

Supplemental Table 1. Patient characteristics in study groups included in blood transcriptomics and plasma metabolomics.

Characteristics	Blood transcriptomics		Plasma metabolomics		
	Cyanotic CHD (n=11)	Control (n=11)	Cyanotic CHD (n=27)	Non-cyanotic CHD (n=11)	Control (n=12)
Female, n (%)	6 (0.55)	6 (0.55)	14 (0.52)	6 (0.55)	6 (0.50)
Gestational age, weeks, median (IQR)	37 (36.5, 37)	35 (34,37)	N/A	N/A	34 (34,35)
Age at collection, months, median (IQR)	0.09 (0.04, 0.25)	0.08 (0.06, 0.13)	0.25 (0.13, 1.38)	6 (4-7.5)	0.13 (0.07, 0.87)
Cardiac phenotypes					
Atrioventricular septal defect	1		1	-	
Hypoplastic left heart syndrome	2		5	-	
Pulmonary atresia	4		5	-	
Transposition of the great arteries	3		3	-	
Truncus arteriosus	-		2	-	
Other single ventricle	-		3	-	
Tetralogy of fallot/DORV	1		8	6	
Aortic stenosis	-		-	1	
Ventricular septal defect	-		-	4	

Note: Tetralogy of fallot/double outlet right ventricle (DORV) patients defined as cyanotic ($\text{SaO}_2 < 92\%$) or non-cyanotic ($\text{SaO}_2 \geq 92\%$). CHD, congenital heart disease; N/A, not available; IQR, interquartile range.

Supplemental Table 2. Comparison of intermediate levels in glycolysis, citric acid cycle, and fatty acid metabolism (medium- and long-chain acylcarnitines) between **A)** females vs. males within each study cohort of cyanotic CHD cases, non-cyanotic (normoxic) CHD cases, and controls without CHD; **B)** cyanotic CHD vs. controls without CHD; and **C)** cyanotic vs. non-cyanotic CHD cases.

A Intermediates	Cyanotic CHD F:M			Non-cyanotic CHD F:M			Controls F:M		
	Fold of Change	p-value	q-value	Fold of Change	p-value	q-value	Fold of Change	p-value	q-value
<i>Glycolysis</i>									
1,5-anhydroglucitol	1.82	0.0283	0.4585	0.25	0.0133	0.2991	1.18	0.7600	0.9980
Glucose	1.09	0.3753	0.6368	0.99	0.9840	0.6867	1.10	0.4216	0.9980
2,3-diphosphoglycerate	5.56	0.0158	0.4585	0.71	0.3029	0.5059	1.56	0.4197	0.9980
3-phosphoglycerate	2.13	0.0283	0.4585	0.48	0.1385	0.4209	0.65	0.6435	0.9980
Pyruvate	0.98	0.7505	0.7755	0.71	0.0384	0.3680	0.88	0.8888	0.9980
Lactate	1.15	0.1875	0.5258	0.82	0.4562	0.5461	1.04	0.7035	0.9980
Glycerate	1.03	0.7001	0.7591	1.47	0.0473	0.3748	1.12	0.5283	0.9980
<i>Citric Acid Cycle</i>									
Citrate	1.18	0.0577	0.4585	0.92	0.4485	0.5444	1.04	0.5965	0.9980
Isocitrate	1.39	0.0158	0.4585	0.88	0.5096	0.5590	0.97	0.9907	0.9980
α -ketoglutarate	1.25	0.5398	0.7241	0.88	0.7261	0.6307	1.52	0.2418	0.9980
Succinate	1.15	0.6517	0.7421	0.91	0.9997	0.6933	1.00	0.8719	0.9980
Fumarate	1.01	0.8131	0.7802	1.08	0.6049	0.5889	1.25	0.2662	0.9980
Malate	1.03	0.8682	0.7951	0.95	0.8504	0.6643	1.09	0.5351	0.9980
2-methylcitrate	0.85	0.3033	0.5977	1.30	0.1672	0.4512	1.54	0.2653	0.9980
<i>Glutamine</i>									
Glutamine	1.01	0.9989	0.8182	1.01	0.9661	0.6803	1.19	0.5163	0.9980
Glutamate	1.33	0.0947	0.4814	1.03	0.7466	0.6367	0.95	0.7146	0.9980
α -ketoglutaramate	0.95	0.3860	0.6391	1.12	0.2237	0.4634	0.85	0.9570	0.9980
<i>Fatty Acid Metabolism (Acylcarnitines)</i>									
Myristoylcarnitine (C14)	1.59	0.0879	0.4814	1.04	0.7837	0.6427	1.27	0.3894	0.9980
Palmitoylcarnitine (C16)	1.45	0.0803	0.4814	1.10	0.2996	0.5035	1.25	0.6464	0.9980
Stearoylcarnitine (C18)	1.56	0.0262	0.4585	0.81	0.2029	0.4613	1.49	0.1718	0.9980
Lignoceroylcarnitine (C24)	1.67	0.1779	0.5242	0.91	0.4759	0.5469	1.12	0.9633	0.9980
Cerotoylcarnitine (C26)	2.08	0.0424	0.4585	0.83	0.4036	0.5296	1.25	0.5146	0.9980

