

Supplementary Table 1. The chromatographic gradient elution conditions.

In arachidonic acid metabolism		In amino acid metabolism and TCA cycle			
(-ESI)		(-ESI)		(+ESI)	
Time/min	B%	Time/min	B%	Time/min	B%
0	35	0	25	0	2
10.0	35	3.5	25	7.0	2
15.0	70	3.6	35	7.1	20
16.0	90	10.0	35	14.0	20
30.0	90				

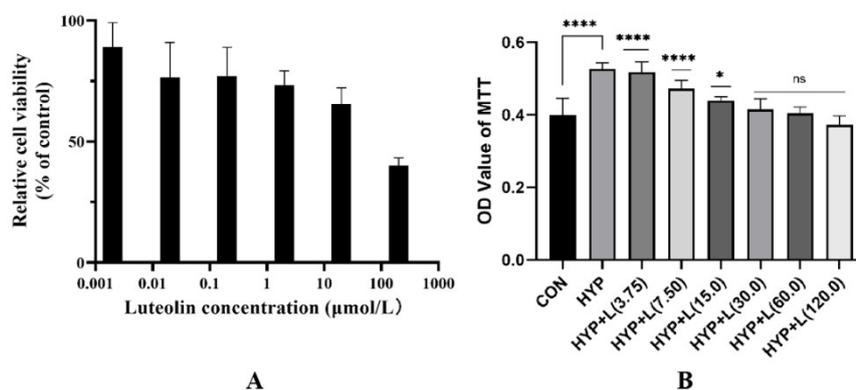
Supplementary Table 2. The MRM conditions of analytes in different pathways.

number	analytes	pathway	ion mode	ion pair	fragmentation voltage/v	collision voltage/v
1	AA	Arachidonic acid metabolism	-ESI	303.1→59.0	135	23
2	DHA	Arachidonic acid metabolism	-ESI	327.2→283.2	135	16
3	14, 15-EpETE	Arachidonic acid metabolism	-ESI	317.3→207.3	135	13
4	PGD2	Arachidonic acid metabolism	-ESI	351.2→315.1	120	13
5	PGE2	Arachidonic acid metabolism	-ESI	351.3→315.2	135	6
6	PGF2 α	Arachidonic acid metabolism	-ESI	353.2→193.1	200	21
7	8-iso-PGF2 α	Arachidonic acid metabolism	-ESI	353.3→193.2	135	24
8	6-keto-PGF1 α	Arachidonic acid metabolism	-ESI	369.3→163.1	160	25
9	TXB2	Arachidonic acid metabolism	-ESI	369.3→169.0	135	6
10	LTB4	Arachidonic acid metabolism	-ESI	335.2→195.2	135	16
11	12-HETE	Arachidonic acid metabolism	-ESI	319.4→257.2	135	18
12	15-HETE	Arachidonic acid metabolism	-ESI	319.3→257.0	135	18
13	5, 6-DiHET	Arachidonic acid metabolism	-ESI	337.3→144.9	135	21
14	PGE2-d4	Internal standard	-ESI	355.2→319.2	135	6
15	15-HETE-d8	Internal standard	-ESI	327.4→265.2	135	15
16	ornithine-d7·HCl	Internal standard	+ESI	140.1→70.2	135	5
17	citric acid-d4	Internal standard	-ESI	195.1→113.0	135	5
18	Citric acid	TCA cycle	-ESI	191.1→111.1	135	7
19	Oxaloacetate	TCA cycle	+ESI	133.1→99.0	135	5
20	L-Malic acid	TCA cycle	-ESI	133.1→114.8	135	10
21	Butane diacid	TCA cycle	-ESI	117.0→73.0	135	11
22	Fumaric acid	TCA cycle	-ESI	115.1→27.1	135	10
23	α -ketoglutarate	TCA cycle	-ESI	145.1→101.1	135	4
24	Aconitic acid	TCA cycle	-ESI	173.1→129.0	135	5
25	L-Aspartic acid	Aspartic acid metabolism	-ESI	132.1→88.1	135	10
26	L-Asparagine	Aspartic acid metabolism	-ESI	131.1→114.1	135	10
27	L-Alanine	Alanine metabolism	+ESI	90.1→44.2	135	4
28	Pyruvate	Alanine metabolism	+ESI	89.0→71.2	135	15
29	Glutamic acid	Glutamate metabolism	-ESI	146.1→102.1	135	9
30	N-acetyl-l-glu	Glutamate metabolism	-ESI	188.1→128.1	135	9
31	N-acetyl-l-orn	Glutamate metabolism	+ESI	175.2→115.1	135	6

