

Supplemental Table 1 – Echocardiography Parameters at Baseline

Echo	Control	Y3-cKO	p-value
IVS;d (mm)	0.67 ± 0.03	0.68 ± 0.04	0.71
IVS;s (mm)	1.04 ± 0.03	1.12 ± 0.04	0.09
LVID;d (mm)	3.85 ± 0.05	4.06 ± 0.10	0.08
LVID;s (mm)	2.74 ± 0.05	2.97 ± 0.10	0.06
LVPW;d (mm)	0.56 ± 0.03	0.64 ± 0.03	0.09
LVPW;s (mm)	0.91 ± 0.03	0.99 ± 0.04	0.10
EF (%)	56.06 ± 1.33	53.15 ± 1.33	0.14
FS (%)	28.2 ± 0.88	27.07 ± 0.8	0.15
HR (bpm)	447.58 ± 14.18	466.20 ± 16.29	0.40

Supplemental Table 1: Echocardiography analysis 1 month after gene knockout, shown as mean ± SEM. n = (10; 15) for (Ctrl; Y3-cKO). Unpaired t-test was used. IVS;d = Interventricular Septum Thickness; diastole. IVS;s = Interventricular Septum Thickness; systole. LVID;d = Left Ventricular Internal Diameter; diastole. LVID;s = Left Ventricular Internal Diameter; systole. LVPW;d = Left Ventricular Posterior Wall Thickness; diastole. LVPW;s = Left Ventricular Posterior Wall Thickness; systole. EF = Ejection Fraction. FS = Fractional Shortening. HR = Heart Rate.

Supplemental Table 2 – Echocardiography Parameters after Transverse Aortic Constriction (TAC)

	Sham		TAC		2 Way ANOVA		
Echo	Control	Y3-cKO	Control	Y3-cKO	Interaction	Genotype	Surgery
IVS;d (mm)	0.74 ± 0.03	0.73 ± 0.08	1.00 ± 0.07	0.81 ± 0.05	0.140	0.110	0.008
IVS;s (mm)	1.17 ± 0.04	1.27 ± 0.08	1.30 ± 0.09	1.28 ± 0.07	0.424	0.563	0.360
LVID;d (mm)	4.19 ± 0.06	4.17 ± 0.15	3.80 ± 0.09	3.76 ± 0.15	0.904	0.815	0.002
LVID;s (mm)	3.01 ± 0.02	2.91 ± 0.13	3.24 ± 0.17	2.93 ± 0.19	0.509	0.189	0.429
LVPW;d (mm)	0.68 ± 0.02	0.60 ± 0.03	0.92 ± 0.03	0.88 ± 0.05	0.437	0.068	0.001
LVPW;s (mm)	1.01 ± 0.04	0.92 ± 0.10	1.06 ± 0.05	1.05 ± 0.08	0.555	0.493	0.225
EF (%)	54.4 ± 1.73	57.9 ± 3.11	32.0 ± 4.78	45.7 ± 4.13	0.210	0.041	0.001
FS (%)	28.0 ± 1.14	30.3 ± 2.10	15.1 ± 2.48	22.7 ± 2.43	0.263	0.038	0.001
HR (bpm)	452.9 ± 13.5	466.9 ± 8.54	468.2 ± 31.06	419.9 ± 16.6	0.171	0.445	0.480

Supplemental Table 2: Echocardiography analysis 6 days after pressure overload surgery, shown as mean ± SEM. n = (7; 5; 8; 8) for (Ctrl Sham; Y3-cKO Sham; Ctrl TAC; Y3-cKO TAC). 2-way ANOVA with multiple comparisons test was used. IVS;d = Interventricular Septum Thickness; diastole. IVS;s = Interventricular Septum Thickness; systole. LVID;d = Left Ventricular Internal Diameter; diastole. LVID;s = Left Ventricular Internal Diameter; systole. LVPW;d = Left Ventricular Posterior Wall Thickness; diastole. LVPW;s = Left Ventricular Posterior Wall Thickness; systole. EF = Ejection Fraction. FS = Fractional Shortening. HR = Heart Rate.

Supplemental Table 3. Differentially Expressed Proteins

Label free Mass Spectrometry was performed on isolated neonatal rat ventricular cardiomyocytes

Differentially expressed proteins are those with a p value < 0.05.

