

SUPPLEMENTAL MATERIAL

Table S1. Characteristics of Donor, DCM and HCM subject.

Subject	Diagnosis	Age(years)	Sex	LVEF (%)	LVEDd (mm)	IVSd (mm)
1	Donor	49	Male	64	46	8
2	Donor	54	Male	68	37	9
3	Donor	32	Male	70	44	7
4	Donor	50	Female	67	45	7
5	DCM	36	Male	35	68	9
6	DCM	55	Male	24	65	10
7	DCM	48	Female	32	70	10
8	DCM	65	Male	28	80	9
9	HCM	30	Male	65	N/A	22
10	HCM	42	Male	55	40	27
11	HCM	56	Male	60	N/A	25
12	HCM	44	Male	58	45	20

LVEF=left ventricular ejection fraction; LVEDd=left ventricular end-diastolic dimension; IVSd=interventricular septal thickness at diastole; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; N/A, not available

Table S2. Echo data of ADAM22-TG and ADAM22-NTG mice with TAC or sham operation.

Parameter	NTG Sham	ADAM22 TG Sham	NTG TAC 4W	ADAM22 TG TAC 4W
IVSD	0.66±0.022	0.66±0.032	0.77±0.031*	0.69±0.037#
LVEDD	3.56±0.134	3.60±0.127	4.58±0.155*	3.91±0.164#
LVPWd	0.66±0.033	0.65±0.034	0.75±0.042*	0.70±0.045#
IVSS	1.03±0.040	1.03±0.047	1.21±0.065*	1.10±0.039#
LVESD	1.91±0.112	1.90±0.076	3.21±0.106*	2.36±0.171#
LVPWS	1.03±0.038	1.03±0.029	1.21±0.055*	1.08±0.054#
EF	79.27±2.453	79.92±3.147	60.27±3.379*	70.83±5.89#
FS	46.3±3.552	47.5±1.730	29.45±2.114*	39.5±2.611#

IVSD=left ventricular wall thickness at end diastole; LVEDD=left ventricular end-diastolic dimension; LVPWd=left ventricular posterior wall thickness at end diastole; IVSS=ventricular septum wall thickness at end systole; LVESD=left ventricular end-systolic dimension; LVPWS= left ventricular posterior wall thickness at end systole; EF=ejection fraction; FS=fractional shortening.

All values are presented as means ± SD. * $P < 0.05$ vs ADAM22 NTG TAC/sham group; # $P < 0.05$ vs ADAM22 TG TAC/sham group.

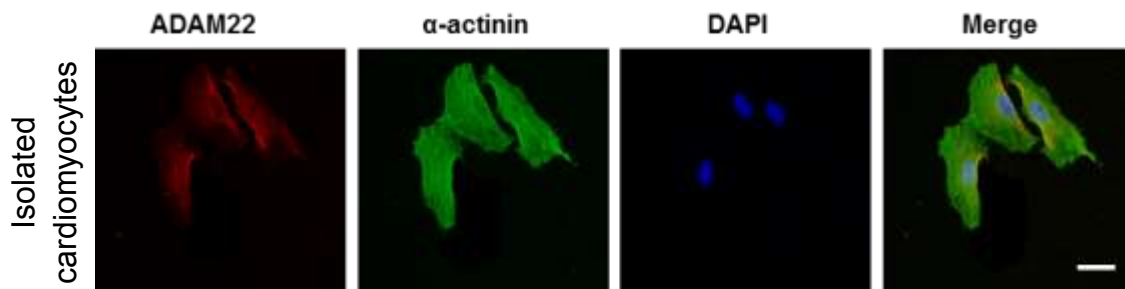
Table S3. Echo data of ADAM22-CKO and ADAM22-Flox mice with TAC or sham operation.

