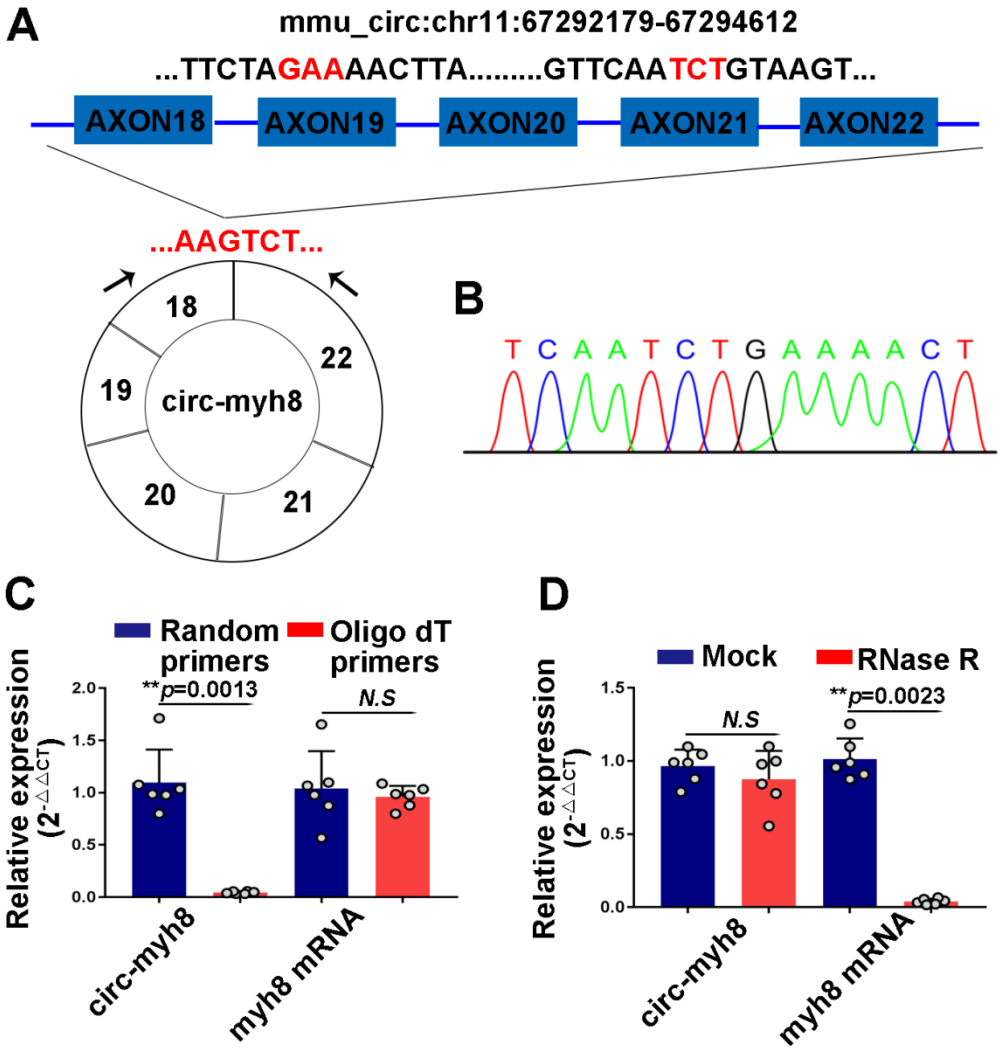