Fold Change is siYthdf3/siNC

n=3 for both groups

Differentially expressed proteins, siYthdf3 vs siNC. p value < 0.05

Accession ID	Gene Name	P Value	Fold Change
P02680	FIBG	0.025	23.3333333
Q811M5	CO6	0.015	13.3333333
Q5RKH6	OS9	0.017	13.3333333
O54937	PDK4	0.016	7.5
Q63258	ITA7	0.0018	4.28571429
P97564	GPAT1	0.0021	4.16666667
Q5BJT4	TXD15	0.041	4.16666667
Q64605	PTPRS	0.046	4.16666667
Q5U1Y0	TM192	0.046	4.16666667
Q5PQM9	KMCP1	0.046	4.16666667
Q5EB73	PGAP4	0.047	4.16666667
P14480	FIBB	0.027	4.0625
O35112	CD166	0.012	3.80952381
P21571	ATP5J	0.016	3
Q7TSN4	PIGW	0.013	2.85714286
P00763	TRY2	0.015	2.85714286
P35952	LDLR	0.02	2.4
Q62725	NFYC	0.016	2.33333333
Q10739	MMP14	0.016	2.33333333
Q9Z2Q7	STX8	0.0071	2.25
P55043	RAD	0.0075	2.25
Q4V7F2	CREL1	0.0062	2.2
Q63377	AT1B3	0.00059	2.14285714
P08050	CXA1	0.0051	2.13888889
O35777	MAGT1	0.048	2.125
B4F795	CTL2	0.023	2.1
Q5FVH0	C1QT5	0.019	2
D4AD37	IMPA3	0.023	2
Q03343	ADCY6	0.045	2

Q62786	FPRP	0.049	2
B5DFN3	UQCC2	0.015	1.88888889
Q80Z70	SE1L1	0.023	1.875
Q9JHW1	CBPD	0.015	1.85
O70513	LG3BP	0.018	1.83333333
Q924Z9	NET1	0.01	1.8125
Q794F9	4F2	0.0023	1.8
P14925	AMD	0.0053	1.73684211
D4A2H2	SPTC1	0.032	1.73684211
P25286	VPP1	0.017	1.64285714
Q6TMA8	ANGL4	0.02	1.63636364
Q08463	FZD1	0.019	1.625
Q07969	CD36	0.0087	1.62068966
P27615	SCRB2	0.00072	1.60526316
Q80WE1	FMR1	0.0068	1.6
Q5XI31	PIGS	0.028	1.5625
Q6P7Q1	BABA2	0.006	1.55555556
D3ZVR7	PXL2B	0.0001	1.5
O35910	MOT4	0.015	1.5
Q6AYQ8	FAHD1	0.018	1.5
Q04400	ADCY5	0.018	1.5
Q63016	LAT1	0.019	1.5
P52590	NU107	0.034	1.5
Q9ES21	SAC1	0.033	1.45945946
Q9QWJ9	NRP1	0.0076	1.45652174
Q5XIB4	UFSP2	0.026	1.45454545
Q5RKI8	MITOS	0.024	1.44776119
Q6P742	PLP2	0.014	1.44444444
Q63060	GLPK	0.0014	1.43478261
P00388	NCPR	0.049	1.43243243
P03889	NU1M	0.024	1.4137931
P97629	LCAP	0.015	1.40322581
P17209	MYL4	0.031	1.40229885
Q9EQG6	KDIS	0.025	1.38181818
P13596	NCAM1	0.0083	1.36619718
Q5XIN6	LETM1	0.0062	1.36607143
Q7TSA0	MIRO2	0.0016	1.36111111
Q5I0K8	RT07	0.046	1.34615385
P31399	ATP5H	0.0011	1.33877551
Q5FVN0	MBOA5	0.0029	1.33333333

