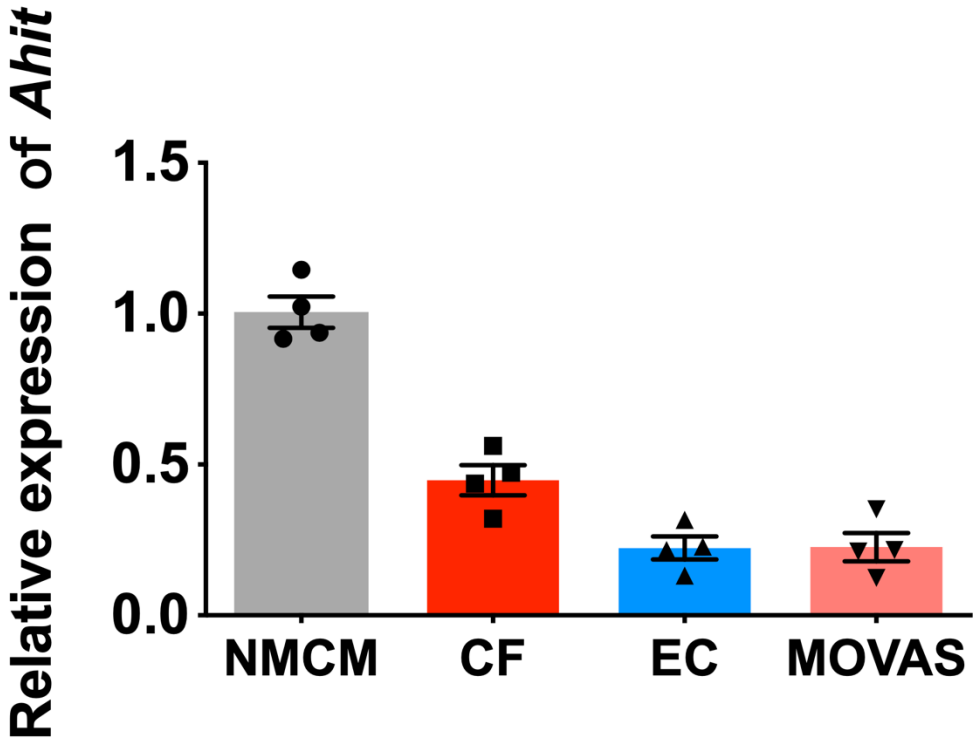
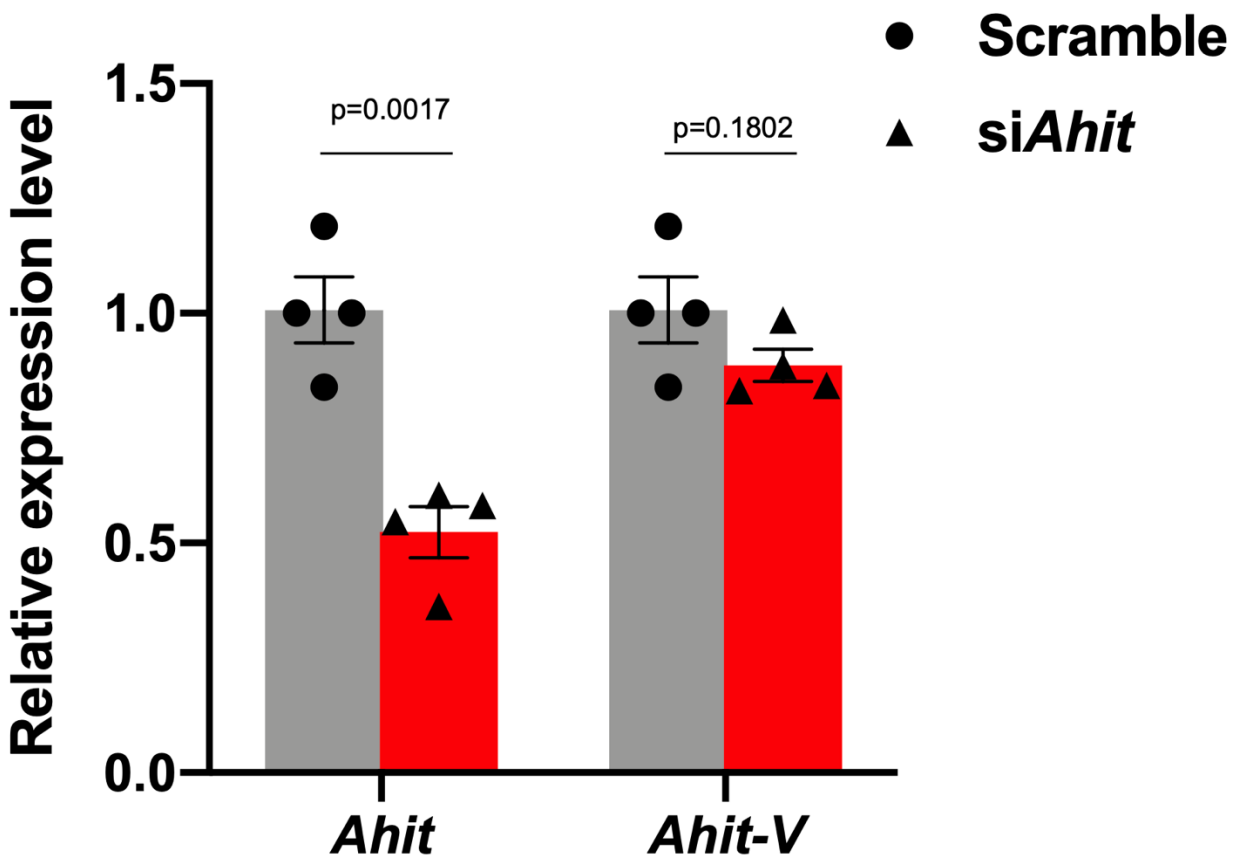
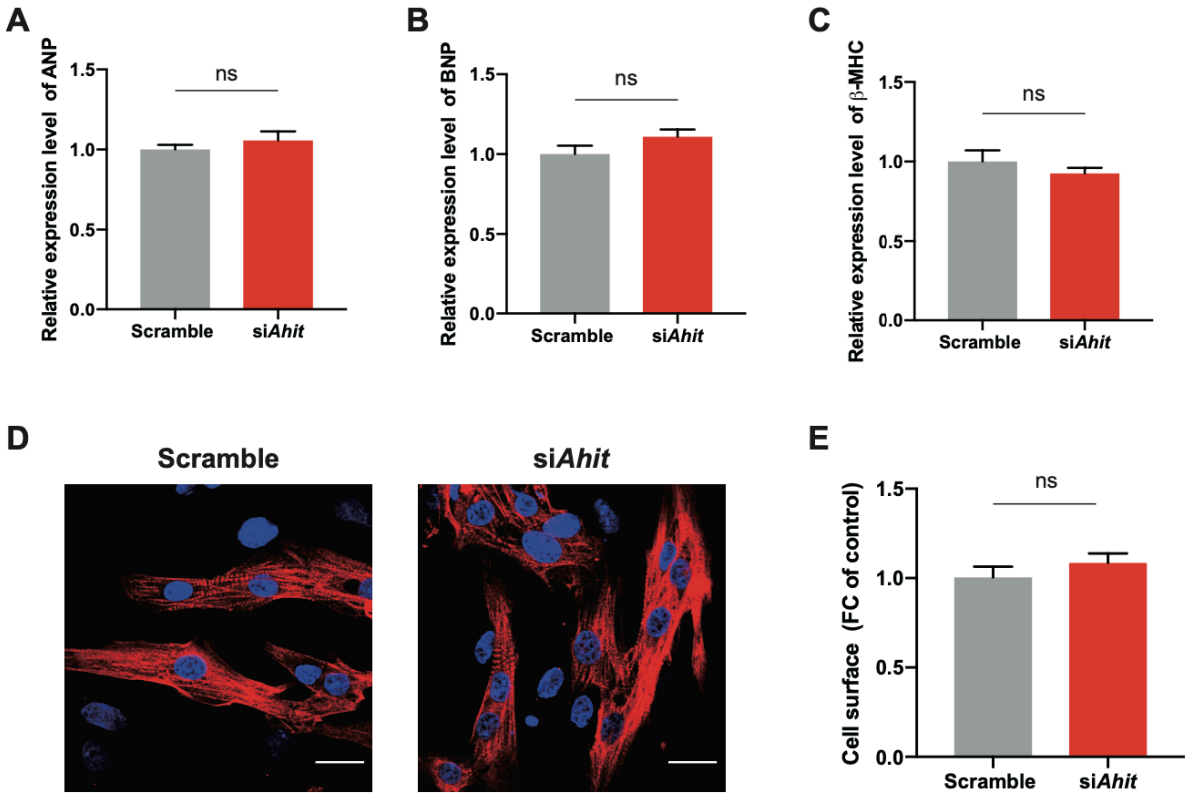
Supplementary materials.