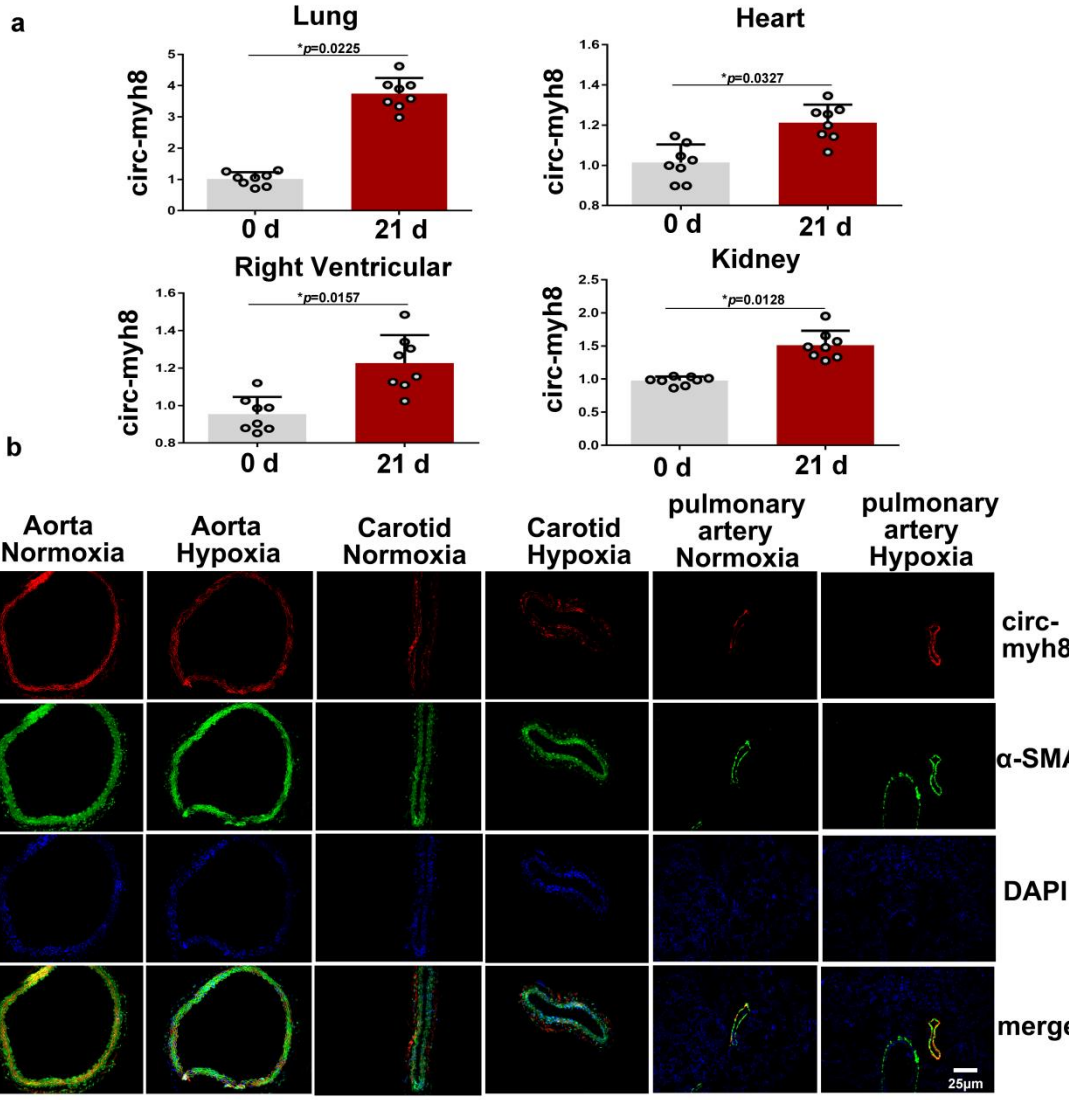
SUPPLEMENTAL MATERIAL

