(μl)	69.49 ± 3.163	66.5 ± 2.325
LV Vol;s(μl)	27.15 ± 4.855	23.99 ± 4.529

EF: Ejection fraction; FS: Shortening fraction; LVAW: Left ventricular anterior wall; LVPW: Left ventricular posterior wall; LVID: Left ventricular internal diameter; LV Vol: Left ventricle volume; d: end-diastolic; s: end-systolic.
Data were presented as mean ± SEM.

Table S2.Echocardiographic analysis of cardiac function of the mice after 2 weeks TAC surgery

Groups	Ctrl (n=4)	cKO (n=4)	Ctrl (n=11)	cKO (n=9)
	sham		TAC	
EF(%)	63.25 ± 4.358	74.2 ± 3.534	67.02 ± 3.376	67.23 ± 4.833
FS(%)	34.09 ± 3.15	42.77 ± 3.147	37.42 ± 2.741	37.79 ± 3.556
LVAW;d(mm)	0.8935 ± 0.02435	0.9769 ± 0.04683	1.072 ± 0.0545	1.317 ± 0.07619 #*
LVAW;s(mm)	1.444 ± 0.09259	1.532 ± 0.06736	1.599 ± 0.05973	1.86 ± 0.09672 *
LVPW;d(mm)	0.8287 ± 0.06159	0.9167 ± 0.07112	0.9596 ± 0.04162	1.132 ± 0.05314 #*
LVPW;s(mm)	1.181 ± 0.0456	1.245 ± 0.1308	1.423 ± 0.0782	1.562 ± 0.07251 #
LVID;d(mm)	3.935 ± 0.0857	3.773 ± 0.1499	3.929 ± 0.1073	3.811 ± 0.1097
LVID;s(mm)	2.597 ± 0.1552	2.162 ± 0.1524	2.48 ± 0.159	2.391 ± 0.1904
LV Vol;d(μl)	67.48 ± 3.406	61.36 ± 5.84	67.85 ± 4.281	63 ± 4.116
LV Vol;s(μl)	24.99 ± 3.57	15.92 ± 2.552	23.42 ± 3.446	21.75 ± 4.294

EF: Ejection fraction; FS: Shortening fraction; LVAW: Left ventricular anterior wall; LVPW: Left ventricular posterior wall; LVID: Left ventricular internal diameter; LV Vol: Left ventricle volume; d: end-diastolic; s: end-systolic.
Data were presented as mean ± SEM. #p<0.05, ##p<0.01 vs. Sham. *p<0.05 vs. Ctrl.

Table S3. Echocardiographic analysis of cardiac function of the mice after 4 weeks TAC surgery

Groups	Ctrl (n=9)	cKO (n=7)	Ctrl (n=10)	cKO (n=14)
	sham		TAC	
EF(%)	65.64 ± 4.755	57.81 ± 3.985	43.53 ± 5.12 ##	51.21 ± 3.491
FS(%)	36.57 ± 3.54	30.47 ± 2.676	21.99 ± 3.213 ##	26.5 ± 2.399
LVAW;d(mm)	0.8594 ± 0.0603	1.004 ± 0.07623	1.286 ± 0.07231 ###	1.375 ± 0.04343 ###
LVAW;s(mm)	1.376 ± 0.08266	1.504 ± 0.07069	1.692 ± 0.1258	1.809 ± 0.04122 ###
LVPW;d(mm)	0.8189 ± 0.05127	0.8448 ± 0.03847	1.023 ± 0.04839 ##	1.306 ± 0.0402 ### ***
LVPW;s(mm)	1.261 ± 0.0755	1.164 ± 0.08355	1.223 ± 0.06281	1.665 ± 0.05578 ### ***
LVID;d(mm)	3.843 ± 0.09253	4.076 ± 0.1358	4.165 ± 0.09444 #	4.18 ± 0.09596
LVID;s(mm)	2.456 ± 0.1819	2.841 ± 0.1721	3.271 ± 0.1927 ##	3.095 ± 0.1542
LV Vol;d(μl)	64.1 ± 3.651	73.92 ± 5.721	77.59 ± 4.02 #	78.51 ± 4.25
LV Vol;s(μl)	22.99 ± 4.126	31.76 ± 4.917	45.34 ± 5.733 ##	39.74 ± 4.253

EF: Ejection fraction; FS: Shortening fraction; LVAW: Left ventricular anterior wall; LVPW: Left ventricular posterior wall; LVID: Left ventricular internal diameter; LV Vol: Left ventricle volume; d: end-diastolic; s: end-systolic.

