Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary Information

Coptis chinensis-induced diarrhea altered gut microbiota and metabolic profiles in rats

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Figure S1. Typical 600 MHz ^{1}H NMR spectra of faecal extracts from control rats (A), CF-treated rats (B), urine from untreated rats (C), CF-treated rats (D) at 7 days treatment. Metabolite keys are shown in Table S1.

Figure S2. PCA scores plots of ^{1}H NMR data of urine (A) and feces (B) are exhibited on day 7, metabolites of urine (C) and feces (D) in control group are analyzed at day -1 and day 7 with PCA model.

Figure S3. DGGE fingerprint for V3 region of fecal 16S rRNA gene on day 21 (recovery for 7 days) dispays at right hand, and its PCA scores plot shows on left.

Table S1. ^{1}H and ^{13}C chemical shifts for metabolites in faeces

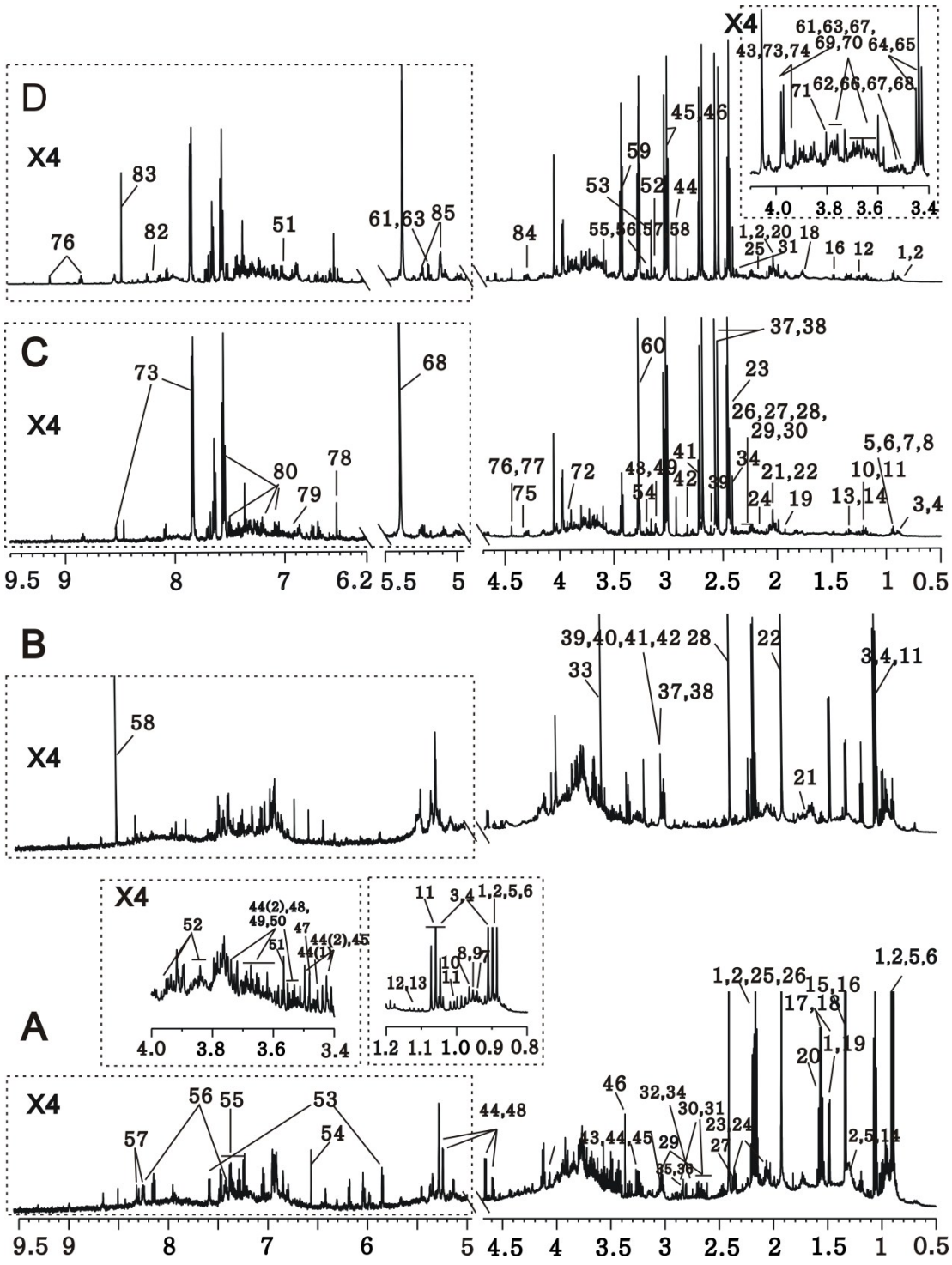
Table S2. ^{1}H and ^{13}C chemical shifts for metabolites in urine