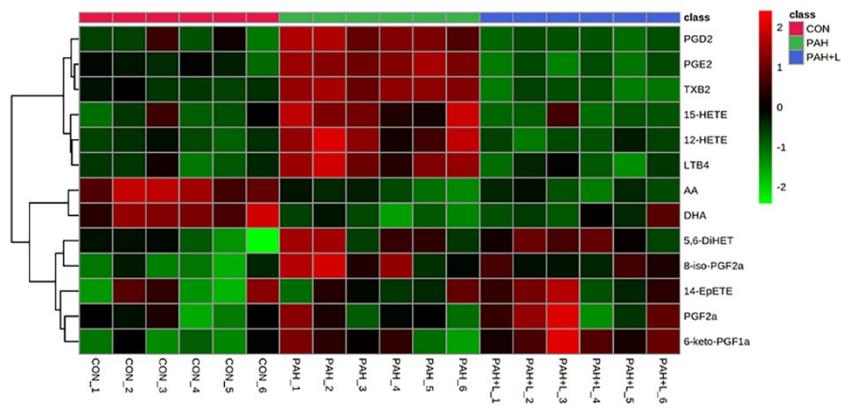
32	Ornithine	Urea cycle	+ESI	133.1→70.2	135	4
33	L-Citrulline	Urea cycle	+ESI	176.2→159.1	135	4
34	L-Arginine	Urea cycle	+ESI	175.1→60.2	135	12

Supplementary Table 3. KEGG pathway enrichment analysis of common targets.

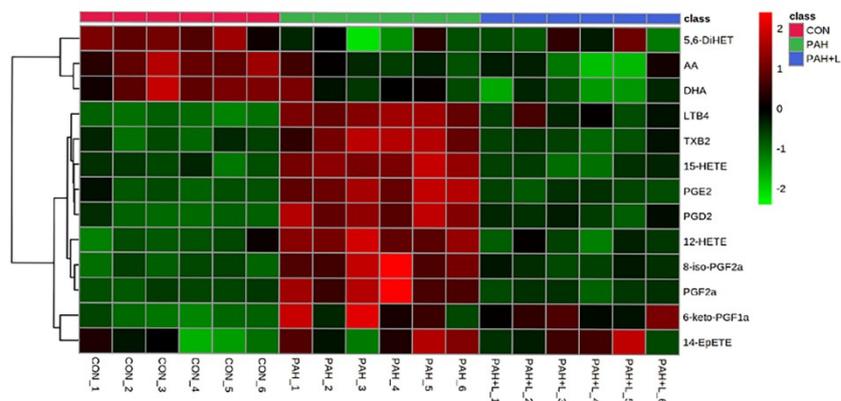
ID	Description	Log10(p-value)	Gene Count
hsa05200	Pathways in cancer	-49.0202	49
hsa05417	Lipid and atherosclerosis	-26.9824	25
hsa01522	Endocrine resistance	-23.207	18
hsa05207	Chemical carcinogenesis - receptor activation	-22.6276	22
hsa05206	MicroRNAs in cancer	-17.7277	21
hsa00020	Citrate cycle (TCA cycle)	-15.9739	10
hsa01521	EGFR tyrosine kinase inhibitor resistance	-14.5454	12
hsa00590	Arachidonic acid metabolism	-14.2416	11
hsa04913	Ovarian steroidogenesis	-13.3815	10
hsa04068	FoxO signaling pathway	-13.2456	13
hsa05210	Colorectal cancer	-12.5176	11
hsa05202	Transcriptional misregulation in cancer	-12.3349	14
hsa04932	Non-alcoholic fatty liver disease	-12.2948	13
hsa04630	JAK-STAT signaling pathway	-12.0475	13
hsa05415	Diabetic cardiomyopathy	-10.8004	13
hsa04917	Prolactin signaling pathway	-10.3531	9
hsa05204	Chemical carcinogenesis - DNA adducts	-10.4112	9
hsa01230	Biosynthesis of amino acids	-10.0759	9
hsa04152	AMPK signaling pathway	-9.54258	10
hsa01523	Antifolate resistance	-8.27908	6



