

Fig.S1 Hematoxylin and eosin staining of mouse myocardial tissues and cytokine measurements.

Fig.S2 PCA score plot of the UPLC/MS serum metabolites data in negative ion mode.

Note: black, control group; red, treatment group.

Fig.S3 Loading-plot of the UPLC/MS serum metabolites data in negative ion mode.

Note: $R^2X = 0.83$, $R^2Y = 0.79$, $Q^2Y = 0.74$.

Fig.S 4 VIP-plot based on the matched PLS-DA model for the interesting variables in negative ion mode.

Fig.S5 Metabolic pathway analysis of serum biomarker metabolites. Note: Red means the strong degree of disturbance, and yellow means the weak degree of disturbance.

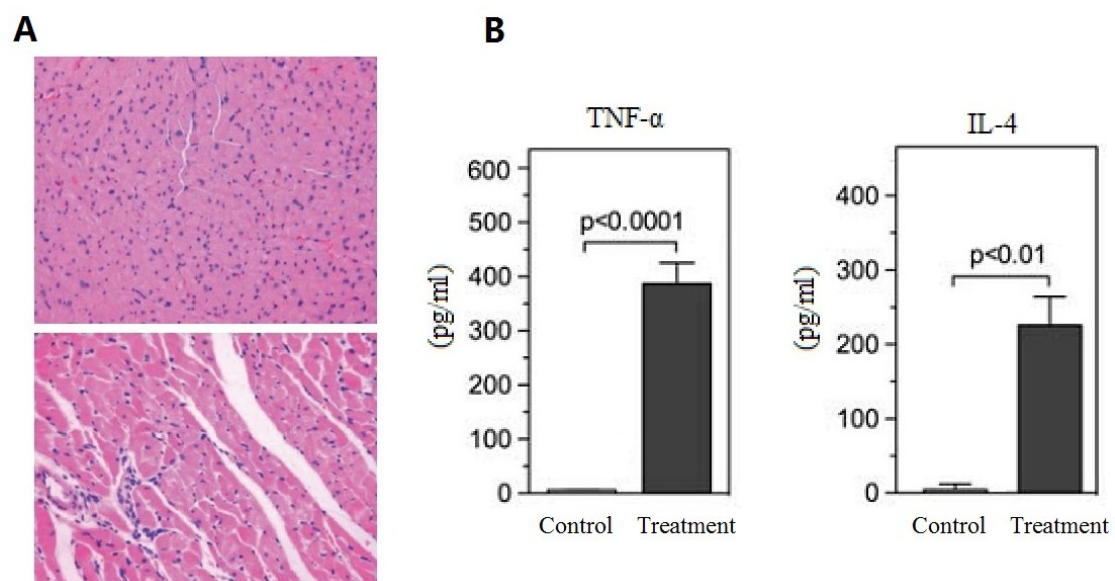