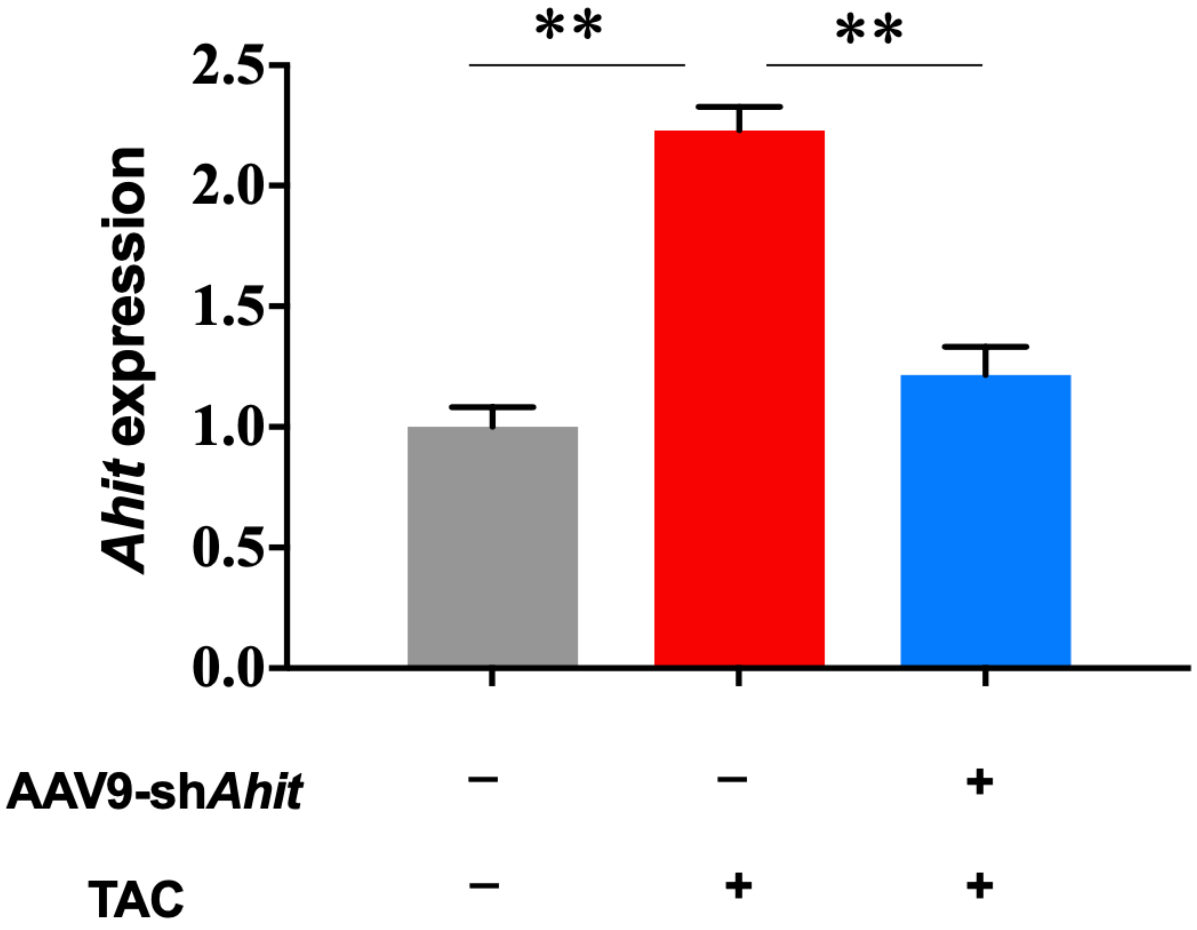
Supplementary Figure 1. The *Ahit* expressions in cardiomyocytes and other cell types. NMCM: Neonatal Mouse Cardiomyocytes; CF: Cardiac fibroblasts; EC: Endothelial cells; MOVAS: Mouse aortic vascular smooth muscle cells (*n*=3, normalized with GAPDH). Data are shown as mean±SEM.



