

SUPPLEMENTARY TABLES

Supplementary Table 1. DNA methylation level at 10 CpG sites of *BMP2* in the second cohorts of VHD-PAH patients and healthy controls.

CpG Position	Mean \pm SD in the VHD-PAH group ($n = 27$)	Mean \pm SD in the control group ($n = 29$)	<i>P</i> value
Pos. 1	3.396% \pm 0.4164%	1.239% \pm 0.5329%	0.0871
Pos. 2	50.05% \pm 3.821%	29.75% \pm 2.932%	0.0059
Pos. 3	4.623% \pm 0.7612%	4.381% \pm 0.6114%	0.8065
Pos. 4	2.479% \pm 0.4316%	1.536% \pm 0.4238%	0.1311
Pos. 5	3.866% \pm 0.8075%	3.941% \pm 0.6784%	0.9436
Pos. 6	5.790% \pm 1.037%	3.437% \pm 0.5867%	0.0880
Pos. 7	15.39% \pm 1.433%	12.91% \pm 0.3509%	0.1510
Pos. 8	6.5395% \pm 1.167%	4.828% \pm 0.6793%	0.2172
Pos. 9	29.06% \pm 2.322%	17.65% \pm 1.655%	0.0001
Pos. 10	20.73% \pm 2.099%	15.05% \pm 1.107%	0.3470
Mean value of 10 CpG sites	13.16% \pm 0.7635%	8.743% \pm 0.5544%	0.0009

Supplementary Table 2. DNA methylation of 10 CpG sites of the *BMP2* promoter in the cardiac valve specimens of the PAH patients.

Methylation (%)	Pos. 1	Pos. 2	Pos. 3	Pos. 4	Pos. 5	Pos. 6	Pos. 7	Pos. 8	Pos. 9	Pos. 10	Mean
Mild PAH	5.75 \pm 1.44	5.67 \pm 1.18	8.59 \pm 3.40	6.87 \pm 0.80	8.44 \pm 0.94	8.08 \pm 0.77	8.23 \pm 0.62	8.00 \pm 0.40	6.68 \pm 1.39	8.35 \pm 0.77	7.47 \pm 0.77
Moderate/ Severe PAH	7.56 \pm 1.65	7.39 \pm 1.87	8.72 \pm 2.60	8.36 \pm 2.15	9.57 \pm 1.67	9.86 \pm 2.36	10.30 \pm 2.45	9.83 \pm 2.41	8.32 \pm 1.35*	10.12 \pm 1.81	8.96 \pm 1.86
<i>p</i>	0.07	0.06	0.93	0.17	0.17	0.08	0.09	0.08	0.04	0.07	0.09

Supplementary Table 3. *BMP2* and *BMP4* protein expression in the human heart valve tissue samples based on immunohistochemistry (IHC).

IHC for protein expression	Tissue	Groups	Percentage contribution of High Positive & Positive (%)	Percentage contribution of Low Positive (%)	Percentage contribution of Negative (%)
<i>BMP2</i>	Lung	control	14.74 \pm 0.7813*	40.33 \pm 0.4954	44.94 \pm 1.145
		PAH	10.02 \pm 1.552	34.71 \pm 3.308	55.27 \pm 4.199*
	Heart	control	8.509 \pm 1.520	56.20 \pm 4.989	35.29 \pm 6.186
		PAH	5.784 \pm 0.3746	50.53 \pm 4.655	43.69 \pm 4.622
<i>BMP4</i>	Lung	control	12.16 \pm 0.6811	22.42 \pm 5.482	66.28 \pm 8.868
		PAH	15.12 \pm 0.8344*	35.88 \pm 1.279*	53.70 \pm 5.432
	Heart	control	2.600 \pm 0.3343	48.92 \pm 3.002	46.51 \pm 3.385
		PAH	1.644 \pm 0.3046	46.57 \pm 0.881	51.79 \pm 0.7491

**P* < 0.05.

Supplementary Table 4. Quantification of fibrosis based on VG and HE staining in the heart and lung of the PAH model mice.

Groups	VG staining	Area fraction %	HE staining	Area fraction %
control	Lung	25.48 ± 1.861*	Lung	16.08 ± 3.322
PAH		32.27 ± 2.644		14.21 ± 3.144
control	Heart	14.89 ± 0.3421	Heart	10.90 ± 2.115
PAH		16.24 ± 4.228		10.86 ± 0.6797

**P* < 0.05.

Supplementary Table 5. Comparisons of sensitivity and specificity for our methods and others in VHD-PAH diagnosis.

VHD group VS. control group	sensitivity	specificity
<i>BMP2</i> mRNA	0.761	0.815
<i>BMP2</i> DNA methylation	0.861	0.833
combination	0.898	0.919
ECG	0.70	0.62
TTE	0.78	0.92