Supplementary information

Supplementary Table S1 NMR data for metabolites detected in urine extracts

Key	Metabolites	δ1 H (ppm)	δ13 C (ppm[a])
1	2-Hydroxy-3-methylvalerate	0.86(t)0.93(d)1.14(m)1.35(m)1.74(m)3.87(d)	—
2	Pantothenic acid	0.84(s)	21.8
3	Isovalerate	0.895(d), 1.929(m), 2.049(d)	24.44, 29.27, 49.26
4	2-Hydroxybutyrate	0.899(m), 1.689(m), 3.996(dd)	10.68, 29.48, 76.07
5	3-Methylglutarate	0.914(d),1.976(d),1.977(q),2.195(m),2.215(s),2.215(t)	—
6	Isovalerylglycine	0.925(d), 1.994(m), 2.166(d), 3.746(d)	24.37, 30.2, 46.93, —
7	Isoleucine	0.936(t), 0.995(d), 1.249(m), 1.452(m), 1.971(m), 3.655(d)	14.7, 17.2, 26.8, 26.8, 62.4
8	Leucine	0.925(d), 0.936(s), 1.703(m), 3.725(d)	23.39, 24.3, 26.62, 56.88
9	Ketoleucine	0.944(d), 2.100(m), 2.617(d)	24.32, 26.2, —
10	Isobutyrate	1.053(d), 2.382(m)	22.04, 39.32
11	Isopropanol	1.146(d), 4.028(m)	26.12, —
12	Ethanol	1.185(t), 3.656(q)	19.54, —
13	3-Hydroxyisovalerate	1.275(s), 2.357(s)	30.2,51.6
14	Threonine	1.330(d), 3.579(d), 4.269(m)	23.5, 63.2, 68.2
15	Lactate	1.331(d),4.115(q)	22.89, 71.40
16	N-Acetyllysine	1.362(m),1.415(m),1.527(m),1.544(m),1.833(m),1.880(m),1.972(s),3.165(t),3.174(t),3.726(t),7.953(s)	—
17	Lysine	1.415(m), 1.719(m), 1.869(m), 3.018(t), 3.741(t)	23.44, 29.72, —, 41.5, 57.58
18	Alanine	1.489(d), 3.780(q)	18.26, 53.32
19	Citrulline	1.558(m), 1.865(m), 3.124(dd), 3.743(t)	—, —, 42, 57.9
20	Ornithine	1.775(m), 1.828(m), 1.929(m), 3.044(t), 3.782(d)	25.5, 25.5, —, 41.12, 56.81
21	N-Acetyltyrosine	1.919(s),2.832(m),3.086(d),4.369(m),6.836(d),7.137(d),7.723(s)	—
22	Acetate	1.927(s)	26.54
23	N-Acetylcarnitine	2.008(s),2.489(m),2.680(d),4.381(m),7.908(s)	—
24	Proline	2.023(m), 2.334(m), 3.320(m), 3.392(m), 4.147(t)	25.78, 32.11, 48.71, 48.71, 63.51
25	N-Acetylglycine	2.044(s), 3.763(d)	24.2, 46.1
26	Glutamate	2.056(m), 2.334(m), 3.741(m,m,q)	30.1, 36.4, 57.6
27	Glutamine	2.138(m), 2.445(m), 3.768(t)	29.53, 32.96, 57.10
28	O-Acetylcholine	2.143(s), 3.202(s), 3.711(t), 4.529(m)	23.4, 56.8, 67.1, 60.2
29	p-Cresol	2.253(s), 6.817(d), 7.130(d)	22.1, 117.9
30	Levulinate	2.211(s), 2.384(t), 2.780(t)	32.42, 34.68, 41.12
31	Acetone	2.229(s)	28.2
32	Acetoacetate	2.266(s), 3.434(s)	32.3
33	p-Cresol glucuronide	2.299(s), 7.055(m), 7.237(m)	22.17, 123.16, 135.68
34	p-Cresol sulfate	2.347(s), 7.217(d), 7.293(d)	—, 121.61, 136.05
35	Pyruvate	2.373(s)	29.5
36	Succinate	2.413(s)	37.3
37	4-Pyridoxine	2.429(s), 7.834(s)	20.39, 138.78
38	2-Oxoglutarate	2.429(t), 2.995(t)	33.2, 39.0
39	5-Aminolevulinate	1.62(m),1.65(m),2.24(t),3.02(t)	38.9, 41.0