Q62639	RHEB	0.038	1.33333333
P29975	AQP1	0.049	1.33333333
Q9JJW3	ATPMD	0.031	1.32911392
P00406	COX2	0.008	1.32743363
P12075	COX5B	0.038	1.32608696
P08753	GNAI3	0.02	1.32258065
P35565	CALX	0.012	1.31972789
B0LPN4	RYR2	0.026	1.30104712
P04897	GNAI2	0.023	1.3
P15999	ATPA	0.025	1.28787879
Q6AXV4	SAM50	0.038	1.264
Q9R066	CXAR	0.018	1.25925926
ANT3_HUMAN		0.041	1.25
Q62902	LMAN1	0.02	1.24285714
Q66HF1	NDUS1	0.044	1.23762376
P49134	ITB1	0.0057	1.23529412
P61621	S61A1	0.015	1.23255814
Q60587	ECHB	0.041	1.2228739
Q9JM53	AIFM1	0.037	1.20930233
P20070	NB5R3	0.039	1.20779221
P0C2X9	AL4A1	0.012	1.18367347
Q63862	MYH11	0.0081	1.17699115
Q5BK63	NDUA9	0.027	1.17261905
Q00657	CSPG4	0.0073	1.144
Q8R4Z9	MFN1	0.0081	1.13953488
P56574	IDHP	0.03	1.05172414
P11980	KPYM	0.021	0.95846645
P68101	IF2A	0.032	0.95698925
Q2PQA9	KINH	0.0041	0.92857143
P29411	KAD3	0.041	0.90217391
Q4QRB4	TBB3	0.026	0.90201005
P68035	ACTC	0.027	0.88774105
P42123	LDHB	0.031	0.88305489
P04797	G3P	0.011	0.87529138
P63102	1433Z	0.034	0.86666667
P82995	HS90A	0.0083	0.86575342
O08730	GLYG	0.0047	0.86419753
P63259	ACTG	0.007	0.86259542
Q9QXQ0	ACTN4	0.012	0.86238532
P07335	KCRB	0.027	0.86231884

Q9ESW0	DDB1	0.042	0.86
P68136	ACTS	0.043	0.85771383
P63159	HMGB1	0.014	0.85454545
P46462	TERA	0.035	0.85377358
Q5XIF6	TBA4A	0.042	0.85326087
Q64057	AL7A1	0.02	0.84782609
P62250	RS16	0.0022	0.84158416
Q6P9V9	TBA1B	0.049	0.8358209
O70196	PPCE	0.018	0.83018868
P05065	ALDOA	0.0087	0.82919255
Q5XID1	CPIN1	0.011	0.82758621
P07483	FABPH	0.022	0.82162162
Q9Z1P2	ACTN1	0.025	0.81944444
P68370	TBA1A	0.042	0.81818182
P05197	EF2	0.0012	0.8083004
P61354	RL27	0.043	0.80821918
P63029	TCTP	0.046	0.80555556
O35115	FHL2	0.02	0.8018018
P50753	TNNT2	0.019	0.8
Q32Q06	AP1M1	0.031	0.8
P97536	CAND1	0.032	0.79640719
P20650	PPM1A	0.016	0.78571429
Q920J4	TXNL1	0.024	0.78504673
D3ZBN0	H15	0.018	0.78333333
P47727	CBR1	0.047	0.78205128
P50399	GDIB	0.016	0.77777778
P50463	CSRP3	0.0076	0.77435897
O08837	CDC5L	0.03	0.77272727
P31044	PEBP1	0.038	0.76829268
P27791	KAPCA	0.0026	0.7625
Q9JJ54	HNRPD	0.021	0.76119403
B0BNA7	EIF3I	0.009	0.75903614
P68182	KAPCB	0.023	0.75903614
P04646	RL35A	0.036	0.75675676
P47860	PFKAP	0.028	0.75449102
Q63798	PSME2	0.042	0.75438596
P13471	RS14	0.012	0.75
Q6RUV5	RAC1	0.014	0.73809524
P09456	KAP0	0.016	0.73504274
Q6PDV7	RL10	0.046	0.73417722