Data were presented as mean ± SEM. #p<0.05, ##p<0.01, ###p<0.001 vs. Sham. ***p<0.001 vs. Ctrl.

Table S4. Echocardiographic analysis of cardiac function of the mice after 4 weeks Ang II infusion

Groups	Ctrl (n=7)	cKO (n=5)	Ctrl (n=7)	cKO (n=5)
	Basic		Ang II	
EF(%)	65.11 ± 2.578	69.86 ± 3.698	57.25 ± 2.883	68.4 ± 3.861 *
FS(%)	35.27 ± 1.891	39.09 ± 2.998	29.8 ± 1.97	37.78 ± 3.177 *
LVAW;d(mm)	0.9797 ± 0.04656	0.949 ± 0.04795	0.9383 ± 0.03923	1.315 ± 0.04046 ### ***
LVAW;s(mm)	1.483 ± 0.04606	1.551 ± 0.06814	1.418 ± 0.09165	1.888 ± 0.05947 ## **
LVPW;d(mm)	0.7826 ± 0.04072	0.9358 ± 0.02044 *	0.8977 ± 0.07116	1.172 ± 0.07726 # *
LVPW;s(mm)	1.197 ± 0.05854	1.367 ± 0.07089	1.256 ± 0.09304	1.571 ± 0.1193
LVID;d(mm)	3.802 ± 0.1127	3.707 ± 0.1703	3.898 ± 0.08539	3.473 ± 0.1284 *
LVID;s(mm)	2.464 ± 0.1185	2.278 ± 0.2112	2.737 ± 0.1012	2.172 ± 0.1709 *
LV Vol;d(μl)	62.53 ± 4.445	59.14 ± 6.398	66.11 ± 3.501	50.35 ± 4.397 *
LV Vol;s(μl)	22.05 ± 2.879	18.76 ± 4.095	28.33 ± 2.509	16.38 ± 2.924 *

EF: Ejection fraction; FS: Shortening fraction; LVAW: Left ventricular anterior wall; LVPW: Left ventricular posterior wall; LVID: Left ventricular internal diameter; LV Vol: Left ventricle volume; d: end-diastolic; s: end-systolic.

Data were presented as mean ± SEM. #p<0.05, ##p<0.01, ###p<0.001 vs. Basic. *p<0.05, **p<0.01, ***p<0.001 vs. Ctrl.