Figure S1. Identification and Validation of a Novel Circular RNA (circ-myh8) in mice PASMCs.



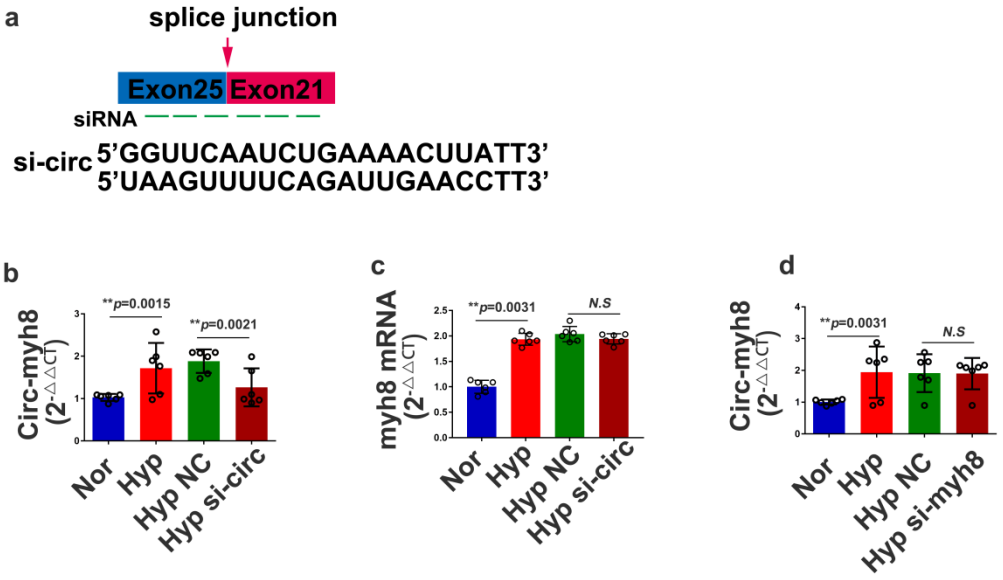
(**a**) Schematic diagram of circ-myh8. Exons 18, 19, 20, 21 and 22 of mice myh8 gene are linked end to end to form a circular structure. (**b**) The Sanger sequencing of the back-splice sites of the PCR products from the designed primers set#2. (**c**) RT-qPCR analysis for the circ-myh8 and myh8 mRNA using the template cDNA reverse-transcribed by random primers and oligo dT primers. (**d**) RT-qPCR assay for the expression of circ- myh8 and myh8 mRNA in PASMCs treated with RNase R. **p<0.01.

Figure S2. Circ-myh8 expression in tissues from hypoxic PH mice.