Table S3. Result from Quantitative Enrichment Analysis for faeces on day 7.

Table S4. Result from Pathway Analysis for faeces on day 7.

Table S5. Result from Quantitative Enrichment Analysis for urine on day 7.

Table S6. Result from Pathway Analysis for urine on day 7.



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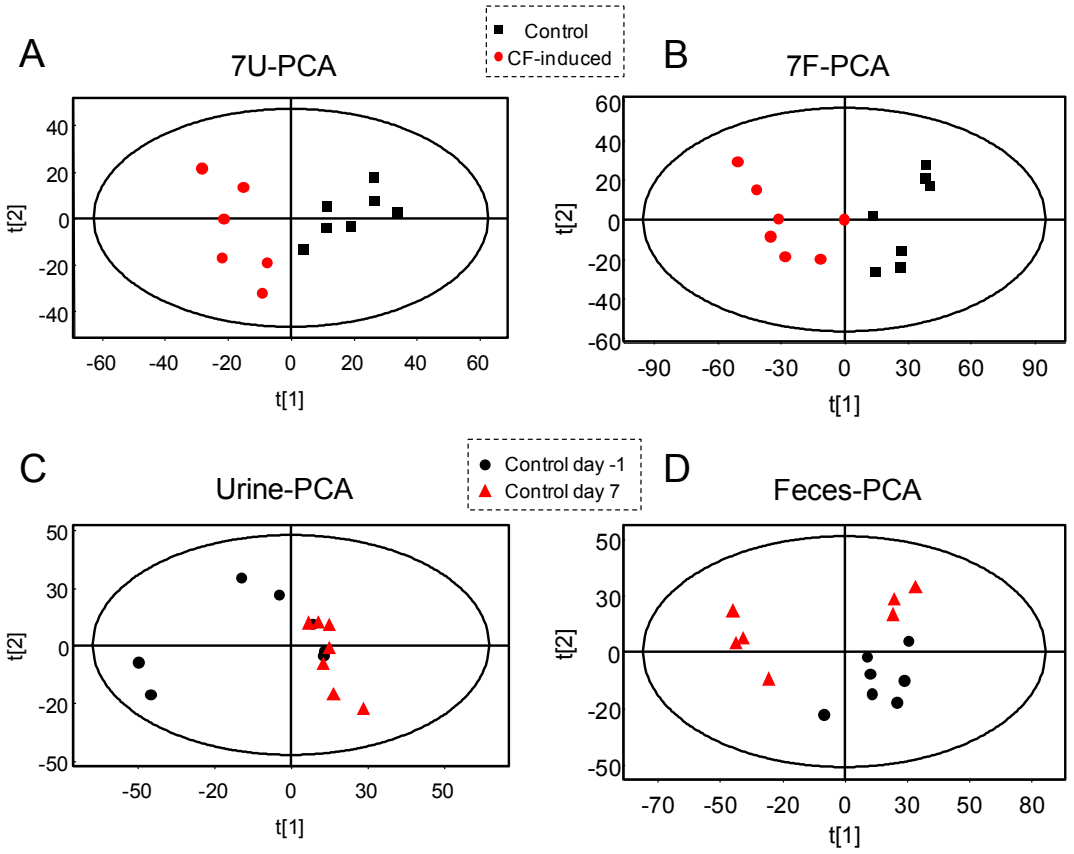

Figure S2. PCA scores plots of ^{1}H NMR data of urine (A) and feces (B) are exhibited on day 7, metabolites of urine (C) and feces (D) in control group are analyzed at day -1 and day 7 with PCA model.