Parameter	α -MHC-MCM	ADAM22-Flox	ADAM22-CKO Sham	α -MHC-MCM	ADAM22-Flox	ADAM22-CKO
	Sham	Sham		TAC 4W	TAC 4W	TAC 4W
IVSD	0.64±0.032	0.65±0.018	0.65±0.033	0.81±0.051*	0.79±0.032*	0.86±0.056 [#]
LVEDD	3.51±0.169	3.53±0.124	3.60±0.173	4.48±0.157*	4.52±0.145*	5.16±0.136 [#]
LVPWd	0.65±0.019	0.64±0.042	0.64±0.026	0.76±0.051*	0.75±0.041*	0.84±0.035 [#]
IVSS	1.03±0.027	1.01±0.036	1.00±0.039	1.21±0.042*	1.22±0.038*	1.27±0.026 [#]
LVESD	1.83±0.091	1.85±0.101	1.90±0.11	3.15±0.151*	3.16±0.103*	4.12±0.150 [#]
LVPWS	1.02±0.042	1.03±0.054	1.03±0.038	1.20±0.075*	1.23±0.048*	1.27±0.061 [#]
EF	81.5±3.605	80.2±3.215	80.1±3.458	62.33±4.01*	62±4.669*	46±4.123 [#]
FS	47.75±1.337	47.33±2.309	46.73±2.68	29.5±2.431*	30.18±2.359*	20.2±2.864 [#]

IVSD=left ventricular wall thickness at end diastole; LVEDD=left ventricular end-diastolic dimension; LVPWd=left ventricular posterior wall thickness at end diastole; IVSS=ventricular septum wall thickness at end systole; LVESD=left ventricular end-systolic dimension; LVPWS= left ventricular posterior wall thickness at end systole; EF=ejection fraction; FS=fractional shortening. All values are presented as means ± SD.

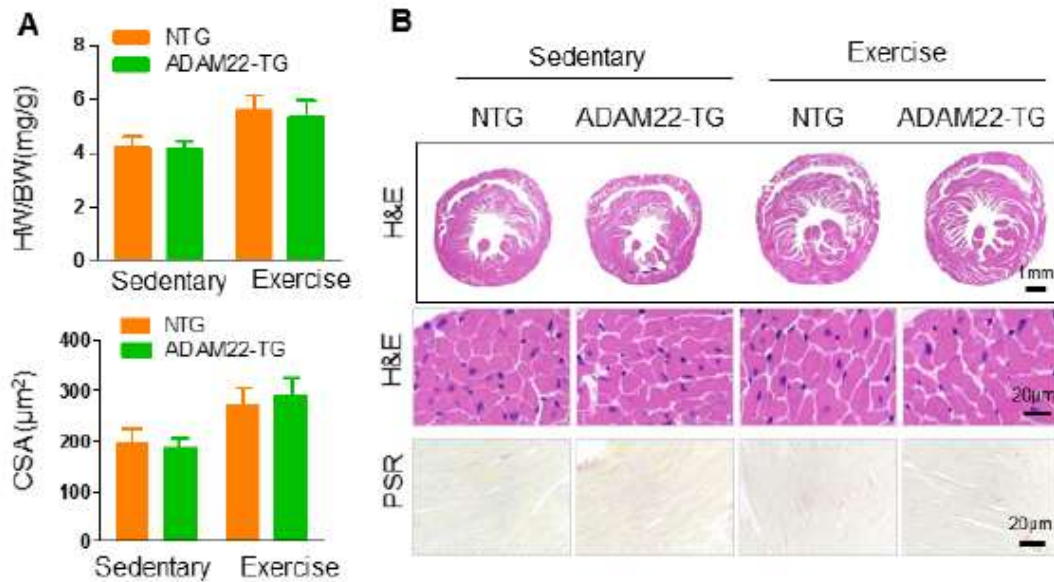
* P <0.05 vs α -MHC-MCM TAC/sham or ADAM22-Flox TAC/sham group; [#] P <0.05 vs ADAM22-CKO TAC/sham group.

Figure S1. The expression of ADAM22 in cardiomyocytes.