40	β-Alanine	2.540(t), 3.196(t)	36.4, 39.97
41	Citrate	2.552(d), 2.658(d)	48.7, 48.7
42	Methylamine	2.613（s)	27
43	Dimethylamine	2.719(s)	36.8
44	Sarcosine	2.729(s),3.602(s)	—
45	Methylguanidine	2.828(s), 3.356(s)	29.47, —
46	Asparagine	2.862(dd), 2.962(m), 3.995(dd)	37.6, 37.6, 54.3
47	Trimethylamine	2.887(s)	47.4
48	N-Methylhydantoin	2.917(s),4.0782(s)	—
49	N,N-Dimethylglycine	2.925(s), 3.712(s)	46.1, 62.2
50	Creatine	3.028(s), 3.926(s)	40.15, 56.25
51	Creatine phosphate	3.030(s),3.993(s)	—
52	Creatinine	3.043(s), 4.052(s)	33.5, 58.39
53	τ-Methylhistidine	3.065(m), 3.681,3.951(m), 7.001(s), 7.677(s)	30.7, 36.5, 58.13, 122.92, —
54	N_6,N_6,N_6-trimethyllysine	3.109(s)	47.14
55	Malonate	3.119(s)	—
56	Cis-aconitate	3.123(s), 5.711(t)	46.7, 127
57	Dimethyl sulfone	3.145(s)	—
58	Histidine	3.144(dd), 3.249(dd), 4.001(q), 7.093(s), 7.844(s)	—, —, —, 119, 139.1
59	N-Nitrosodimethylamine	3.162(s), 3.802(s)	32.16, 39.86
60	Phenylalanine	3.117(dd), 3.270(dd), 4.001(q), 7.323(d), 7.365(t), 7.42(m)	38.9, 38.9, 58.9, 132.2, 129.8, 131.9
61	Choline	3.191(s), 3.504(t), 4.085(m)	56.9, 70.1, 58.2
62	Phosphorylcholine	3.203(s), 3.671(t), 4.190(dd)	56.0, 68.56, 60.33
63	Taurine	3.243(t), 3.435(t)	49.5, 37.5
64	β-Glucose	3.243(t), 3.478(m), 3.492(m), 3.864(m), 3.927(s), 4.660(d)	—, —, —, 63.26, 63.26, 98.39
65	Trimethylamine-N-oxide	3.266(s)	61.5
66	Betaine	3.273(s), 3.927(s)	57, 68
67	Lactose	3.276(t),3.507(m),3.604(m),3.710(m),3.768(m),3.847(m), 3.936(m), 4.455(d), 4.660(d), 5.211(d)	76.16, —, —, —, 64.68, 63.52, —, 104.59, 98.91, 93.9
68	trans-Aconitate	3.435(s), 6.571(s)	39.2, 133.4
69	4-Hydroxyphenylacetate	3.437(s),6.850(d),7.154(d)	—
70	p-Hydroxyphenylacetate	3.445(s), 6.865(d), 7.169(d)	46.5, 118.59, 133.69
71	Homogentisate	3.463(s),6.691(dd),6.700(s),6.793(d)	—
72	Glycerol	3.551(t), 3.634(m), 3.767(m)	65.2, 65.2, 74.7
73	2-Hydroxyphenylacelate	3,52(s)6.90(d)6.93(d)7.17(d)7.20(t)	47.04, 119.45, 124.19, 132.91
74	Ethylene glycol	3.662(s)	—
75	Glycogen	3.633(m), 3.657(m), 3.829,3.874,3.975,5.394(s)	72.59, 79.59,72.56,63.26,101.78
76	N-Phenylacetylglycine	3.665(s),3.744(d),7.344(d),7.349(t),7.410(t),7.977(s)	—
77	Mannitol	3.677(dd), 3.770(m), 3.805(d), 3.873(dd)	65.37, 72.8, 72.66, 66.69
78	Phenylacetylglycine	3.680(s), 3.746(d), 7.365(t), 7.425(t)	44.42, —, 131.12, 130.89
79	Indole-3-acetate	3.681(s), 7.161(t), 7.216(t), 7.507(d), 7.635(d)	36.65,121.26,126.49,114.38, 121.37
80	Guanidoacetate	3.801(s)	47.5

