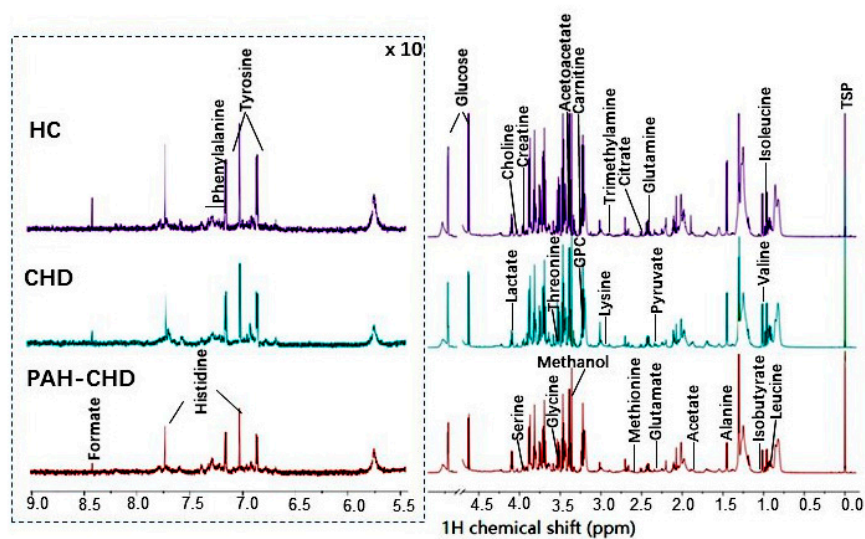


# **NMR-based Metabolomic Analysis of Plasma in Patients with Adult Congenital Heart Disease and Associated Pulmonary Arterial Hypertension: A Pilot Study**

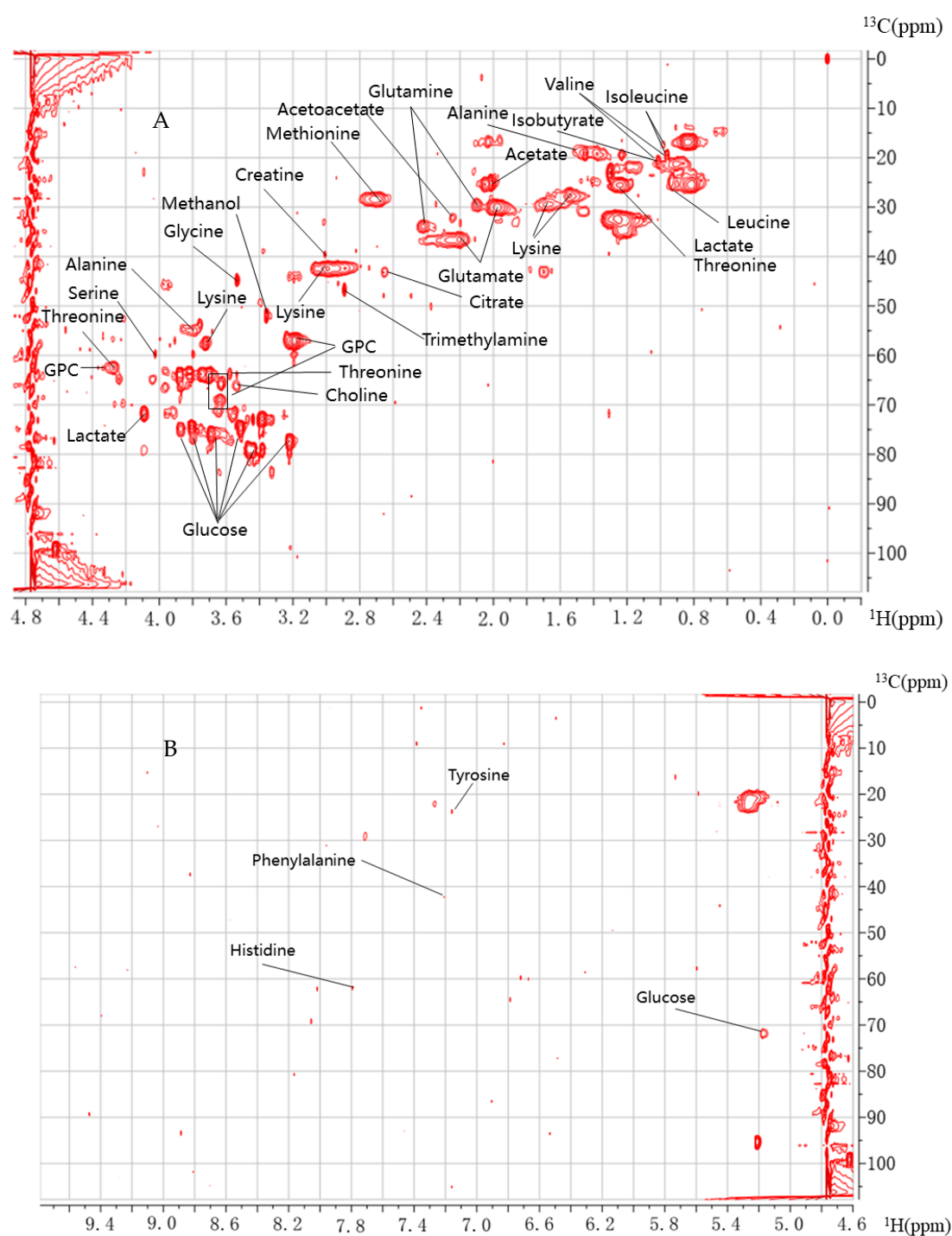
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5 Supplementary Figures;