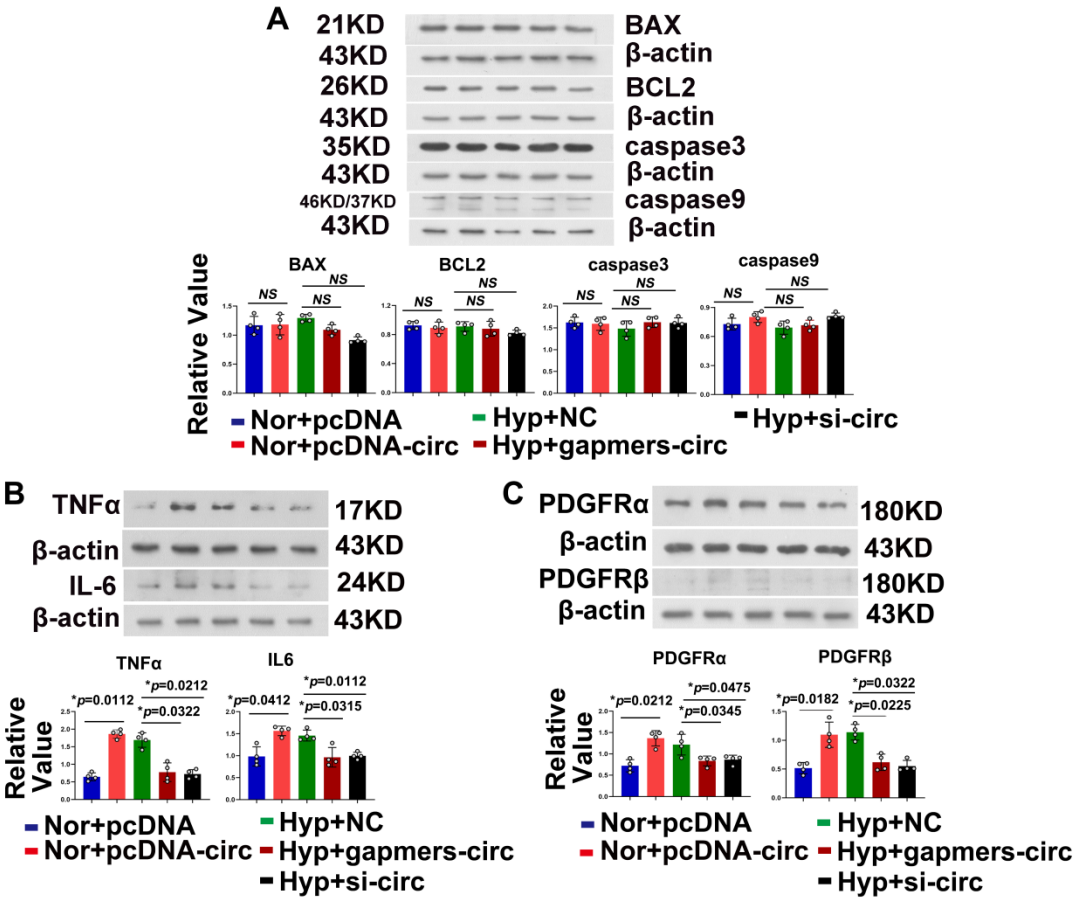
(**a**) RT-qPCR assay for circ-myh8 expression in different mice tissues. (**b**) Fluorescent in situ hybridization (FISH) for circ-myh8 (red) and immunofluorescence (IF) for α-smooth muscle actin (green) in different vascular from mice. The profiles of colocalization were also provided. Scale bar, 25 μm. * $p < 0.05$.

Figure S3. siRNA-specific silencing circ-myh8 contain head-to-tail junctions.



(**a**) Schematic illustration of two siRNAs targeting the back-splice junction of circ-myh8 (si-circ1 and nd si-circ2).circ-myh8 primer is a base sequence containing head-to-tail junctions and upstream and downstream. (**b**) RT-qPCR assay of interfering efficacy on circ-myh8 expression after transfection of the si-circ into PASMCs, and exposure to hypoxia for 24 h. (**c**) RT-qPCR assay of myh8 mRNA expression after transfection of the si-circ into PASMCs, and exposure to hypoxia for 24 h. (**d**) RT-qPCR assay of circ-myh8 expression after transfection of the si-myh8 into PASMCs, and exposure to hypoxia for 24 h. Nor represents normoxia, Hyp represents hypoxia, veh represents vehicle, and NC represent negative control. **p < 0.01.

Figure S4. Relation of Circ-myh8 with apoptosis, inflammation factor and PDGFR.



PASMCs were transfected with circ-myh8 plasmid or pcDNA following cultured in normoxia condition for 24h. For the circ-myh8 knockdown, PASMCs were transfected with circ-myh8 siRNA, gapmers, or NC then exposure to hypoxia (0.3% FiO2) for 24h. Represent images and summarized data of Bax, BCL2, caspase 3 and caspase 9 (A), TNFα and IL-6 (B), PDGFRα and PDGFRβ (C). Nor represents normoxia, Hyp represents hypoxia, veh represents vehicle, and NC represent negative control, PDGFR represents platelet-derived growth factor receptor, TNF α represents tumor necrosis factor alpha, and IL6 represents interleukin-6.

Figure S5. Circ-myh8 cannot bind to KAT5, KAT7 and KAT8. RNA pull-down assay followed by western blot for candidate proteins KAT1 (a), KAT5 (b) and KAT8 (c). KAT represents lysine acetyltransferase.