Fig.S1

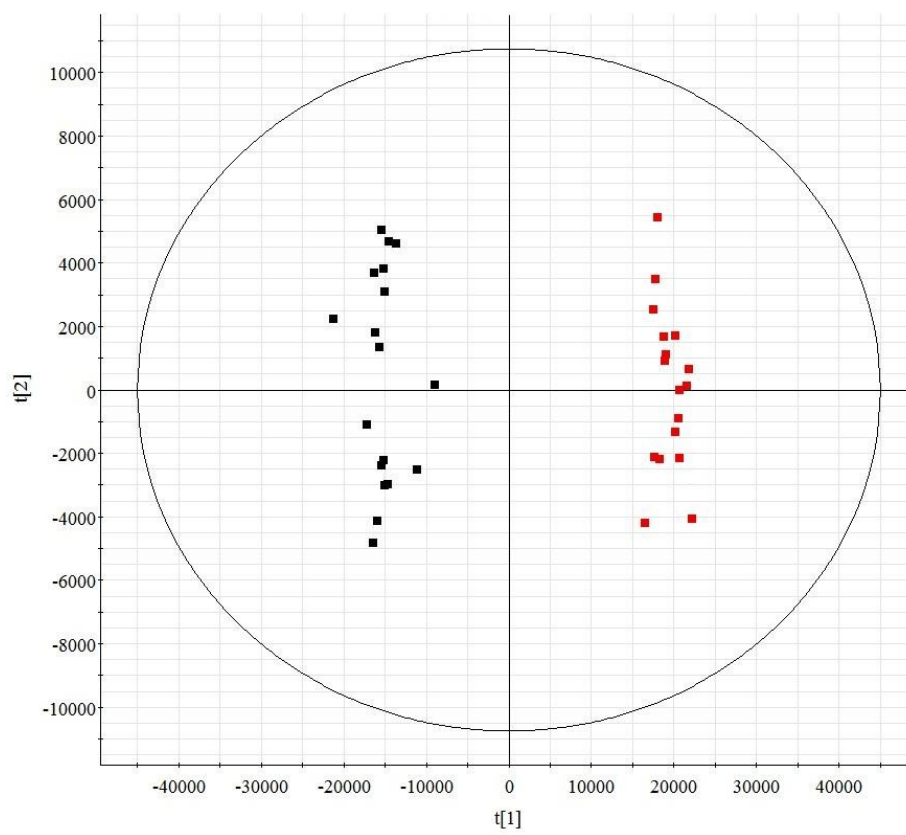


Fig.S2

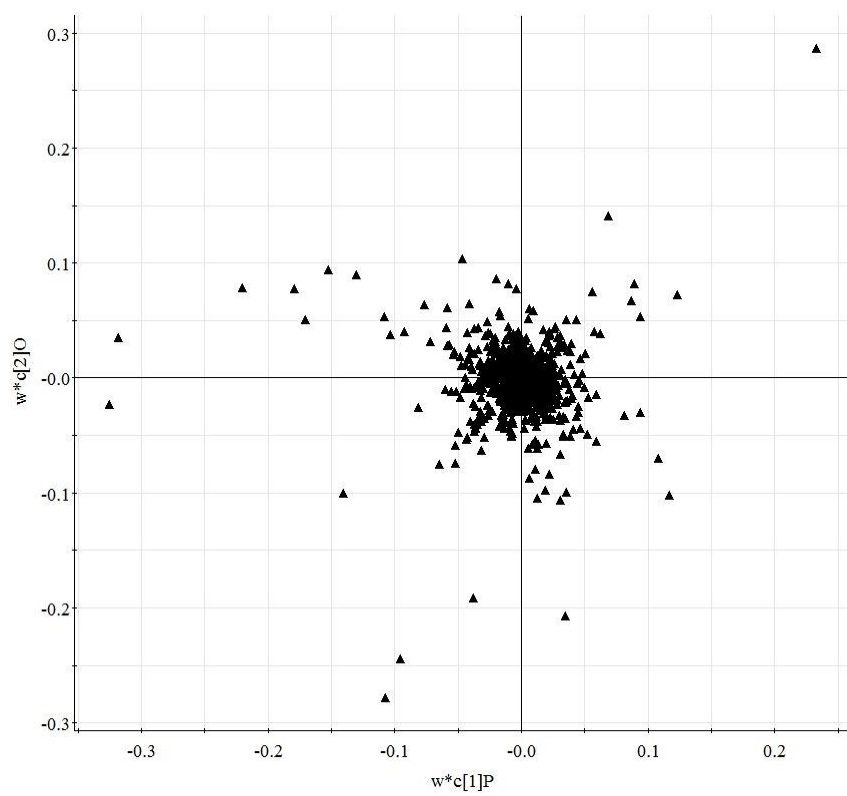


Fig.S3

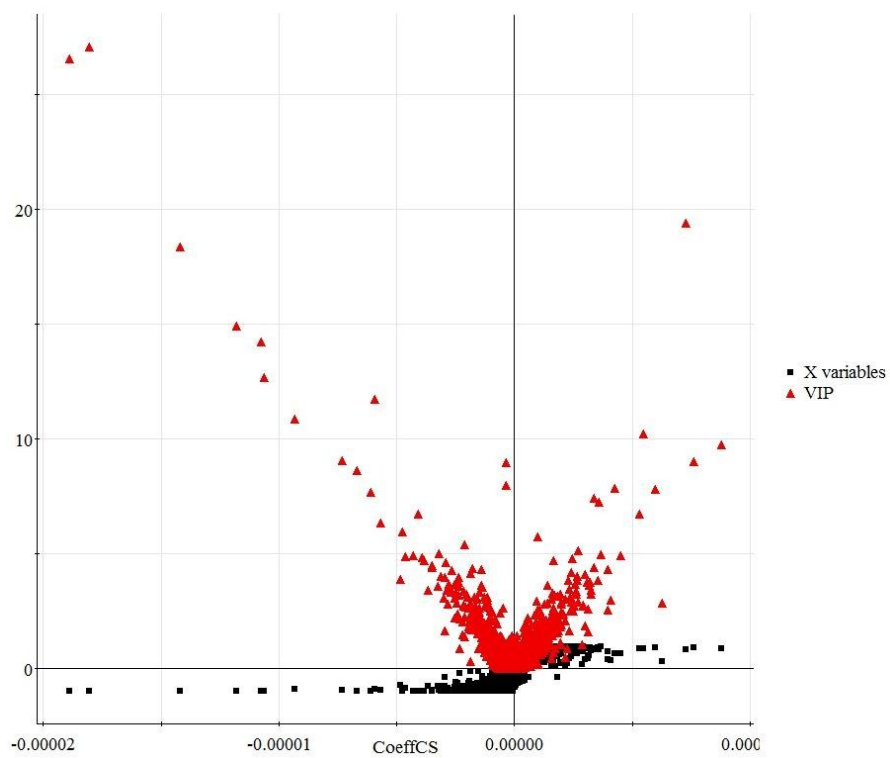


Fig.S4

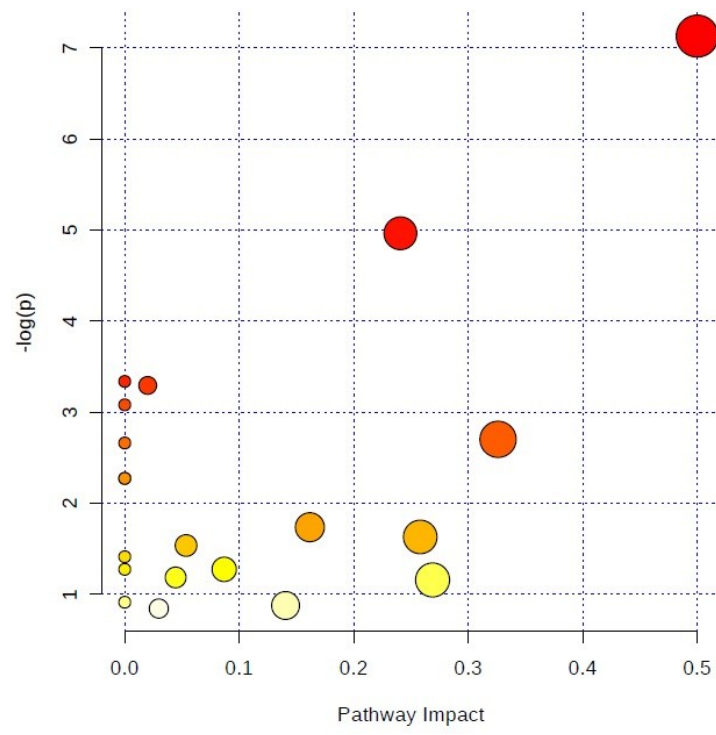


Fig.S5

Table S1. Information of biomarker metabolites detected by UPLC/MS in positive and negative ion mode.