1 Supplementary Table.



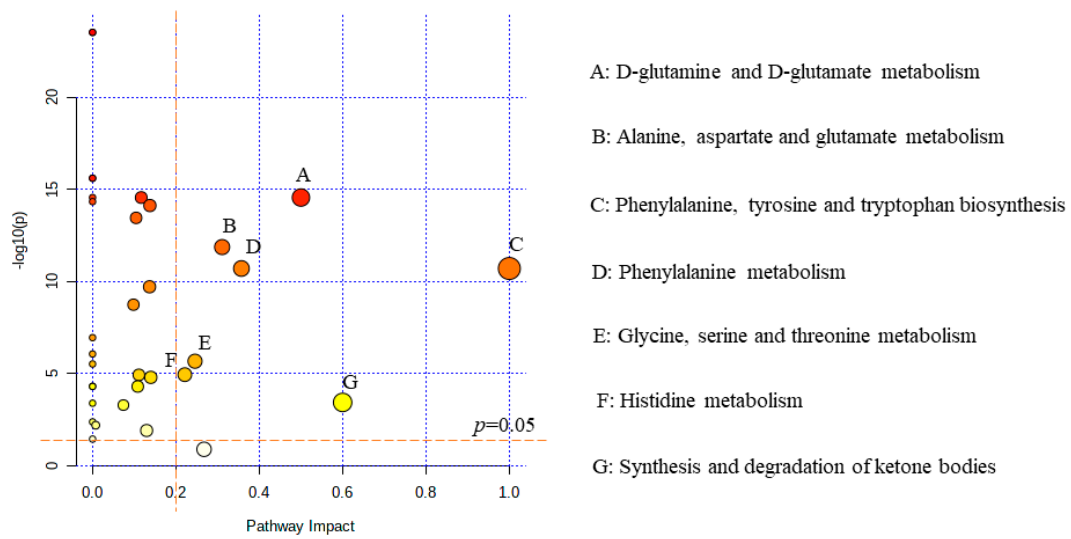
**Figure S1.** The typical 1D  $^1\text{H}$ -NMR spectra recorded on the three group of plasma and resonance assignments of metabolites. Spectral region of  $\delta 5.1\text{--}4.5$  ppm (water resonance) was removed and the region of  $\delta 9.0\text{--}5.3$  ppm was amplified 10 times to make the peaks of low concentration metabolites easy to recognize. PAH-CHD, pulmonary arterial hypertension associated with congenital heart disease; CHD, congenital heart disease; HC, healthy control; GPC, glycerylphosphorylcholine.