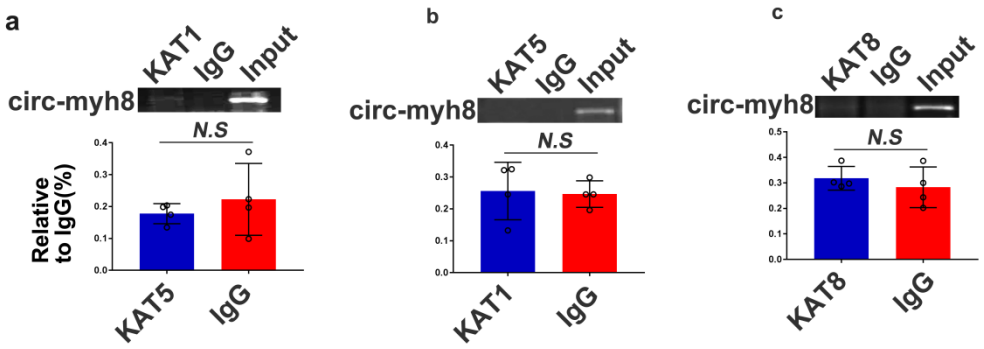
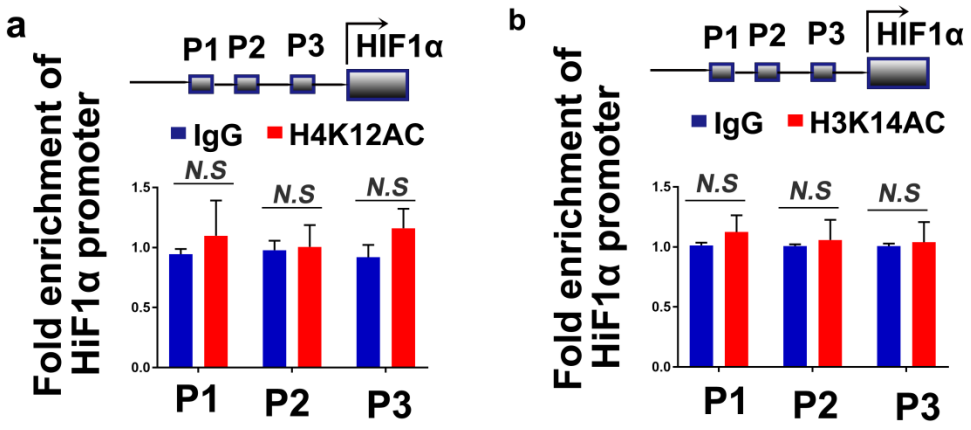


Figure S6. No acetylation occurred at H4K12 and H3K14 sites in HIF1α promoter region.



(**a**) ChIP assay for H4K12ac level and H3K14ac level (**b**) in HIF1α promoter regions. Final DNA extractions were PCR amplified using primers that cover P1 (-5837bp to -5675bp), P2 (-803bp to -554bp) and P3 (-403bp to -172bp) sites in HIF1α promoter. HIF1α represents hypoxia inducible factor alpha, H4K12AC represents acetylation of lysine 12 of histone H4, H3K14AC represents acetylation of lysine 14 of histone H3.

Table S1. Clinical information of the PH patients.

Patient	Diagnosis	Origin	Sex	Age	mPAP (mmHg)	（PAWP） (mmHg)	RAP (mmHg)	PVR (WU)	CO (L/min)	LVEF (%)
1	IPAH	Surgery	F	39	72	7	2	29.54	2.2	51%
2	PAH-CTD	Surgery	F	31	55	11	4	20.00	2.2	67%
3	IPAH	Surgery	F	52	60	14	11	8.07	5.7	65%
4	IPAH	Surgery	M	66	57	7	9	14.70	3.4	64%
5	IPAH	Surgery	F	71	38	13	19	6.76	3.7	74%
6	Group 2 PH	Surgery	F	50	41	15	13	13.52	2.3	61%
7	Group 2 PH	Surgery	F	45	43	17	19	15.30	1.7	67%
8	Group 2 PH	Surgery	F	43	73	18	4	28.79	1.8	53%
9	IPAH	Surgery	F	35	64	10	19	28.42	1.9	72%
10	IPAH	Surgery	F	26	35	8	5	4.90	5.5	61%