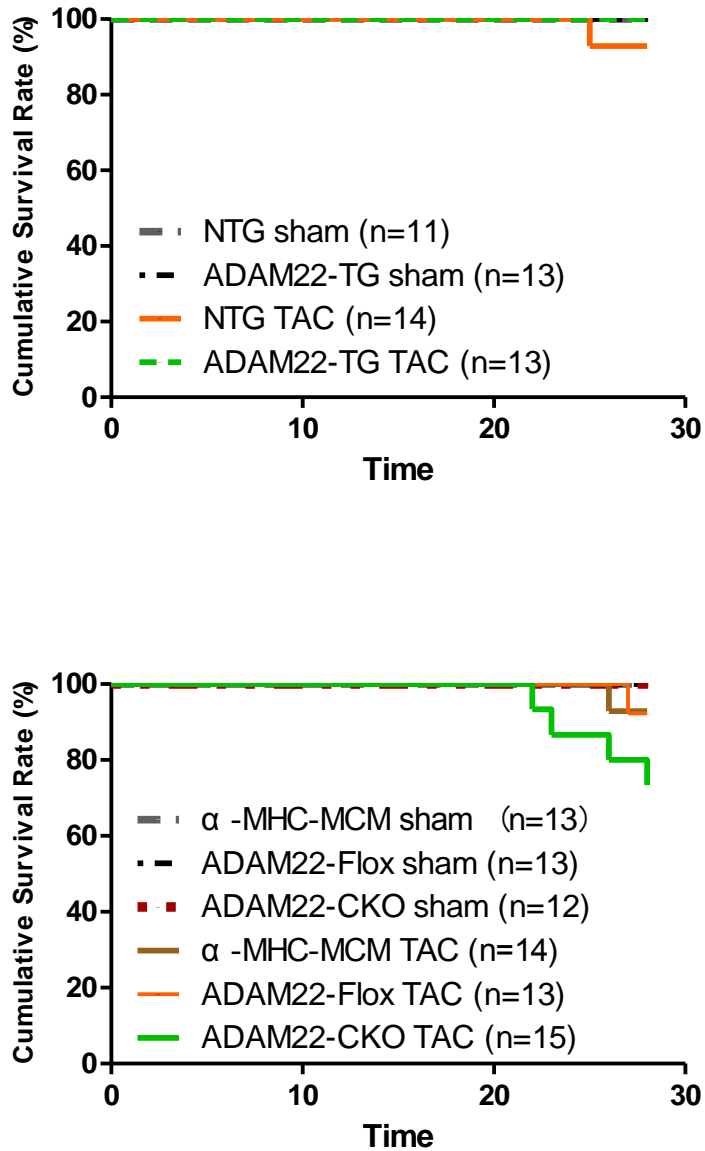
Immunofluorescence staining of ADAM22 on isolated cardiomyocytes labeled by specific marker α -actinin. (scale bar = 20 μ m)

Figure S2. The influence of ADAM22 on physiological cardiac hypertrophy.