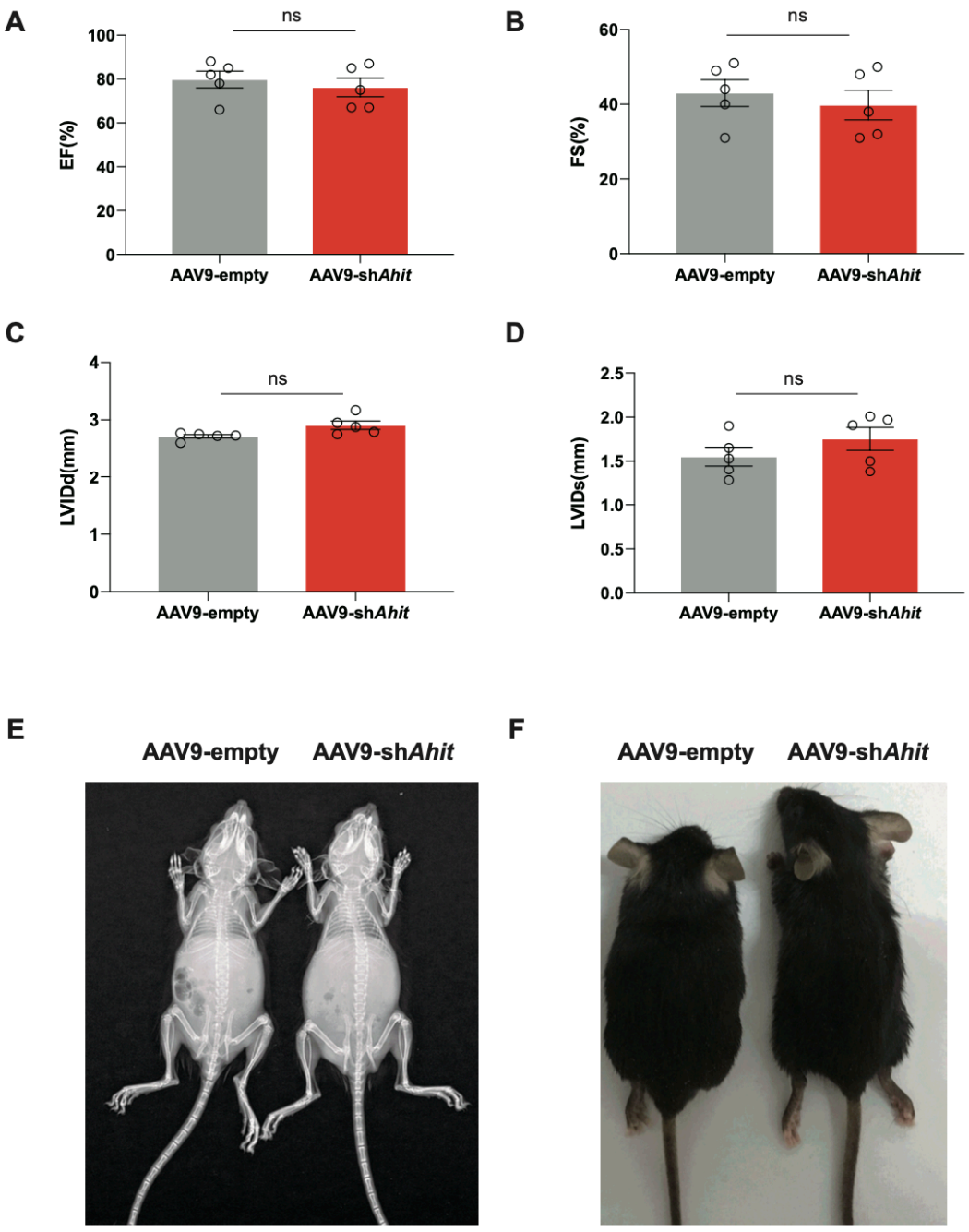
Supplementary Figure 2. The expression of *Ahit* and *Ahit*-V in NRCMs with *Ahit* knockdown. NRCMs were transfected with siRNA targeting *Ahit* (si*Ahit*) or scramble for 24 h, and analyzed by qRT-PCR (*n* =3, Student's t-test). Data are shown as mean±SEM.