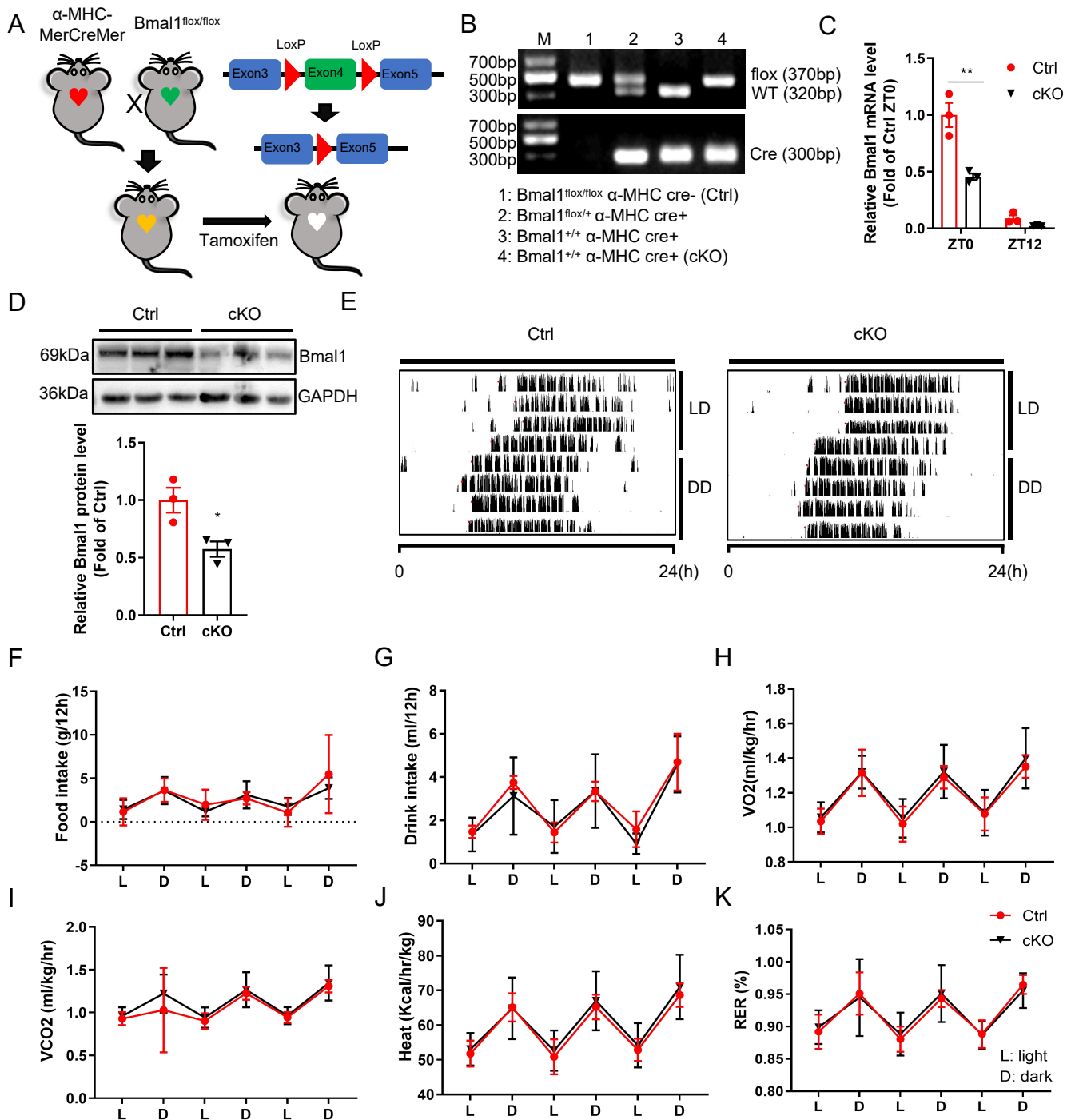


Figure S1. Generation and characterization of the cKO mice.

A. Schematic showing the generation of inducible cardiomyocyte specific $Bmal1$ knockout (cKO mice. The locations of loxP sites flanked the exon 4 of the $Bmal1$ gene.

B. Genotyping tests show the bands for $Bmal1$ flox (370bp), $Bmal1^{+/+}$ (320bp), and the α -MHC-Cre (300bp).

C. $Bmal1$ mRNA expression in the heart tissues measured at ZT0 (light on) and ZT12 (light off). $n=3$ mice per group.

D. $Bmal1$ protein expression in the heart tissues measured at ZT0. $n=3$ mice per group.

E. Representative double-plotted actograms of wheel-running activity of the cKO and Ctrl mice.

F-K. Circadian rhythms of food intake, drink intake, oxygen consumption (VO_2), carbon dioxide production (VCO_2), heat production and respiratory exchange ratio (RER) of the cKO and Ctrl mice. $n=4-5$ mice per group. Data were presented as mean \pm SEM, * $p<0.05$, ** $p<0.01$ vs. Ctrl.