CO: cardiac output; iPAH: idiopathic pulmonary arterial hypertension; F: female; LVEF: left ventricle ejection fraction; Group 2 PH: PH due to left heart disease; M: male; mmHg: millimetres of mercury; mPAP: mean pulmonary artery pressure; PAWP: pulmonary artery wedge pressure; PVR: pulmonary vascular resistance; RAP: right atrial pressure; WU: Wood units.

Table S2. siRNA and gapmers sequence, FISH probe, Biotin-circ-myh8 probe.

Name	sequence（5’-3’）
NC	UUCUCCGAACGUGUCACGUTT
NC	ACGUGACACGUUCGGAGAATT
Si-circ-nyh8	GGUUCAAUCUGAAAACUUATT
Si-circ-myh8	UAAGUUUUCAGAUUGAACCTT
Si-myh8	CGACAAGGUUCUAUCAGAAUG
Si-myh8	UUCUGAUAGAACCUUGUCGAA
Gapmers-circ-myh8	AUUUAAGTTTTCAGAUUGA
FISH probe	GTTTATTTAAGTTTTCAGATTG
Biotin-circ-myh8 probe	GUACGAAGUGAGGGUGUGUA

Table S3. Primer sequence.

Name	sequence（5’-3’）
mmu-circ-myh8(F1)	TTTGGACACACCAAGGTTTTCT (630bp)
mmu-circ-myh8(R1)	GTGATCGATATCAATAGAGCCCAG (630bp)
mmu-circ-myh8(F2)	GCTGGAGGAGAAGATGGTCACT (115bp)
mmu-circ-myh8(R2)	GAAGTGAGGGTGTGTACTTCTCAGA (115bp)
mmu-myh8(F1)	CACCTGGAGCGGATGAAGAAGAAC (327bp)
mmu-myh8(R1)	CTCAGCCTCCTCAGCCTGTCTC (327bp)
mmu-myh8(F2)	AGACGGAGAGGAGCAGGAAGATTG (100bp)
mmu-myh8(F2)	TTGGTGTTGATGAGGCTCGTGTTC (100bp)
Mmu-HIF1α(F)	CCACCACAACTGCCACCACTG (141bp)
Mmu-HIF1α(R)	TGCCACTGTATGCTGATGCCTTAG (141bp)
Mmu-HIF1β(F)	CCGAGAATGGCTGTGGATGAGAAC (140bp)
Mmu-HIF1β(R)	GGATGGTGTTGGACAGTGTAGGC (140bp)
Mmu-HIF2α(F)	GATATGGCAGCGGTGTGACAGTC (115bp)
Mmu-HIF2α(R)	CCCTCATAGCGGCAACAGCAC (115bp)
Mmu-HIF2β(F)	TGGAGCCAGGAGCACAGGATG (121bp)
Mmu-HIF2β(F)	CCAACACGCCACAGTACATCTACC (121bp)
HIF1α-promoter1(F)	TGGCTTGATTTTTGTCAGTAA (162bp)
HIF1α-promoter1(R)	CAAACTTTGAGACTTGAAATG (162bp)
HIF1α-promoter2(F)	GCATCCATTTAAGATGATCTTTG (249bp)
HIF1α-promoter2(R)	GGCCAAAGTTTGACTACTGAG (249bp)
HIF1α-promoter3(F)	TCAACTGGAAACTCGGGCGG (232bp)
HIF1α-promoter3(R)	CGAGCGACGGGTGCGGCTGAG (232bp)