B

Intermediates	Cyanotic CHD vs. Non-cyanotic CHD			Cyanotic CHD vs. Non-cyanotic CHD (males)			Cyanotic CHD vs. Non-cyanotic CHD (females)		
	Fold of Change	p-value	q-value	Fold of Change	p-value	q-value	Fold of Change	p-value	q-value
<i>Glycolysis</i>									
1,5-anhydroglucitol	0.19	4.1x10⁻⁵	6.6x10⁻⁵	0.08	0.0001	0.0003	0.58	0.0105	0.0235
Glucose	0.96	0.2657	0.0983	0.91	0.2842	0.0931	1.00	0.7312	0.3939
2,3-diphosphoglycerate	3.49	0.1991	0.0782	0.87	0.3146	0.1006	6.84	0.0247	0.0389
3-phosphoglycerate	1.71	0.0656	0.0316	0.77	0.6721	0.1720	3.44	0.0075	0.0194
Pyruvate	0.98	0.3447	0.1195	0.84	0.1419	0.0570	1.15	0.9289	0.4496
Lactate	1.32	0.0113	0.0073	1.10	0.5288	0.1450	1.54	0.0005	0.0075
Glycerate	1.09	0.3733	0.1271	1.34	0.0995	0.0440	0.94	0.6048	0.3506
<i>Citric Acid Cycle</i>									
Citrate	0.86	0.0141	0.0088	0.75	0.0188	0.0128	0.96	0.5077	0.3074
Isocitrate	0.74	0.0020	0.0017	0.58	0.0090	0.0069	0.91	0.2699	0.2046
α -ketoglutarate	1.57	0.0086	0.0058	1.31	0.2541	0.0861	1.84	0.0184	0.0316
Succinate	2.97	1.5x10⁻⁷	1.1x10⁻⁶	2.61	0.0098	0.0074	3.32	1.7x10⁻⁵	0.0020
Fumarate	1.24	0.1120	0.0483	1.29	0.2467	0.0845	1.21	0.3702	0.2474
Malate	1.36	0.0346	0.0187	1.30	0.2379	0.0825	1.41	0.0772	0.0874
2-methylcitrate	2.81	2.3x10⁻⁶	7.1x10⁻⁶	3.56	1.8x10⁻⁵	0.0001	2.31	0.0187	0.0320
<i>Glutamine Metabolism</i>									
Glutamine	1.00	0.6184	0.1878	1.00	0.7243	0.1819	0.99	0.7375	0.3959
Glutamate	0.81	0.0098	0.0064	0.70	0.0364	0.0208	0.90	0.2278	0.1827
α -ketoglutaramate	2.29	4.0x10⁻⁸	5.1x10⁻⁷	2.12	8.5x10⁻⁶	7.8x10⁻⁵	1.99	0.0033	0.0130
<i>Fatty Acid Metabolism (Acylcarnitines)</i>									
Myristoylcarnitine (C14)	0.97	0.1119	0.0483	0.76	0.0621	0.0307	1.16	0.8140	0.4175
Palmitoylcarnitine (C16)	1.00	0.2183	0.0839	0.86	0.0995	0.0440	1.12	0.9515	0.4551
Stearoylcarnitine (C18)	0.77	0.0045	0.0034	0.53	0.0014	0.0017	1.03	0.6345	0.3593
Lignoceroylcarnitine (C24)	0.38	9.5x10⁻⁹	1.8x10⁻⁷	0.27	4.4x10⁻⁶	0.0001	0.49	0.0006	0.0075
Cerotoylcarnitine (C26)	0.34	4.0x10⁻⁹	1.3x10⁻⁷	0.20	2.2x10⁻⁶	0.0001	0.50	0.0007	0.0075