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 siAhit on cellular and molecular phenotype of NRCMs without hypertrophic stimulation. A-C. The mRNA expressions of hypertrophy marker genes ANP (A), BNP (B), and  $\beta$ -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-shAhit and AAV-empty mouse heart after TAC. The result was detected with qRT-PCR in sham, TAC with AAV9-empty, and TAC with AAV9-shAhit (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 shAhit. 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-shAhit 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 foldenrichment 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.

Supp	lemen	tary	Figure	8
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NW Score -658	Identities 1238/2273 (54%)	Gaps 509/2273 (22%)	Strand Plus/Plus					
mMEF2A 1 hMEF2A 1	ACAGTGATTGTGCTCTGCTAAT	TTCTTAG- TAGCTGTGCTCCACAAA	ACTTAGCCTTCCACTT	7 60	mMEF2A hMEF2A	456 589	TTTTAAAATCCTCCCTGCAGCCTGCGCACAGGCCTTTTCCTCTCAAAGGGCCTCACAGGC 	515 622
nMEF2A 8 bMFF2A 61	ттесттететесттесттест	TCCTTCCTTCTTACCACTGCCT.	GCAATGATA TCTCAC.AG	16 120	nMEF2A	516 623	TAGAGGGGAAGATAACAGCTCCCTGCCACCCCCCCCCCC	575 638
mMEF2A 17 hMEF2A 121	TTGTGATGCAGA-TGCTG GGCTACGG.	GAGAAAAAGGGTTCTCTCTAAAAG G. G. G. GA G T GGT	CTGTGCAAACAGCCTT IGACT	71 180	nMEF2A hMEF2A	576 639	CC-GAGGCCCTGAGTAGAAGCCCTGCCTTATTTTCCACTGTCTGGTAATCTCGTATC . TT. T. AG. T C T. CA T TG. C C	632 689
nMEF2A 72 hMEF2A 181	TTCCCTTGGCTGCAC	CTTATGGCCAAGTCCTCTGCCTG .CA.TTGTT.A	GCTTCTAGGGTGAC A. A. T. TG A	122 240	nMEF2A hMEF2A	633 690	TCTGTACTGCCTTTGTGTCAGCCTCTCTCCAGCACATTGCCTTGTTGTCCTTGAGGGAGG	692 749
nNEF2A 123 hNEF2A 241	CAAAAGCATTAGGCGATGGG-A TG.AT.	ATGGG-TGGACAGGCTGGAGTTGA ACGTC	AGTCTCCTGTGTTCCA	180 296	nMEF2A hMEF2A	693 750	AAGCCAGAGAGCCTCCAGCTTCCTTTGTAACTTCCCAGTTCCTCCGC CCTTGACTCACAGCCTCT.	739 809
mMEF2A 181 hMEF2A 297	GGAGGACTGCAAACAG-AAG	GCAGGGATGGGGGAGCTAT .GTGCCAGTGA	IGAGAGAGTCAAATGT AG.T.ACA.	233 353	nMEF2A hMEF2A	740 810	ACATCTGCTCACCCACCCCCAAAGACTTGTTTTAAAGCCCTAACCACAGAATTGAGCCTC T	799 864
mMEF2A 234 hMEF2A 354	CTTCTGAAACAATTTGTCCTCT	TTGTCCTTCCCTCTCTCAGGO	TGAAAAGCTGGTG C.GCGCA	291 408	nMEF2A hMEF2A	800 865	TCATTTTCGAATGAGGGTTTGTGCCCATTGCATGGGCAGCTCTGGGTT C.ACAAACAACCATTT.C.C.T.T.A.CAC	847 924
mMEF2A 292 hMEF2A 409	AGAAG-GGCCTAGTCTTCACTC	CTCCTTTACCTTTAG G. GCCC AC. CCAG C. A	TTTTAGTGGA-AATCA AATGT.	341 468	nMEF2A hMEF2A	848 925	CGGATACCAGCCATCACATTCTTATTACCTCTACAGCGGT-AGCAACTTTTGGGG-GTGA . AC G. AG AC. GTGGCC. CG. AA. A T A G GG CA AT. A	905 984
mMEF2A 342 hMEF2A 469	CCAGAA-CAGC-CATTCTCTTG TT. A. CT. TT. T. G. C	GAGTAGAACAGTTGAATACAGCT	IGCTGCGGCTTCT C. GCTA	396 528	nMEF2A hMEF2A	906 985	GCACCAGCAGAGAGTCACCCCCATAAGCCTTCTCTGGACAAAATCAGTAAGTA	965 1044