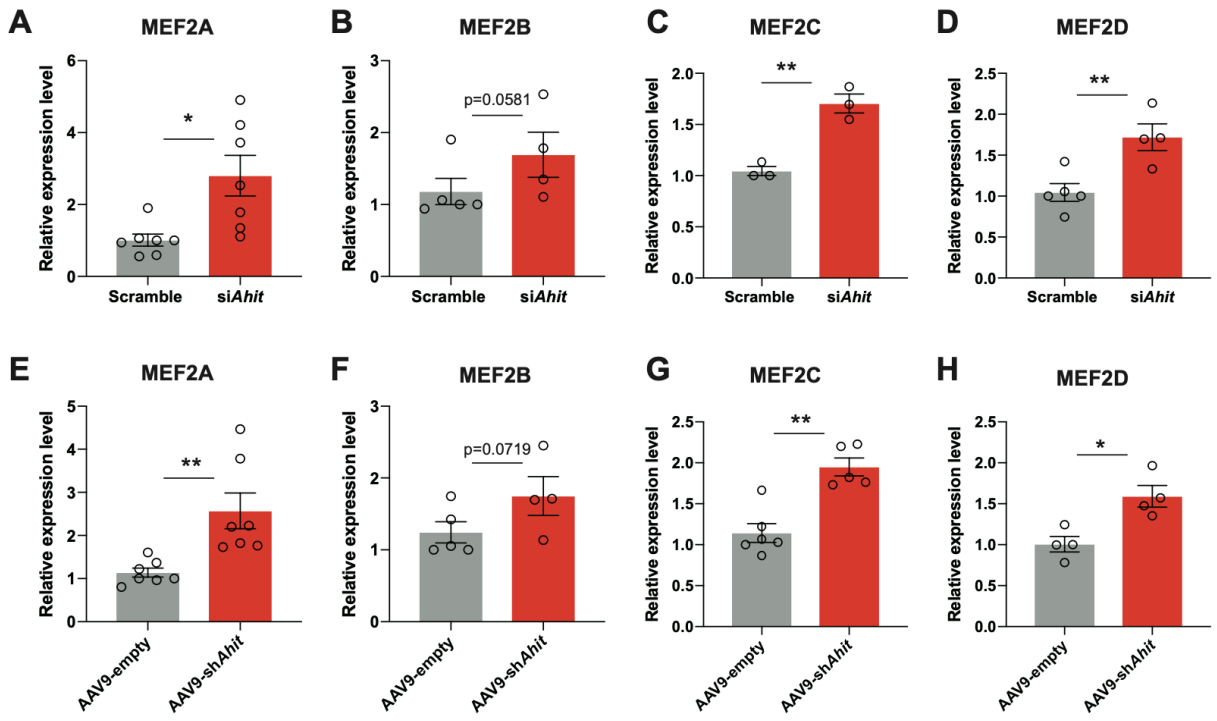
Supplementary Figure 3. The effect of si*Ahit* on cellular and molecular phenotype of NRCMs without hypertrophic stimulation. A-C. The mRNA expressions of hypertrophy marker genes ANP (**A**), BNP (**B**), and β-MHC (**C**) after *Ahit* knockdown (*n*=3/group). **D.** Cellular phenotype and fold-change of the cell surface area after *Ahit* knockdown. (4 slides/group with 10 fields/slide) Data are shown as mean±SEM.