81	Glycolate	3.932(s)	64.19
82	Hippurate	3.975(d), 7.553(t), 7.642(t), 7.837(d), 8.508(s)	46.1, 131.5, 134.9, 129.9
83	4-Hydroxyhippurate	3.978(s), 6.976(d), 7.765(d)	—
84	Tartrate	4.329(s)	77.38
85	Trigonelline	4.438(s), 8.084(t), 8.837(t), 9.122(s)	51.3, 130.8, —, —
86	1-Methylnicotinamide	4.476(s), 8.181(t), 8.894(d), 8.960(d), 9.272(s)	50.85, 131.14, —, —, —
87	Allantion	5.39(s)	—
88	Fumarate	6.524(s)	137.5
89	p-Hydroxybenzoate	6,970(m), 7.759(m)	117.2, 133.68
90	Benzoate	7.474(t),7.546(t),7.863(d)	—
91	Xanthine	7.909(s)	141.77
92	Hypoxanthine	8.22(s),8.20(s)	145.2, 147.5
93	Oxypurinol	8.209(s)	129.09
94	Formate	8.467(s)	172.4

Note: a indicates the displacement value of $^1H/^{13}C$ is based on the HSQC spectra. "—" indicates the corresponding displacement value of ^{13}C is not found in the HSQC spectra, and the attribution of metabolite is a reference only the ^1H displacement in NOESY spectra.
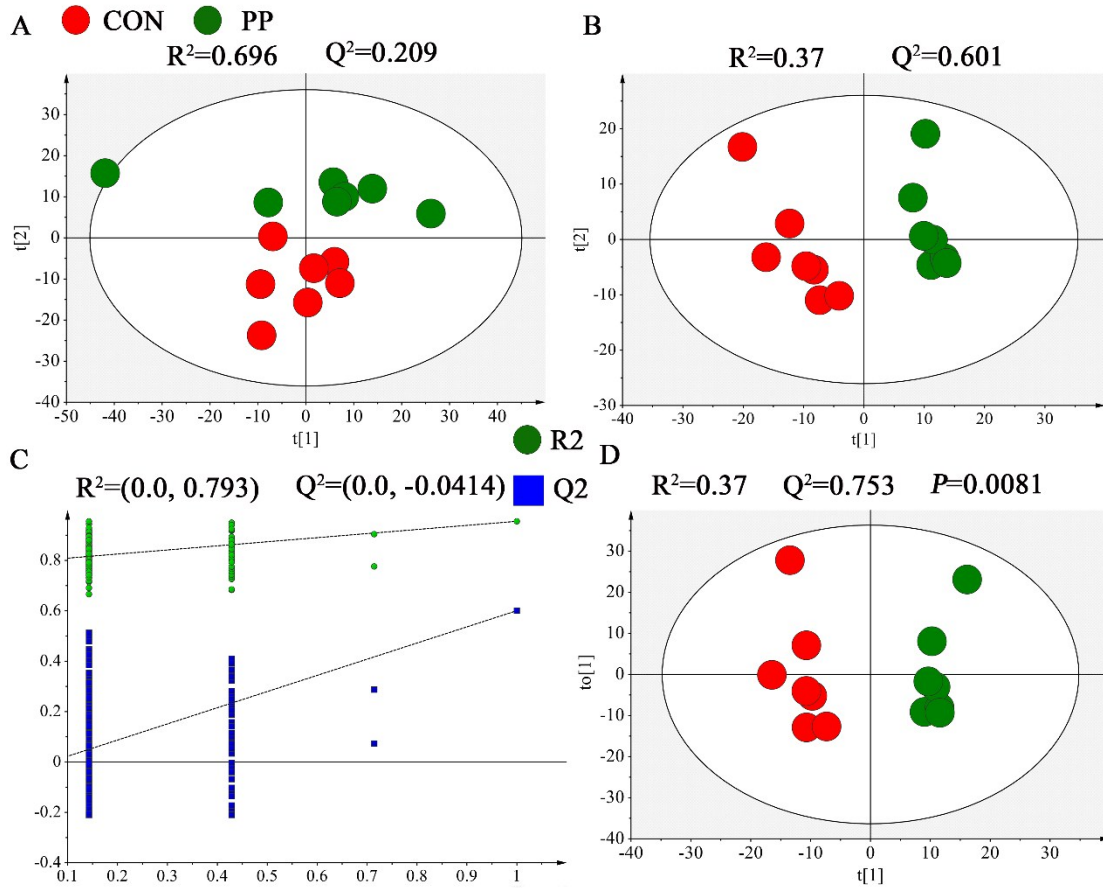
Supplementary Table S2 NMR data for metabolites detected in feces extracts