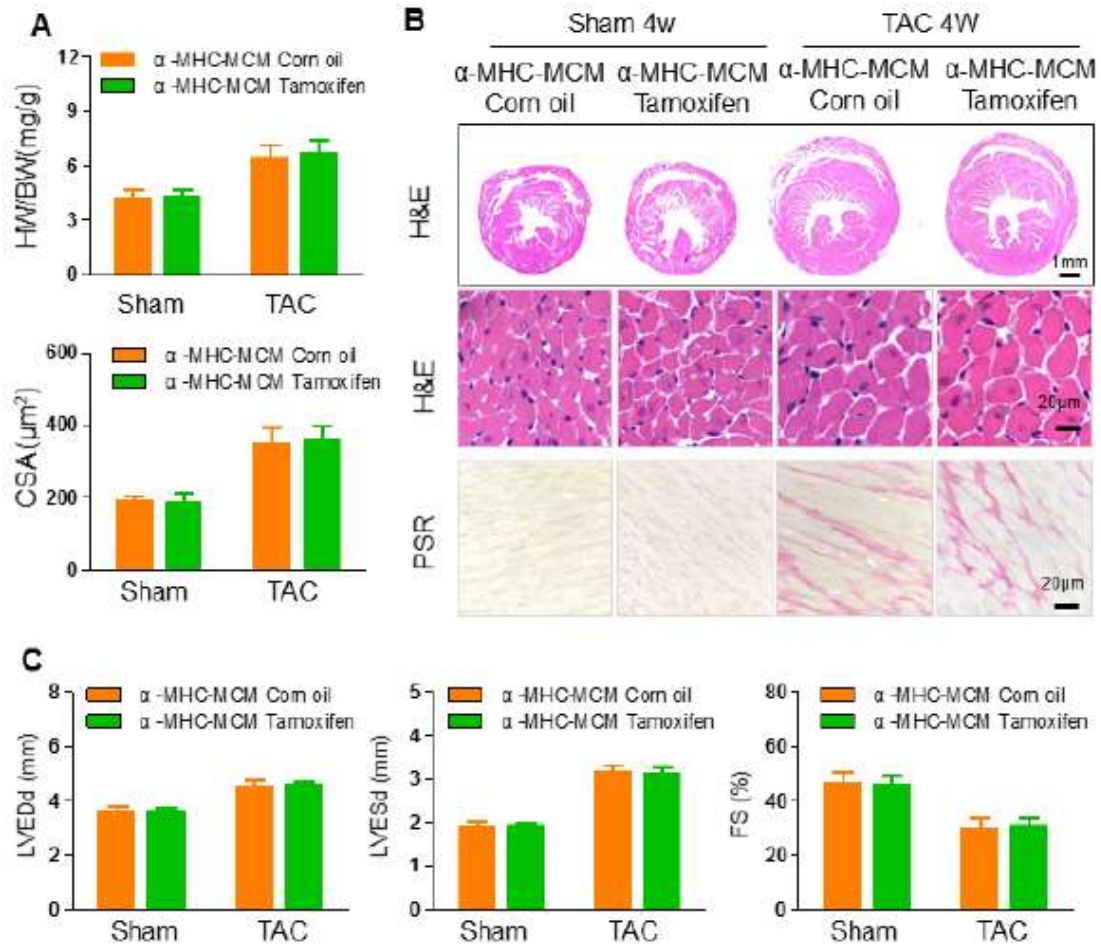
(A) The HW/BW ratios and analyses of the cardiac cross-sectional areas from ADAM22-TG and NTG mice under sedentary or exercise condition (n=7 mice in NTG group and n=12 mice in TG group were measured). (B) Histological analyses of whole heart stained with H&E (scale bar = 1 mm or 20 μm) and cardiac interstitial fibrosis after picrosirius red staining in the indicated groups. (scale bar = 20 μm , n=7 mice in NTG group and n=12 mice in TG group were measured).

Figure S3. Survival data in mice upon TAC.