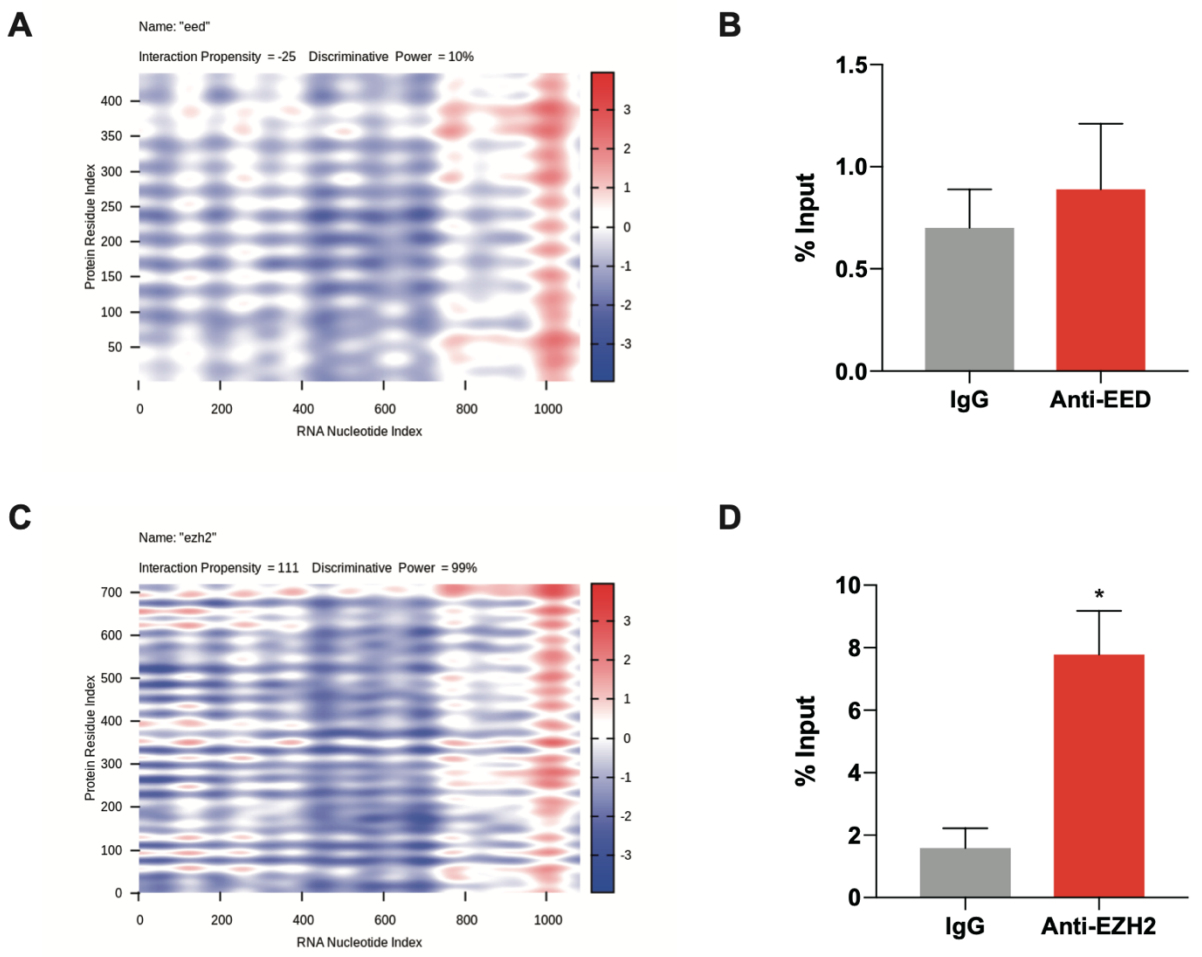
Supplementary Figure 4. The *Ahit* expression in AAV-sh*Ahit* and AAV-empty mouse heart after TAC. The result was detected with qRT-PCR in sham, TAC with AAV9-empty, and TAC with AAV9-sh*Ahit* (*n*=3, ***P* < 0.01 versus the sham group, one-way ANOVA, Holm-Sidak test). Data are shown as mean±SEM.



Supplementary Figure 5. Basic cardiac function and growth of mice injected with AAV9-empty and sh*Ahit*. A-D. Echocardiography analyses of cardiac function between the two groups. EF: Left ventricular ejection fraction; FS: Fractional shortening; LVIDd: Left ventricular internal dimension at end-diastole; LVIDs: Left ventricular internal dimension at end-systolic pressure (*n*=5/group). **E** and **F**. X-ray (**E**) and gross appearance (**F**) of the two groups of mice.