Key	Metabolites	δ1 H (ppm)	δ13 C (ppm[a])
1	α-Keto-β-methyl-valerate	0.887(t), 1.104(d), 1.47(m),1.687(m), 2.923(m)	12.9, 16.5, 27.4, 27.4, 42.2
2	Caproate	0.887(t), 1.292(m),1.309(m), 1.556(m), 2.178(t)	16.23, 32.69, 23.66, 29.05, 39.54
3	Butyrate	0.899(t), 1.562(m), 2.150(t)	16.0, 22.1, 42.3
4	3-Methyl-2-oxovalerate	0.899(t), 1.093(d), 1.438(m), 1.662(m), 2.928(m)	13.2, 16.4, 26.8, 26.8, 45.9
5	Valerate	0.899(t), 1.309(m), 2.178(d)	16.39, 23.94, 39.56
6	α-Ketoisocaproate	0.920(s), 2.054(m), 2.616(d)	25.0, 26.3, 46, 181.6
7	Leucine	0.925(d), 0.936(s), 1.703(m), 3.725(d)	23.39, 24.3, 26.62, 56.88
8	Isoleucine	0.936(t), 0.995(d), 1.249(m), 1.452(m), 1.971(m), 3.655(d)	14.7, 17.2, 26.8, 26.8, 62.4
9	Valine	0.979(d), 1.013(d), 2.275(m), 3.617(d)	19.6, 20.5, 32.2, 63.4
10	Propionate	1.061(t), 2.191(q)	12.95, 33.35
11	Methylsuccinate	1.104(d), 2.134(d), 2.633(m)	20.68, 44.43, —
12	α-Ketoisovalerate	1.127(d), 3.022(m)	18.8, 39.5
13	n-Heptanoate	1.309(m)	30.22
14	Threonine	1.330(d), 3.579(d), 4.269(m)	23.5, 63.2, 68.2
15	Lactate	1.331(d),4.115(q)	22.89, 71.40
16	Lysine	1.415(m), 1.719(m), 1.869(m), 3.018(t), 3.741(t)	23.44, 29.72, —, 41.5, 57.58
17	Cadaverine	1.483(d), 1.724(m), 3.022(t)	25.96, 29.37, 41.41
18	Alanine	1.489(d), 3.780(q)	18.26, 53.32
19	5-Aminovalerate	1.624(t), 1.650(t), 2.237(m), 3.022(m)	25.58, 29.76, 39.35, 41.37
20	Acetate	1.927(s)	26.54
21	Proline	2.023(m), 2.334(m), 3.320(m), 3.392(m), 4.147(t)	25.78, 32.11, 48.71, 48.71, 63.51
22	Glutamate	2.056(m), 2.334(m), 3.741（m,m,q）	30.1, 36.4, 57.6
23	Glutamine	2.138(m), 2.445(m), 3.768(t)	29.53, 32.96, 57.10
24	Methionine	2.141(s), 2.169(m), 2.648(t), 3.853(m)	16.0, 31, 56.7