P14173	DDC	0.0061	0.72727273
P52925	HMGB2	0.029	0.72151899
P85968	6PGD	0.015	0.71666667
P21531	RL3	0.037	0.71578947
P80385	AAKG1	0.035	0.71428571
Q63270	ACOC	0.036	0.71428571
Q3B8Q1	DDX21	0.009	0.7125
P50878	RL4	0.016	0.7079646
Q71UF4	RBBP7	0.011	0.70422535
Q6AXQ0	SAE1	0.022	0.7
Q7M0E3	DEST	0.036	0.69565217
Q6AYR6	HDHD2	0.029	0.69230769
Q5XI22	THIC	0.011	0.69090909
P34926	MAP1A	0.035	0.69047619
P07323	ENOG	0.00079	0.6875
Q4V8K3	NAA11	0.038	0.6875
P32362	DCUP	0.043	0.68181818
P47245	NRDC	0.02	0.67857143
Q9ER30	KLH41	0.00058	0.67741935
Q9WUH4	FHL1	0.00079	0.66451613
P18395	CSDE1	0.0038	0.66197183
P45592	COF1	0.045	0.65432099
Q62920	PDLI5	0.00038	0.64942529
P62755	RS6	0.036	0.64912281
Q3MIE4	VAT1	0.00046	0.64705882
SYH_HUMAN		0.04	0.64285714
Q62658	FKB1A	0.034	0.64150943
Q4G069	RMD1	0.035	0.63636364
Q62698	DC1L2	0.036	0.63333333
Q5I0K3	CLYBL	0.0011	0.62962963
Q66HG9	MAVS	0.023	0.625
O08653	TEP1	0.0025	0.61904762
Q66HC1	TDRD3	0.012	0.61904762
Q4V7D7	RBM22	0.021	0.61538462
Q6AYK6	CYBP	0.041	0.61111111
P97571	CAN1	0.039	0.60869565
O88656	ARC1B	0.0071	0.60526316
O55012	PICAL	0.0066	0.6
F1LP64	TRIPC	0.019	0.6
Q5U1X1	ORN	0.019	0.6

Q8VIF7	SBP1	0.015	0.59090909
P31232	TAGL	0.0099	0.58385093
Q5XIB3	ARHL1	0.022	0.57894737
Q6AY53	DHYS	0.047	0.57142857
B3DMA2	ACD11	0.026	0.5625
Q8VHT6	AS3MT	0.021	0.55555556
P00787	CATB	0.016	0.54285714
Q9QZR6	SEPT9	0.0051	0.53571429
Q5XIC8	ALKB3	0.0009	0.52941176
Q5XIE2	MTEF2	0.025	0.52941176
P18445	RL27A	0.018	0.52631579
Q4KM86	GGACT	0.0001	0.5
O70277	TRIM3	0.0001	0.5
O08836	IGBP1	0.0001	0.5
P25886	RL29	0.021	0.5
P0C5E3	PALLD	0.026	0.5
P85971	6PGL	0.032	0.5
Q80WL2	BYST	0.017	0.47619048
O35760	IDI1	0.021	0.47368421
O88350	RBBP9	0.011	0.47058824
B0BN85	SGT1	0.034	0.44827586
O70467	ANM3	0.011	0.42857143
Q5XI01	LARP7	0.018	0.42857143
Q6IMX7	HPBP1	0.004	0.41176471
P62994	GRB2	0.017	0.39130435
Q6VV72	IF1A	0.003	0.38461538
Q9JIH7	WNK1	0.027	0.38461538
Q6MGB6	RING1	0.019	0.35
O55173	PDPK1	0.0001	0.33333333
Q6P7A2	UBE4A	0.00075	0.33333333
O70199	UGDH	0.0013	0.31428571
Q6BBI8	UFC1	0.03	0.3
O08874	PKN2	0.013	0.2625
Q4V7F3	OSGP2	0.014	0.2625
P51952	CDK7	0.049	0.24
Q08290	CNN1	0.031	0.21428571
Q5BK56	GSTM4	0.036	0.2
P57113	MAAI	0.0088	0.18333333
Q4KLJ8	PDCL3	0.0078	0.15
Q9QYU4	CRYM	0.011	0.15

Q6IRK9	CBPQ	0.012	0.075
B0BN49	RBMX2	0.018	0.075
Q9ES73	MAGD1	0.019	0.075
Q5U2V4	PLBL1	0.0066	0.06
Q8CGS4	CHMP3	0.028	0.05
O55166	VPS52	0.0011	0.0375
Q4V8K5	BROX	0.008	0.03333333
P52287	GBB3	0.0001	0.025