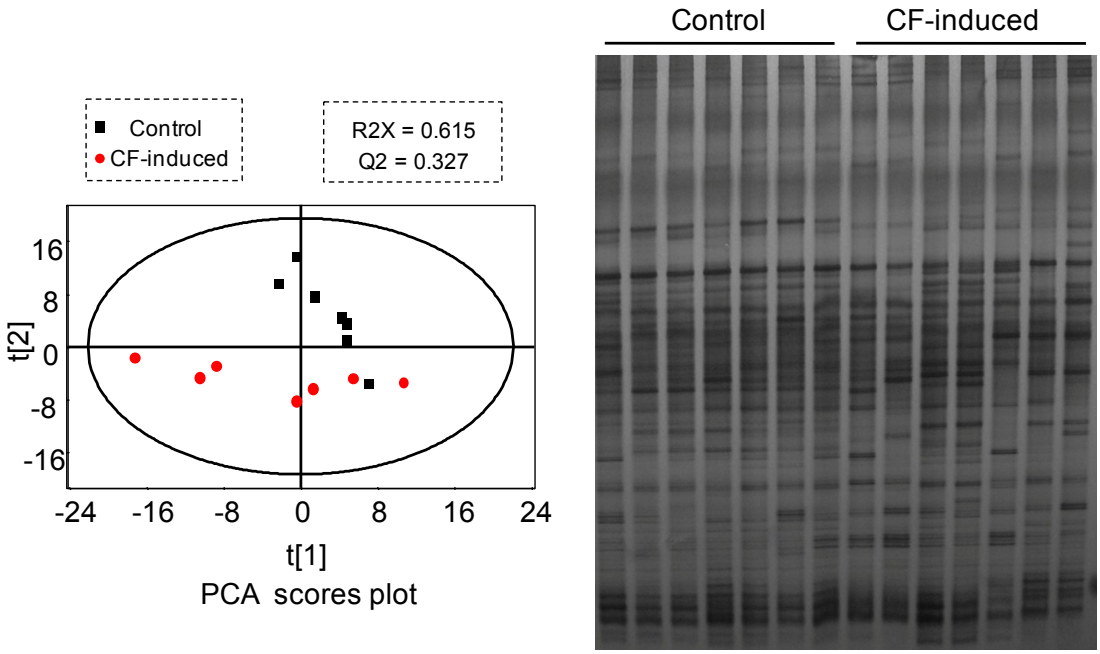

Figure S3. DGGE fingerprint for V3 region of fecal 16S rRNA gene on day 21 (recovery for 7 days) dispays at right hand, and its PCA scores plot shows on left.