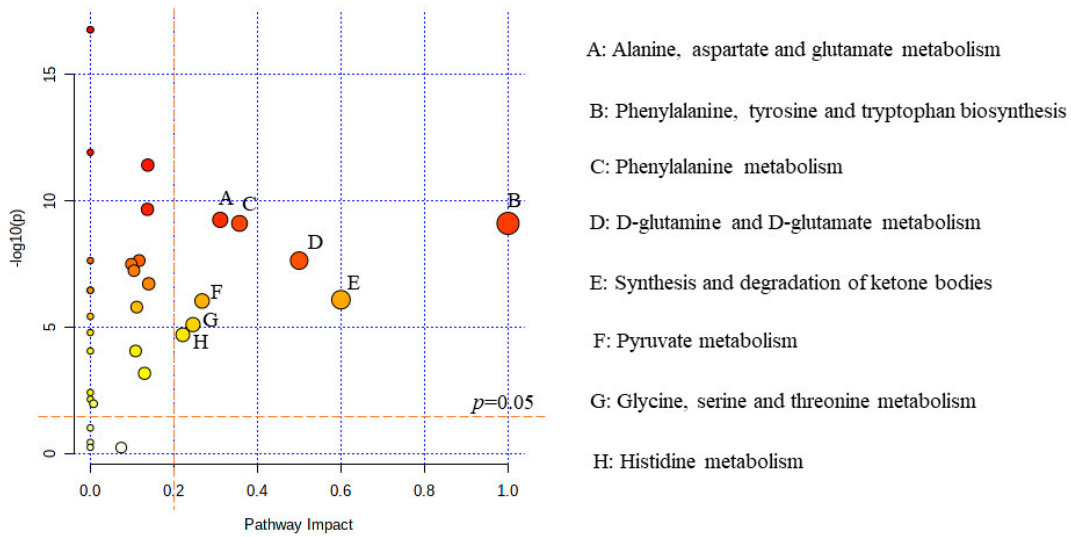
**Figure S2.** 2D  $^1\text{H}$ - $^{13}\text{C}$  heteronuclear single quantum coherence (HSQC) spectrum and resonance assignments of metabolites.



**Figure S3.** 2D  $^1\text{H}$ - $^1\text{H}$  total correlation spectroscopy (TOCSY) spectrum and resonance assignments of metabolites.



**Figure S4.** Metabolic pathway analysis for identifying significantly altered metabolic pathways in CHD relative to HC.



**Figure S5.** Metabolic pathway analysis for identifying significantly altered metabolic pathways in PAH-CHD relative to HC.

**Table S1.** Relative levels of metabolites identified from 1D <sup>1</sup>H-NMR spectra (mean ± SD)

Metabolites	PAH-CHD	CHD	HC
Leucine	1.258±0.280	1.554±0.371	1.246±0.202
Isoleucine	0.505±0.102	0.574±0.146	0.433±0.097
Valine	1.558±0.287	1.806±0.334	1.355±0.248
Isobutyrate	0.056±0.021	0.047±0.014	0.015±0.012
Alanine	2.444±0.570	3.071±0.723	2.722±0.563
Acetate	0.323±0.140	0.218±0.066	0.142±0.029
Glutamate	1.296±0.252	1.211±0.228	0.911±0.315
Pyruvate	0.260±0.039	0.280±0.071	0.238±0.084
Glutamine	4.298±0.758	4.881±0.700	3.271±0.487
Citrate	0.912±0.266	0.758±0.161	0.480±0.101
Methionine	0.499±0.093	0.547±0.083	0.354±0.061
Trimethylamine	0.047±0.011	0.041±0.009	0.022±0.007
Lysine	2.718±0.308	2.781±0.280	1.741±0.248
GPC	0.274±0.175	0.367±0.092	0.303±0.073
Carnitine	0.106±0.030	0.100±0.025	0.072±0.015
Methanol	1.989±0.420	2.293±0.483	0.863±0.504
Glucose	32.976±4.044	38.480±5.739	35.066±4.912
Acetoacetate	0.361±0.091	0.317±0.085	0.246±0.053
Glycine	1.285±0.735	2.070±0.653	1.705±0.242
Threonine	3.183±2.270	1.161±0.356	0.966±0.320
Creatine	0.576±0.149	0.557±0.143	0.323±0.069
Serine	3.031±0.364	2.731±0.394	2.202±0.328
Choline	0.539±0.390	0.792±0.467	0.484±0.150
Lactate	6.386±1.709	4.579±1.263	4.271±1.208
Tyrosine	0.254±0.059	0.239±0.048	0.192±0.038
Phenylalanine	0.162±0.074	0.137±0.050	0.053±0.023
Histidine	0.378±0.060	0.417±0.059	0.366±0.048
Formate	0.071±0.061	0.033±0.010	0.026±0.011

Abbreviations: PAH-CHD, pulmonary arterial hypertension associated with congenital heart disease; CHD, congenital heart disease; HC, healthy control; GPC, glycerylphosphorylcholine.