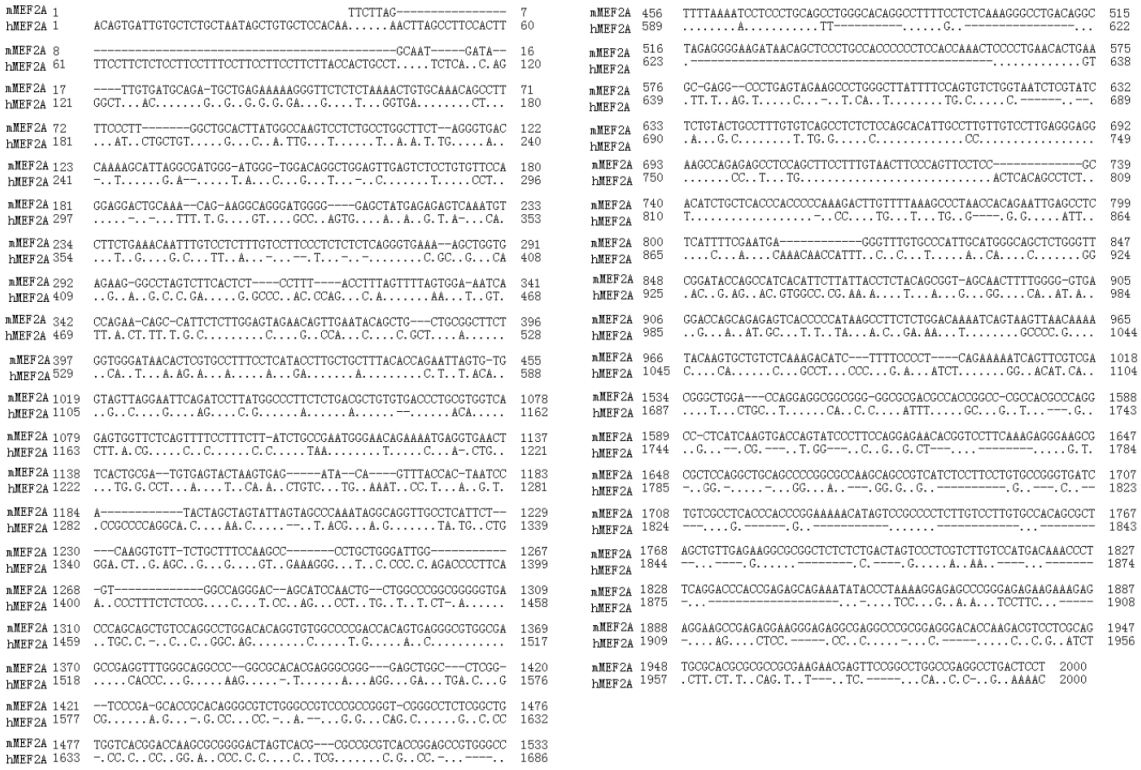
Supplementary Figure 6. The expressions of the MEF2 family genes, MEF2A, MEF2B, MEF2C, and MEF2D, after *Ahit* knock-down *in vitro* and *in vivo*. A-D, qRT-PCR analysis of MEF2A (**A**), MEF2B (**B**), MEF2C (**C**), and MEF2D (**D**) expressions in the NMCMs transfected with *Ahit* or scramble siRNA (n=3, $^{*}P < 0.05$; $^{**}P < 0.01$ versus scramble, Student's t-test). **E-H**, Cardiac *in vivo* expression of MEF2A (**E**), MEF2B (**F**), MEF2C (**G**), and MEF2D (**H**) in AAV9-sh*Ahit* infected mice detected by qRT-PCR (n=5, $^{*}P < 0.05$; $^{**}P < 0.01$ versus AAV9-empty, Student's t-test). All data are shown as the mean±SEM.



Supplementary Figure 7. Interaction between *Ahit* and other PRC2 components. **A and C.** Online prediction between *Ahit* and EED **(A)**, *Ahit* and EZH2 **(C)** on catRAPID website. **B and D**. RNA immunoprecipitation (RIP) of EED and *Ahit* **(B)**, EZH2 and *Ahit* **(D)** in NMCMs. Bars represent fold-enrichment of *Ahit* immunoprecipitated by specific EED or EZH2 antibody or anti-IgG (n=4. *P < 0.05 versus IgG, Student's t-test). Data are shown as mean±SEM.

Supplementary Figure 8

NW Score	Identities	Gaps	Strand
-658	1238/2273 (54%)	509/2273 (22%)	Plus/Plus



Supplementary Figure 8. The evolutionary conservation of the MEF2A promoter regions between human and mouse. This result was blasted through NCBI (https://blast.ncbi.nlm.nih.gov/Blast.cgi).