Table S1. ^{1}H and ^{13}C chemical shifts for metabolites in faeces

keys	metabolites	δ1 H (ppm)	δ13 C (ppm[a])
1	isocaproate	0.882(d), 1.449(m), 1.483(d), 2.191(t)	—, 37.57, 30.72, 39.33
2	caproate	0.887(t), 1.292(ov),1.309(m), 1.556(m), 2.178(t)	16.23, 32.69, 23.66, 29.05, 39.54
3	*α*-keto-*β*-methyl-valerate	0.887(t), 1.104(d), 1.687(m), 2.923(m)	—
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	butyrate	0.899(t), 1.562(m), 2.150(t)	16.0, 22.1, 42.3
7	*α*-ketoisocaproate	0.920(s), 2.054(m), 2.616(d)	—
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	leucine	0.925(d), 0.936(s), 1.703(m), 3.725(d)	23.39, 24.3, 26.62, 56.88
10	valine	0.979(d), 1.013(d), 2.275(m), 3.617(d)	19.6, 20.5, 32.2, 63.4
11	propionate	1.061(t), 2.191(q)	12.95, 33.35
12	methylsuccinate	1.104(d), 2.134(d), 2.633(m)	20.68, 44.43, —
13	*α*-ketoisovalerate	1.127(d), 3.022(m)	18.8, 39.5
14	*n*-heptanoate	1.309(m)	30.22
15	lactate	1.331(d),4.115(q)	22.89, 71.40
16	threonine	1.330(d), 3.579(d), 4.269(m)	23.5, 63.2, 68.2
17	lycine	1.415(m), 1.719(m), 1.869(m), 3.018(t), 3.741(t)	23.44, 29.72, —, 41.5, 57.58
18	cadaverine	1.483(d), 1.724(m), 3.022(t)	25.96, 29.37, 41.41
19	alanine	1.489(d), 3.780(q)	18.26, 53.32
20	5-aminovalerate	1.624(t), 1.650(t), 2.237(m), 3.022(m)	25.58, 29.76, 39.35, 41.37
21	glutarate	1.775(ov), 2.181(t)	26.15, 39.44
22	acetate	1.927(s)	26.54
23	glutamate	2.056(m), 2.334(m), 3.741（m,m,q）	—
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	methionine	2.141(s), 2.169(m), 2.648(t), 3.853(m)	16.0, 31, 56.7
26	glutamine	2.138(m), 2.445(m), 3.768(t)	29.53, 32.96, 57.10
27	pyruvate	2.373(s)	29.5
28	succinate	2.413(s)	37.3
29	*α*-ketoglutarate	2.443(t), 3.011(t)	33.4, 38.3
30	desaminotyrosine	2.463(t), 2.835(t), 6.859(d),7.191(d)	42.87,33.72, 118.54, 132.6

31	3-phenylpropionate	2.496(t), 2.883(d), 7.274(t), 7.325(d), 7.375(m)	—, 34.44, —, —, 131.18
32	aspartate	2.666(dd), 2.805(dd), 3.898(dd)	39.3, 39.3, 55.1
33	sarcosine	2.704(s), 3.597(s)	34.86, 53.7
34	dimethylamine	2.719(s)	36.8
35	asparagine	2.862(dd), 2.962(m), 3.995(dd)	—
36	trimethylamine	2.871(s)	47.4
37	creatine	3.028(s), 3.926(s)	40.15, 56.25
38	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
39	malonate	3.112(s)	50.13
40	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
41	ethanolamine	3.134(d), 3.817(d)	45.38, 60.22
42	histidine	3.144(dd), 3.249(dd), 4.001(q), 7.093(s), 7.844(s)	—, —, —, 119, 139.1
43	choline	3.191(s), 3.504(t), 4.085(m)	56.9, 70.1, 58.2
44	*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
	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
45	taurine	3.243(t), 3.435(t)	49.5, 37.5
46	methanol	3.366(s)	51.17
47	3-hydroxyphenylacetate	3.490(s), 6.794(m), 6.872(ov), 7.258(ov)	47.04,119.45, 124.19, 132.91
48	*β*-arabinose	3.525(dd), 3.671(t), 3.856(dd), 3.945(m), 4.523(d)	—, 69.8, 70.6, —, 99.7
	α-arabinose	3.850(d), 3.906(m), 3.993(t), 4.023(d), 5.251(d)	—, —, 72.3, 66.37, 93.94
49	phenylacetate	3.542(s), 7.317(m), 7.375(m)	47.21,129.57, 131.08
50	*α*-xylose	3.545(dd), 3.630(m), 3.671(t), 5.203(d)	—
51	glycine	3.566(s)	44.5
52	serine	3.828(dd), 3.949(dd), 3.981(dd)	59.32, —, —
53	uracil	5.805(d), 7.540(d)	104.2, 146.2
54	fumarate	6.524(s)	137.5
55	urocanate	6.40(d), 7.318(d),7.434(s), 7.885(s)	133.42,124.74, 141.43, 134.16
56	imidazole	7.327(s), 8.297(s)	123.24, 133.94
57	adenine	8.195(s), 8.213(s)	144.2, 156.2
58	formate	8.467(s)	—