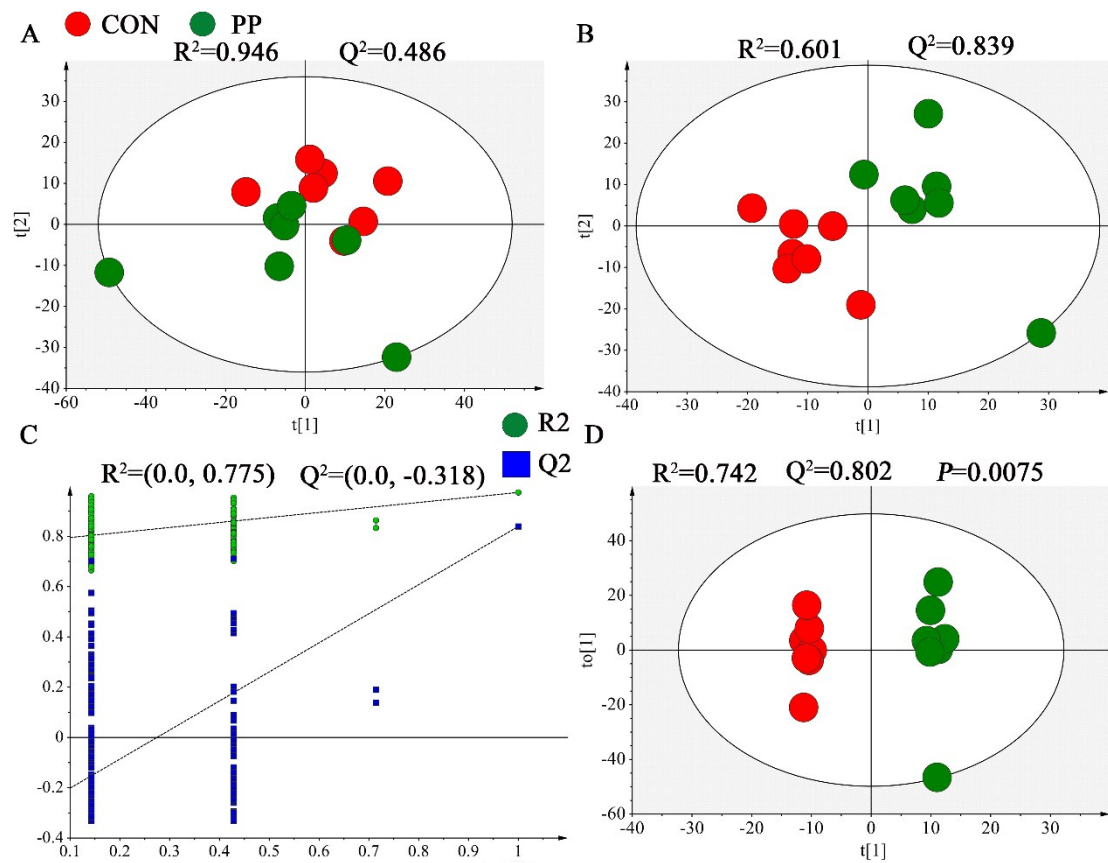| 25	Pyruvate	2.373(s)	29.5
26	Succinate	2.413(s)	37.3
27	Desaminotyrosine	2.463(t), 2.835(t), 6.859(d),7.191(d)	42.87,33.72, 118.54, 132.6
28	3-Phenylpropionate	2.496(t), 2.883(d), 7.274(t), 7.325(d), 7.375(m)	—, 34.44, —, —, 131.18
29	Aspartate	2.666(dd), 2.805(dd), 3.898(dd)	39.3, 39.3, 55.1
30	Sarcosine	2.704(s), 3.597(s)	34.86, 53.7
31	Dimethylamine	2.719(s)	36.8
32	Asparagine	2.862(dd), 2.962(m), 3.995(dd)	37.6, 37.6, 54.3
33	Trimethylamine	2.871(s)	47.4
34	Creatine	3.028(s), 3.926(s)	40.15, 56.25
35	Tyrosine	3.068(d), 3.140(dd), 3.943(d), 6.906(dd), 7.197(d)	37.91,37.87,59.39,118.8, 133.39
36	Malonate	3.112(s)	50.13
37	Phenylalanine	3.117(dd), 3.270(dd), 4.001(q), 7.323(d), 7.365(t), 7.42(m)	38.9,38.9,58.9,132.2,129.8,131.9
38	Ethanolamine	3.134(d), 3.817(d)	45.38, 60.22
39	Histidine	3.144(dd), 3.249(dd), 4.001(q), 7.093(s), 7.844(s)	—, —, —, 119, 139.1
40	Choline	3.191(s), 3.504(t), 4.085(m)	56.9, 70.1, 58.2
41	β-Glucose	3.243(t), 3.478(m), 3.492(m), 3.864(m), 3.927(s), 4.660(d)	—, —, —, 63.26, 63.26, 98.39
42	Taurine	3.243(t), 3.435(t)	49.5, 37.5
43	Betaine	3.27(s),3.91(s)	57.0, 68.0
44	Nethanol	3.366(s)	51.17
45	α-Glucose	3.417(m),3.546(m),3.726(m),3.742(m),3.772(m), 3.869(m), 5.210(d)	72.4, 74.3, 75.4, —, —, 75.2, 94.9
46	β-Arabinose	3.525(dd), 3.671(t), 3.856(dd), 3.945(m), 4.523(d)	—, 69.8, 70.6, —, 99.7
47	Phenylacetate	3.542(s), 7.317(m), 7.375(m)	47.21,129.57, 131.08
48	Glycine	3.566(s)	44.5