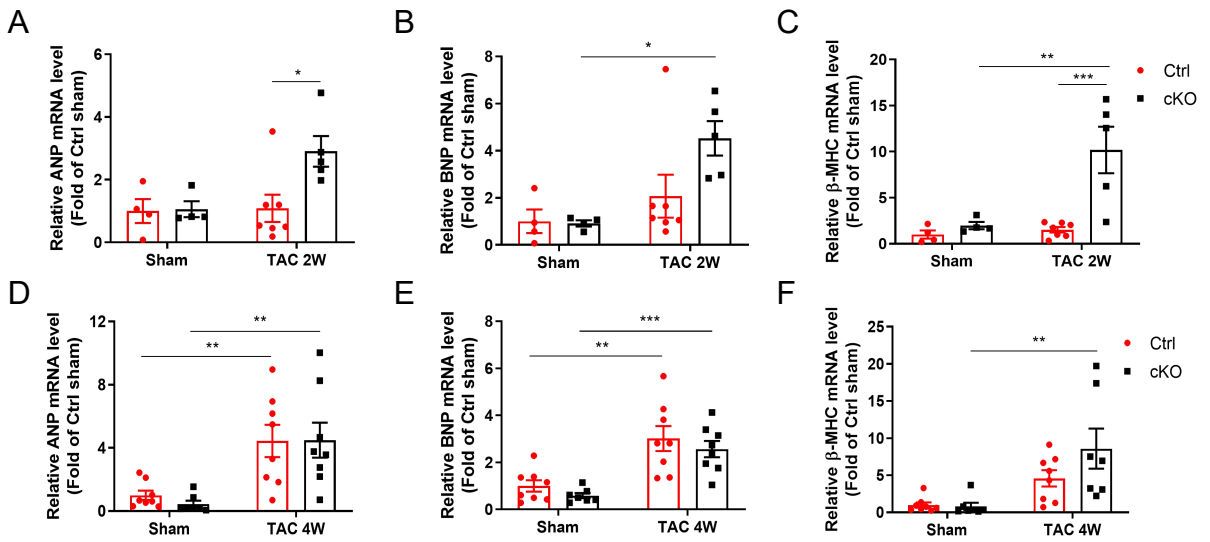


Figure S2. Hypertrophy related gene expression in Ctrl and cKO mice after TAC surgery.

A-C. qRT-PCR analysis of the mRNA levels of ANP, BNP and β-MHC in the hearts of Ctrl and cKO mice in response to 2 weeks TAC surgery. n=4-7 mice per group.

D-F. qRT-PCR analysis of the mRNA levels of ANP, BNP and β-MHC in the hearts of Ctrl and cKO mice in response to 4 weeks TAC surgery. n=7-8 mice per group.

Data were presented as mean ± SEM, *p<0.05, **p<0.01, ***p<0.001.

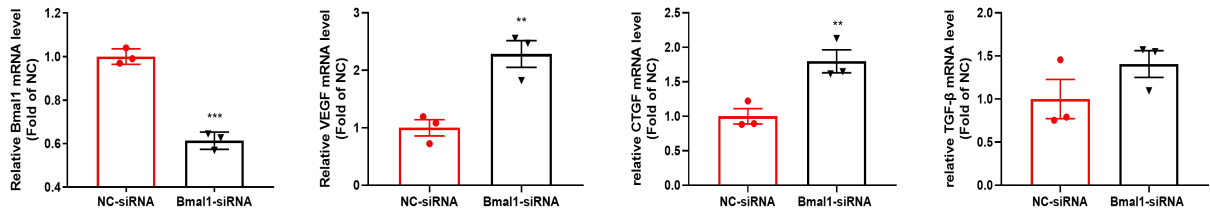


Figure S3. Silencing Bmal1 in cardiomyocytes promotes fibrogenic gene expression in neonatal rat ventricular cardiomyocytes (NRVMs). NRVMs were transfected with negative control (NC) or Bmal1 siRNA for 24h and treated with PE for 6h. Bmal1, VEGF, CTGF and TGFβ mRNA expression was determined by qRT-PCR. n=3 per group.