Table S2. ^{1}H and ^{13}C chemical shifts for metabolites in urine

keys	metabolites	δ1 H (ppm)	δ13 C (ppm[a])
1	triglyceride	0.895(m), 1.303(m), 2.041(m), 2.242(m), 2.754(m), 5.315(m)	—
2	isovalerate	0.895(d), 1.929(m), 2.049(d)	24.44, 29.27, 49.26
3	2-hydroxybutyrate	0.899(m), 1.689(m), 3.996(dd)	10.68, 29.48, 76.07
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	leucine	0.925(d), 0.936(s), 1.703(m), 3.725(d)	23.39, 24.3, 26.62, 56.88
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	ketoleucine	0.944(d), 2.100(m), 2.617(d)	24.32, 26.2, —
9	isobutyrate	1.053(d), 2.382(m)	22.04, 39.32
10	isopropanol	1.146(d), 4.028(m)	26.12, —
11	ethanol	1.185(t), 3.656(q)	19.54, —
12	3-hydroxyisovalerate	1.275(s), 2.357(s)	30.2,51.6
13	threonine	1.330(d), 3.579(d), 4.269(m)	23.5, 63.2, 68.2
14	lactate	1.331(d),4.115(q)	22.89, 71.40
15	lysine	1.415(m), 1.719(m), 1.869(m), 3.018(t), 3.741(t)	23.44, 29.72, —, 41.5, 57.58
16	alanine	1.489(d), 3.780(q)	18.26, 53.32
17	citrulline	1.558(m), 1.865(m), 3.124(dd), 3.743(t)	—, —, 42, 57.9
18	ornithine	1.775(m), 1.828(m), 1.929(m), 3.044(t), 3.782(d)	25.5, 25.5, —, 41.12, 56.81
19	acetate	1.927(s)	26.54
20	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
21	*N*-acetylglycine	2.044(s), 3.763(d)	24.2, 46.1
22	glutamate	2.056(m), 2.334(m), 3.741（m,m,q）	—
23	glutamine	2.138(m), 2.445(m), 3.768(t)	29.53， 32.96， 57.10
24	*O*-acetylcholine	2.143(s), 3.202(s), 3.711(t), 4.529(m)	23.4, 56.8, 67.1, 60.2
25	acetylcarnitine	2.159(s), 2.504(m), 2.631(m), 3.202(s), 3.621(d), 3.829(dd)	22.4, 44.0, 44.0, 57.5, 70.9,70.9
26	levulinate	2.211(s), 2.384(t), 2.780(t)	32.42, 34.68, 41.12
27	acetone	2.229(s)	28.2
28	*p*-cresol	2.253(s), 6.817(d), 7.130(d)	—
29	acetoacetate	2.266(s), 3.434(s)	32.3
30	*p*-cresol glucuronide	2.299(s), 7.055(m), 7.237(m)	22.17, 123.16, 135.68

31	pyruvate	2.373(s)	29.5
32	*p*-cresol sulfate	2.347(s), 7.217(d), 7.293(d)	—, 121.61, 136.05
33	carnitine	2.41(t), 3.230(s), 3.405(m), 4.554(m)	—, 57.51, 71.6, 66.38
34	succinate	2.413(s)	37.3
35	2-oxoglutarate	2.429(t), 2.995(t)	33.2, 39.0
36	4-pyridoxate	2.429(s), 7.834(s)	20.39, 138.78
37	citrate	2.552(d), 2.658(d)	48.7, 48.7
38	*β*-alanine	2.540(t), 3.196(t)	36.4, 39.97
39	methylamine	2.613(s)	27
40	aspartate	2.666(dd), 2.805(dd), 3.898(dd)	39.3, 39.3, 55.1
41	dimethylamine	2.719(s)	36.8
42	methylguanidine	2.828(s), 3.356(s)	29.47, —
43	asparagine	2.862(dd), 2.962(m), 3.995(dd)	—
44	*N*,*N*-dimethylglycine	2.925(s), 3.712(s)	46.1, 62.2
45	creatine	3.028(s), 3.926(s)	40.15, 56.25
46	creatinine	3.043(s), 4.052(s)	33.5, 58.39
47	*τ*-methylhistidine	3.065(m), 3.681,3.951(m), 7.001(s), 7.677(s)	30.7, 36.5, 58.13, 122.92, —
48	*N*6,*N*6,*N*6-trimethyllysine	3.109(s)	47.14
49	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
50	*cis*-aconitate	3.123(s), 5.711(t)	46.7, 127
51	histidine	3.144(dd), 3.249(dd), 4.001(q), 7.093(s), 7.844(s)	—, —, —, 119, 139.1
52	dimethyl sulfone	3.145(s)	—
53	*N*-nitrosodimethylamine	3.162(s), 3.802(s)	32.16, 39.86
54	choline	3.191(s), 3.504(t), 4.085(m)	56.9, 70.1, 58.2
55	phosphorylcholine	3.203(s), 3.671(t), 4.190(dd)	56.0, 68.56, 60.33
56	glycerophosphocholine	3.223,3.689(m), 3.925(m), 4.317(dd)	55.97, 68.1, 73.93, 64.44
57	*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
58	taurine	3.243(t), 3.435(t)	49.5, 37.5
59	trimethylamine-N-oxide (TMAO)	3.266(s)	61.5
60	betaine	3.273(s), 3.927(s)	57, 68
61	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