49	Serine	3.828(dd), 3.949(dd), 3.981(dd)	59.32, —, —
50	α-arabinose	3.850(d), 3.906(m), 3.993(t), 4.023(d), 5.251(d)	—, —, 72.3, 66.37, 93.94
51	Uracil	5.805(d), 7.540(d)	104.2, 146.2
52	Fumarate	6.524(s)	137.5
53	Urocanate	6.40(d), 7.318(d),7.434(s), 7.885(s)	133.42,124.74, 141.43, 134.16
54	Imidazole	7.327(s), 8.297(s)	123.24, 133.94
55	Adenine	8.195(s), 8.213(s)	144.2, 156.2

Note: Note: a indicates the displacement value of $^1H/^{13}C$ is based on the HSQC spectra. "—" indicates the corresponding displacement value of ^{13}C is not found in the HSQC spectra, and the attribution of metabolite is a reference only the ^1H displacement in NOESY spectra.

Supplementary Figure S1

Fig. S1 ^{1}H-NMR-based metabonomic analysis of urine samples. PCA (A) and PLS-DA (B) score plots derived from the ^{1}H-NMR spectra of urine extracts obtained from CON and PP groups, and cross validation (C) by permutation test at day 14. OPLS-DA (D) score plot derived from the ^{1}H-NMR spectra of urine extracts showing the discrimination between CON and PP groups at day 14.

Supplementary Figure S2

Fig. S2 ^{1}H-NMR-based metabonomic analysis of feces samples. PCA (A) and PLS-DA (B) score plots derived from the ^{1}H-NMR spectra of feces extracts obtained from CON and PP groups, and cross validation (C) by permutation test at day 14. OPLS-DA (D) score plot derived from the ^{1}H-NMR spectra of feces extracts showing the discrimination between CON and PP groups at day 14.