Supplementary Table 1. Patients' conditions

Control patients

Gender	Age	Blood pressure（mmHg）	cardiac hypertrophy
Female	72	115/87	-
Female	72	114/76	-
Female	74	112/73	-
Female	65	128/86	-
Female	76	107/60	-
Female	64	110/67	-
Female	75	110/64	-
Male	71	139/84	-
Male	64	145/80	-
Male	75	128/80	-
Male	70	125/80	-
Male	18	109/63	-
Male	25	101/60	-
Male	69	125/88	-
Male	64	115/75	-

Hypertensive heart disease patients

Gender	Age	Blood pressure（mmHg）	cardiac hypertrophy
Female	72	190/110	+
Female	73	170/100	+
Female	78	180/95	+
Female	91	190/110	+
Female	74	180/100	+
Female	82	215/90	+
Male	74	185/115	+
Male	84	126/88	+
Male	69	126/76	+
Male	68	175/105	+
Male	68	105/65	+

Supplementary Table 2. Primers list

Gene	Species	Forward Primer	Reverse Primer
ANP	Rattus norvegicus	TGAGCCGAGACAGCAAACAT	CAATATGGCCTGGGAGCCAA
BNP	Rattus norvegicus	CAGAAGCTGCTGGAGCTGATA	GGCGCTGTCTTGAGACCTAA
β-MHC	Rattus norvegicus	CCGAGTCCCAGGTCAACAAG	CTTGGAGCTGGGTAGCACAA
GAPDH	Rattus norvegicus	GCCCAGCAAGGATACTGAGA	GATGGTATTCGAGAGAAGGGAGG
Ahit	Rattus norvegicus	CGGAATGGGTCTGGAATGGT	TGGAACAAGCGGACGTAACA
MEF2A	Mus musculus	GAAAGCAGGACGAACTCGGA	AGTATCAGGGTCTGGGCTGT
Neat1	Mus musculus	ACCCTTTTTCATGGGGGTAG	GCTGGATGGAGGCTTGTTTA
18S	Mus musculus	CGCGGTTCTATTTTGTTGGT	AGTCGGCATCGTTTATGGTC
snoRNA	Mus musculus	CAGAGTAGCGAGGACTTGAAGAG	GCTGGTTCGTCTATCTTGTGGG
***Ahit*-V**	Mus musculus	ACGGTGCCTTACTGACACAC	ATTGCTCTGGCTGTAGGGTG
Ahit	Mus musculus	ACCCAAGGAAAACCCTGTTGA	GAACTAACGGGGAAGTGCGA
GAPDH	Mus musculus	CCACTCTTCCACCTTCGATG	CCACCACCCTGTTGCTGT A
***Ahit*-P1**	Mus musculus	AGGCAAGCATGAACCTGTCA	AGGGACCCTAATGACCTCCC
***Ahit*-P2**	Mus musculus	TGTCGGCTTCTCTTTGGAGC	ATGGCTCCTAGGTGGTCAGT
***Ahit*-P3**	Mus musculus	AAGTGTTGGGAGGCCACTATG	TCCAGTGACTCCTCCAGGTA
***Ahit*-P4**	Mus musculus	GCTTTGGGGAACCAGCATTG	TGAAGCGACCCACTTTCCTC
***Ahit*-P5**	Mus musculus	GGGCTCTTTCCTCCCCATTC	CTGGTAAACAACCCGCAGGA