Supplementary Figure 1. Determination of concentration of luteolin used for PASCs. (A) MTT assay the IC₅₀ value of the luteolin in PASCs. (B) The numbers of PASCs after administering various concentrations of luteolin. CON, control; HYP, hypoxia; HYP + L, hypoxia + luteolin. * $P < 0.05$, * $P < 0.001$, **** $P < 0.0001$ vs. CON.**

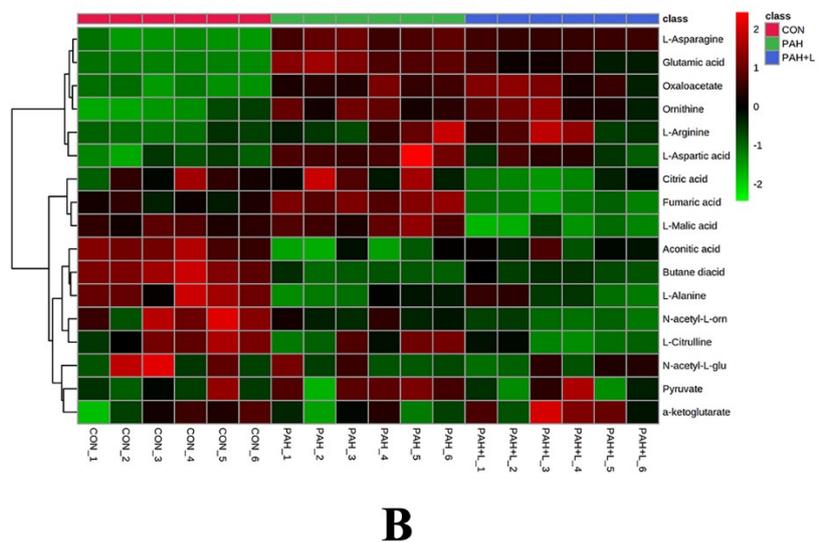
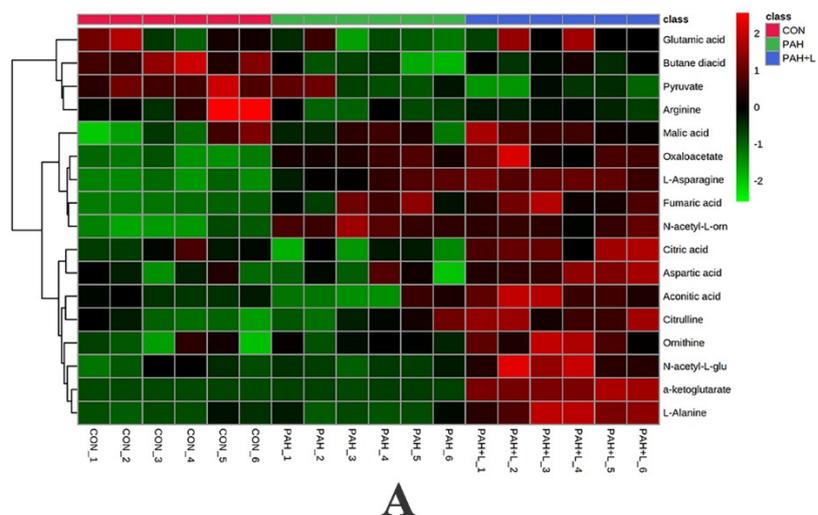


A



B

Supplementary Figure 2. The heatmaps of the metabolites in arachidonic acid pathway. (A) Metabolites were determined in the plasma samples, and (B) in lung tissue samples.



Supplementary Figure 3. The heatmaps of the metabolites in amino acid pathway and TCA cycle. (A) Metabolites were determined in the plasma samples, and (B) in lung tissue samples.