mMEF2A397 hMEF2A529	GGTGGGATAACACTCGTGCCTT	TCCTCATACCTTGCTGCTTTACA	ACCAGAATTAGTG-TG	455 588	nMEF2A hMEF2A	966 1045	TACAAGTGCTGTCTCAAAGACATCTTTTCCCCTCAGAAAAATCAGTTCGTCGA CCaCGCTCCCG.AATCTGG.ACAT.CA	1018 1104
mMEF2A 1019 hMEF2A 1105	GTAGTTAGGAATTCAGATCCTT GCGAGC	ATGGCCCTTCTCTGACGCTGTG	IGACCCTGCGTGGTCA	1078 1162	nMEF2A hMEF2A	1534 1687	CGGGCTGGACCAGGAGGCGCGCGGGGGGGCACCGGCC-CGCCACGCCAGG TCTGCTCAC.CATTTGCGTG.	1588 1743
nMEF2A 1079 hMEF2A 1163	GAGTGGTTCTCAGTTTTCCTTT CTT. A. CG C C	CTT-ATCTGCCGAATGGGAACAC	GAAAATGAGGTGAACT	1137 1221	nMEF2A hMEF2A	1589 1744	CC-CTCATCAAGTGACCAGTATCCCTTCCAGGAGAACACGGTCCTTCAAAGAGGGGAAGGG GG	1647 1784
mMEF2A 1138 hMEF2A 1222	TCACTGCGATGTGAGTACTA	AGTGAGATACAC CA.A.CTGTCTGAAAT.	TTTACCAC-TAATCC .CC.TAG.T.	1183 1281	nMEF2A hMEF2A	1648 1785	CGCTCCAGGCTGCAGCCCCGGCGCCAAGCAGCCGCCTCATCTCCTTTCCTGCCCGGGTGATC GGGGAGG.GGG	1707 1823
nMEF2A 1184 hMEF2A 1282	ATACTAGCTA . CCGCCCCAGGCA. C AA.	GTATTAGTAGCCCAAATAGGCAG CA.G	GTTGCCTCATTCT TA.TGCTG	1229 1339	nMEF2A hMEF2A	1708 1824	TGTCGCCTCACCCGCGAAAAACATAGTCCGCCCCCTTTGTCCTTGTGCCCCACGGGCT	1767 1843
mMEF2A 1230 hMEF2A <sup>1340</sup>	CAAGGTGTT-TCTGCTTTC GGA.CTG.AGCGG.	CAAGCCCCTGCTGGGA	ATTGG CC. C. AGACCCCTTCA	1267 1399	nMEF2A hMEF2A	1768 1844	AGCTGTTGAGAAGGGCGGGGCTCTCTGAGTAGTCCCTCGTCTTGTCCATGACAAACCCT	1827 1874
nMEF2A 1268 hMEF2A 1400	-GTGGCCAG ACCCTTTCTCTCCGC.	GGACAGCATCCAACTGCTC	GCCCCGGCGGGGGGTGA	1309 1458	nMEF2A hMEF2A	1828 1875	TCAGGACCCACCGAGAGCAGAAATATACCCTAAAAGGAGAGCCCCGGGAGAAGAAGAG 	1887 1908
nMEF2A 1310 hMEF2A 1459	CCCAGCAGCTGTCCAGGCCTGG TGC.CCCGGC.A	GACACAGGTGTGGCCCCGACCACA	AGTGAGGGGCGTGGCGA	1369 1517	nMEF2A hMEF2A	1888 1909	AGGAAGCCCAGAGGAAGGGACAGGCCAGGCCCCCGGAGGGACACCAAGACGTCCTCCGCAG , AG, CTCC, CC. , C,, C. , C. , C.	1947 1956
mMEF2A 1370 hMEF2A <sup>1518</sup>	GCCGAGGTTTGGGCAGGCCC CACCCGAAG	-GGCGCACACGAGGGCGGGGA	AGCTGGCCTCGG- .GATGA.CG	1420 1576	nMEF2A hMEF2A	1948 1957	TCCCCACGCCGCCGCGAAGAACCAGTTCCCGCCCGGCCGAGGCCTGACTCCT 2000 .CTT.CT.T.CAG.T.TTCCAC.CG.AAAAC 2000	
mMEF2A 1421 hMEF2A 1577	TCCCGA-GCACCGCACAGGG CGA.GG.CC	CGTCTGGGCCGTCCCGCCGGGT . CC A G. G CAC	-CGGGCCTCTCGGCTG G. C G C. CC	1476 1632				
nMEF2A 1477 hMEF2A 1633	TGGTCACGGACCAAGCGCGGGG CC. C CC GG. A CCC.	ACTAGTCACGCGCCGCGTCA	ACCGGAGCCGTGGGCC	1533 1686				

Supplemen	tary Figure	e 8. Th	e evolutior	nary co	nservation	of the	e MEF2A	promoter	regions
between	human	and	mouse.	This	result	was	blasted	through	NCBI
(https://blast.ncbi.nlm.nih.gov/Blast.cgi).									

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	-

## Supplementary Table 1. Patients' conditions

## 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-МНС	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	IncRNA	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	LOC1008622	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