Supplementary Table 3. The top 20 up-regulated ncRNAs

Probe Set ID	lncRNA	P-value	FDR	Fold-change	style	TAC 2W1	TAC 2W2	TAC 2W3	sham 1	sham 2	sham 3
17432861	**Gm13054-00**	0.0000508	0.00097	2.34	**up**	7.19917	6.773957	6.816598	5.560976	5.877608	5.664166
17492031	**4833412C05**	0.0005493	0.00299	2.24	**up**	4.328189	5.020806	4.439967	3.646907	3.165509	3.179484
17284354	**Ighv1-47-20**	0.0074278	0.0161	2.15	**up**	5.825106	5.24115	6.155831	4.950842	4.104911	4.854156
17284356	**Ighv1-54-20**	0.0012106	0.0046	2.13	**up**	5.61173	5.252519	6.013564	4.68402	4.254404	4.658948
17497783	**Gm22019-20**	0.0030595	0.00839	2.12	**up**	5.383635	5.495275	4.878191	4.079642	4.626595	3.794038
17249829	**LOC100862**	0.0013807	0.00496	2.05	**up**	7.419577	6.675532	6.859843	6.122295	5.994383	5.731214
17225169	**Snora75**	0.0194548	0.0343	1.98	**up**	4.306142	5.289876	4.224824	3.273994	4.100536	3.433555
17458677	**Gm20297**	0.0011527	0.00452	1.95	**up**	4.099085	4.731099	4.024061	2.514409	2.701237	2.66096
17278757	**Gm24564-20**	0.0025984	0.00747	1.93	**up**	4.576254	4.576254	4.859112	3.26167	4.157985	3.678313
17288107	**Mir27b**	0.0005297	0.0029	1.89	**up**	4.773398	4.971069	4.728637	3.580769	4.112498	4.034415
17260931	**Mir1933**	0.0060548	0.0138	1.83	**up**	4.354985	4.603126	3.663538	3.297647	3.308748	3.368515
17284314	**Ighv7-3-201**	0.0050719	0.012	1.79	**up**	4.4392	4.598856	4.835496	4.090337	3.048213	3.937337
17288105	**Mir23b**	0.0439697	0.0652	1.79	**up**	4.857151	5.34798	4.711966	3.345747	4.49321	4.564165
17491596	**Snord116**	0.030266	0.0483	1.77	**up**	4.022402	5.039968	5.034625	3.954946	4.161333	3.51315
17457804	**LOC665506**	0.0369548	0.0572	1.75	**up**	6.074794	6.293189	6.069461	6.027606	4.650615	5.32629
17459415	**Igk-V28**	0.0000082	0.000615	1.72	**up**	7.3159	7.30661	7.331053	6.449608	6.556776	6.597958
17264180	**Gm12295**	0.0400718	0.0609	1.71	**up**	4.7357	6.052444	5.649583	4.695332	4.6282	4.799949
17491537	**Gm26504**	0.0416898	0.0624	1.7	**up**	4.03064	5.026043	5.102505	4.012105	4.249637	3.607674
17344140	**D17H6S56E-**	0.0011994	0.00458	1.7	**up**	5.237349	4.858284	5.400797	4.297372	4.523228	4.382611
17464530	**Gm20559**	0.0132643	0.0253	1.7	**up**	7.034883	7.417033	7.005577	6.900485	6.046176	6.220438

Supplementary Table 4. Online-predicted binding between *Ahit* and MEF2A promoter on LongTarget website

QueryStart	QueryEnd	StartInSeq	EndInSeq	LncRNA	Species	Chromosor	Diretion	StartInGen	EndInGeno	MeanStabil	MeanIdenti	Strand	Rule	Score	Nt(bp)	Class	MidPoint	Center	TFO_sequence	TTS_sequence
1023	1093	1967	1896	mouse_lncl	mouse_mm	chr7	L	67374754	67374825	1.38	62.5	AntiPlus	9	1.46	72	1	1058	1059	AACTTTTGATATTTTAACAGCTGACTTTACAATGTAATAAAATAAAAATTCCCCCAAAGAAAAAAAAAAAA	TCTTCGCGGCGCGCGTGCGCACTGCGAGGACGTCTTGGTGTCCCTCCGCGGGCCTCGCCTCTCCCTTCCTCT
1026	1094	1943	1875	mouse_lncl	mouse_mm	chr7	L	67374733	67374801	1.63	62.32	AntiPlus	9	1.61	69	1	1060	1059	TTTTGATATTTTAACAGCTGACTTTACAATGTAATAAAATAAAAATTCCCCCAAAGAAAAAAAAAAAAA	CGAGGACGTCTTGGTGTCCCTCCGCGGGCCTCGCCTCTCCCTTCCTCTCGGCTTCCTCTCTTTCTTCTC
1029	1094	1937	1873	mouse_lncl	mouse_mm	chr7	L	67374731	67374795	1.61	68.18	AntiPlus	9	1.95	66	1	1061	1059	TGATATTTTAACAGCTGACTTTACAATGTAATAAAATAAAAATTCCCCCAAAGAAAAAAAAAAAAA	CGTCTTGGTGTCCCTCCGCGGGCCTCGCCTCTCCCTTCCTCTCGGCTTCCTCTCTTTCTTCTCTC
683	774	1009	1090	mouse_lncl	mouse_mm	chr7	R	67373867	67373948	1.05	60.22	AntiMinus	15	0.77	93	2	728	728	GTCAATGCCATGTAGCCTTTCACGCTATTCCATCAGCTTGGTCCAGAGTTTTAGCATCTGGCACAACTGTTCTACATCAGTGTTTTTCAGAG	GTTCGTCGAGTAGTTAGGAATTCAGATCCTTATGGCCCTTCTCTGACGCTGTGTGACCCTGCGTGGTCAGAGTGGTTCTCAG
572	624	1925	1871	mouse_lncl	mouse_mm	chr7	L	67374729	67374783	1.05	63.64	AntiPlus	18	1.29	55	3	598	598	AGAACAGCCAGGAGTACATAATGAAACCCTGTGTCAAAACACAACCAACAAAC	CCTCCGCGGGCCTCGCCTCTCCCTTCCTCTCGGCTTCCTCTCTTTCTTCTCTCCC
86	133	572	521	mouse_lncl	mouse_mm	chr7	L	67373379	67373430	1.01	65.38	AntiPlus	10	1.42	52	4	109	109	GCAGCAGTCCCAGCACCCCGCCCCCAACCTCAGGCATGAAGAGCAAGG	CAGTGTTCAGGGGAGTTTGGTGGAGGGGGGTGGCAGGGAGCTGTTATCTTCC