NO.	VIP	Rt min	M/Z Calculated	M/Z Determined	Mass Error (ppm)	Scan Mode	Formula	Metabolites
1	10.1458	1.13	130.0506	130.0503	0.88	ESI ⁺	C ₅ H ₇ NO ₃	Pyroglutamic acid
2	10.02623	2.34	118.0863	118.0866	1.72	ESI ⁺	C ₅ H ₁₁ NO ₂	5-Aminopentanoic acid
3	11.4403	2.46	138.0529	138.0533	1.34	ESI ⁺	C ₇ H ₇ NO ₂	p-Aminobenzoic acid
4	19.7646	3.51	193.0189	193.0190	-0.35	ESI ⁺	C ₆ H ₁₀ O ₇	Citric acid
5	36.5573	4.53	182.0814	182.0812	-0.59	ESI ⁺	C ₉ H ₁₁ NO ₃	L-Tyrosine
6	13.0287	5.04	130.0862	130.0867	3.06	ESI ⁺	C ₆ H ₁₁ NO ₂	Pipecolic acid
7	37.9863	5.42	150.0582	150.0586	2.08	ESI ⁺	C ₅ H ₁₁ NO ₂ S	L-Methionine
8	24.0192	5.75	130.0354	130.0348	1.73	ESI ⁺	C ₅ H ₉ NO ₃	Pyrrolidonecarboxylic acid
9	24.528	6.92	165.0555	165.0549	1.05	ESI ⁺	C ₉ H ₈ O ₃	Phenylpyruvic acid
10	13.0143	7.94	132.1018	132.1023	1.42	ESI ⁺	C ₆ H ₁₃ NO ₂	D-Leucine
11	11.6872	1.94	369.2267	369.2272	1.06	ESI ⁻	C ₂₀ H ₃₂ O ₆	6-Keto-prostaglandin F1a
12	18.348	2.83	540.3237	540.3241	-0.55	ESI ⁻	C ₂₈ H ₄₆ NO ₇ P	LysoPC(20:5(5Z,8Z,11Z,14Z,17Z))
13	14.9047	2.99	564.3311	564.3304	1.24	ESI ⁻	C ₂₆ H ₄₈ NO ₇ P	LysoPC(18:2(9Z,12Z))
14	12.703	3.21	303.2468	303.2471	-2.93	ESI ⁻	C ₂₀ H ₃₀ O ₂	Arachidonic acid
15	11.7306	3.43	319.2287	319.2290	1.44	ESI ⁻	C ₂₀ H ₃₀ O ₃	20-Hydroxyeicosatetraenoic acid
16	26.5472	3.72	301.2296	301.2301	0.43	ESI ⁻	C ₂₀ H ₂₈ O ₂	Retinyl ester
17	27.0859	4.56	74.04029	74.04020	1.15	ESI ⁻	C ₂ H ₃ NO ₂	Glycine
18	10.8746	4.98	338.1398	338.1401	1.70	ESI ⁻	C ₁₆ H ₁₉ NO ₇	5-Hydroxytryptophol glucuronide
19	10.2361	5.79	188.0497	188.0496	-0.23	ESI ⁻	C ₁₀ H ₅ NO ₃	Kynurenic acid
20	14.2222	6.24	310.1308	310.1310	1.57	ESI ⁻	C ₁₂ H ₁₅ N ₅ O ₅	1,7-Dimethylguanosine
21	19.3829	7.08	267.1252	267.1257	0.87	ESI ⁻	C ₁₁ H ₁₄ N ₄ O ₄	Acetylcarnosine

Table S2. The pathway analysis of the differential metabolites.

N o	Pathway	Tot al	Expecte d	Hit s	Raw p	Log(p)	FDR	Impa ct
1	Phenylalanine, tyrosine and tryptophan biosynthesis	4	0.0480	2	0.0008	7.1285	0.0658	0.50
2	Arachidonic acid metabolism	36	0.4319	2	0.0672	2.6999	0.8197	0.33
3	Glycine, serine and threonine metabolism	31	0.3719	1	0.3149	1.1555	1	0.27
4	Glyoxylate and dicarboxylate metabolism	18	0.2160	1	0.1963	1.6279	1	0.26
5	Phenylalanine metabolism	11	0.1320	2	0.0070	4.9625	0.2868	0.24
6	Retinol metabolism	16	0.1920	1	0.1765	1.7346	1	0.16
7	Tyrosine metabolism	44	0.5279	1	0.4169	0.8750	1	0.14
8	Cysteine and methionine metabolism	27	0.3239	1	0.2803	1.2719	1	0.09
9	Citrate cycle (TCA cycle)	20	0.2399	1	0.2158	1.5336	1	0.05
10	Glycerophospholipid metabolism	30	0.3599	1	0.3064	1.1828	1	0.04
11	Primary bile acid biosynthesis	46	0.5519	1	0.4312	0.8411	1	0.03
12	Glutathione metabolism	26	0.3119	2	0.0372	3.2917	0.7547	0.02
13	Ubiquinone and other terpenoid-quinone biosynthesis	3	0.0360	1	0.0356	3.3358	0.7547	0
14	Aminoacyl-tRNA biosynthesis	69	0.8278	3	0.0460	3.0788	0.7547	0
15	Cyanoamino acid metabolism	6	0.0720	1	0.0700	2.6596	0.8197	0
16	Methane metabolism	9	0.1080	1	0.1032	2.2710	0.9404	0
17	Nitrogen metabolism	9	0.1080	1	0.1032	2.2710	0.9404	0
18	Lysine degradation	23	0.2759	1	0.2441	1.4103	1	0
19	Porphyrin and chlorophyll metabolism	27	0.3239	1	0.2803	1.2719	1	0
20	Biosynthesis of unsaturated fatty acids	42	0.5039	1	0.402	0.910	1	0