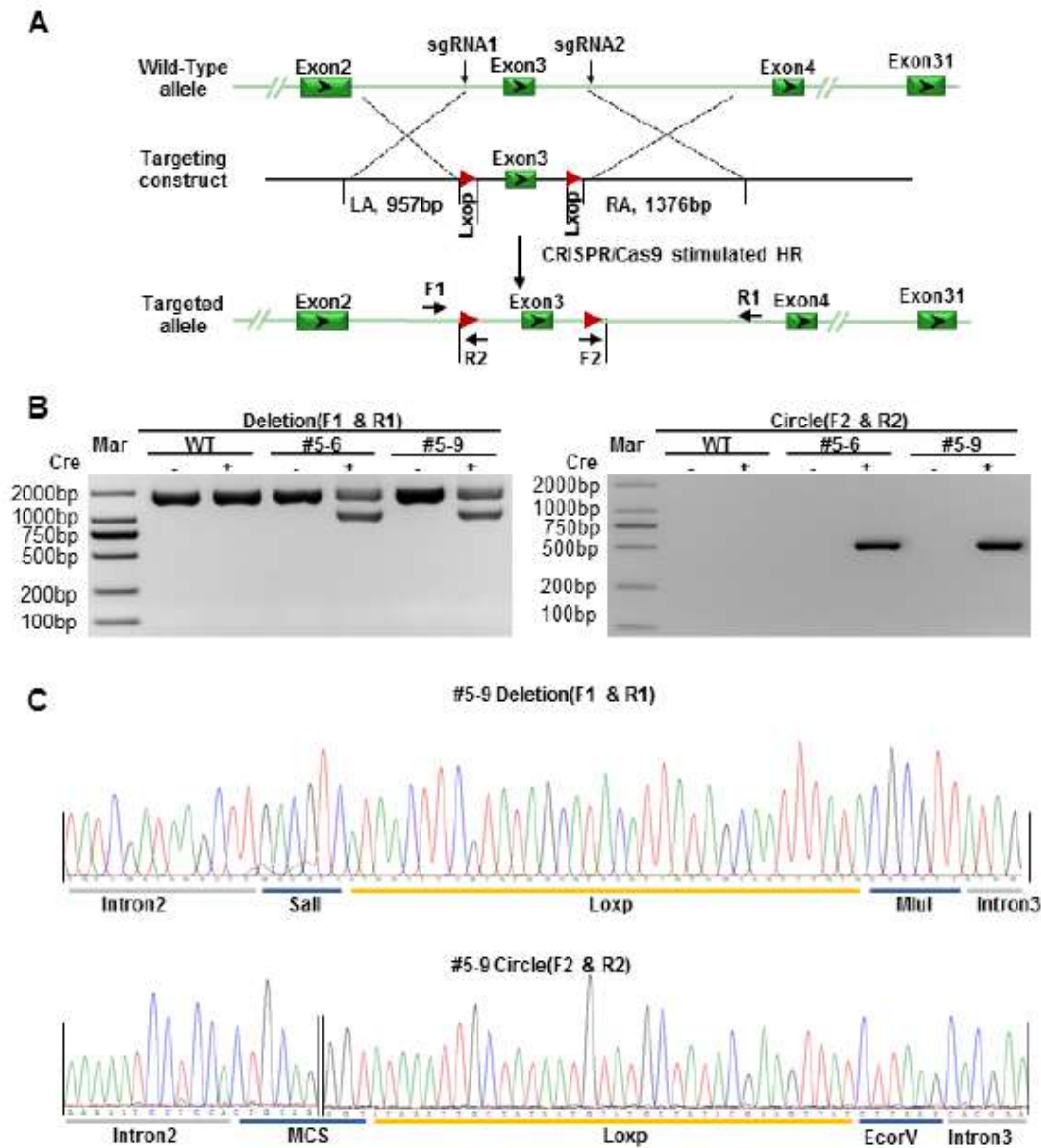
(A) Survival data of cardiac-specific conditional ADAM22 knockout, α -MHC-MCM and ADAM22-Flox mice upon TAC and sham operation. (B) Survival data of cardiac-specific ADAM22 transgenic and control mice upon TAC and sham operation.

Figure S4. The effect of tamoxifen injection on cardiac function of α MHC-MerCreMer.



(A) The HW/BW ratios and analyses of the cardiac cross-sectional areas from α -MHC-MCM mice injected corn oil or tamoxifen under TAC or sham operation (n=8 mice were measured per group). (B) Histological analyses of whole heart stained with H&E (scale bar = 1 mm or 20 μm) and cardiac interstitial fibrosis after picrosirius red staining in the indicated groups. (scale bar = 20 μm , n=8 mice were measured per group). (C) The levels of LVEDd, LVESd and FS in the indicated groups (n=8 mice per group).

Figure S5. Generation of cardiac-specific conditional ADAM22 knockout mice and identification.



(A) Illustration of cardiac-specific conditional ADAM22 knockout mice. **(B)** Amplification of the entire region covering the floxed exon 1, exon 2, and homology arm using the F1/R1 primer (left) and the circle excised by Cre using the F2/R2 primer (right). **(C)** DNA sequence of the truncated fragment amplified by the F1/R1 primer (upper) and the circular PCR products amplified by the F2/R2 primer (below). Western blot analysis of ADAM22 expression in different tissues of ADAM22-CKO and WT mice (n=8 mice per group; *P<0.05 vs. WT group).