62	tryptophan	3.298(dd), 3.498(dd),4.089(q), 7.204(t), 7.310,7.507(m), 7.701(d)	—
63	*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
64	*trans*-aconitate	3.435(s), 6.571(s)	39.2, 133.4
65	*p*-hydroxyphenylacetate	3.445(s), 6.865(d), 7.169(d)	46.5, 118.59, 133.69
66	3-hydeoxyphenylacetate	3.490(s), 6.794(m), 6.872(ov), 7.258(ov)	47.04, 119.45, 124.19, 132.91
67	glycerol	3.551(t), 3.634(m), 3.767(m)	—
68	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
69	mannitol	3.677(dd), 3.770(m), 3.805(d), 3.873(dd)	65.37, 72.8, 72.66, 66.69
70	phenylacetylglycine	3.680(s), 3.746(d), 7.365(t), 7.425(t)	44.42, —, 131.12, 130.89
71	guanidoacetate	3.801(s)	47.5
72	glycolate	3.932(s)	64.19
73	hippurate	3.975(d), 7.553(t), 7.642(t), 7.837(d), 8.508(s)	46.1, 131.5, 134.9, 129.9
74	4-hydroxyhippurate	3.978(s), 6.976(d), 7.765(d)	—
75	tartrate	4.329(s)	77.38
76	trigonelline	4.438(s), 8.084(t), 8.837(t), 9.122(s)	51.3, 130.8, —, —
77	1-methylnicotinamide	4.476(s), 8.181(t), 8.894(d), 8.960(d), 9.272(s)	50.85, 131.14, —, —, —
78	fumarate	6.524(s)	137.5
79	*p*-hydroxybenzoate	6,970(m), 7.759(m)	117.2, 133.68
80	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
81	xanthine	7.909(s)	141.77
82	oxypurinol	8.209(s)	129.09
83	formate	8.467(s)	—
84	glycylproline	1.832(m), 1.973(m), 2.137(m), 2.242(m), 2.346(m), 3.545(m), 3.942(s), 4.223(dd), 4.267(ov)	25.28, 26.24, —, 32.22, 33.97, 49.0, 42.66, —, —
85	fucose	1.187(d), 1.213, 3.434(t), 3.550(t), 3.620(dd), 3.725(d), 3.746(d), 3.793(m), 3.829(dd), 3.969(t), 4.002(m), 4.036(d), 4.083(dd), 4.177(q), 4.535(d), 5.189(d), 5.263(d)	18.16, 17.83, —, —,76.98, 74.67, 70.9, 72.86, 72.16—, —, —, —, 69.75, 99.63, 95.61, —

[a] corresponding values in the two columns are chemical shifts of $^{1}H/^{13}C$ pairs detected in the HSQC experiment. Signals marked '-' in the ^{13}C column were not found by HSQC; in that case, ^{1}H shifts are from TOCSY.

Table S3. Result from Quantitative Enrichment Analysis for faeces on day 7.

	Total Cmpd	Hits	Statistic Q	Expected Q	Raw p	Holm p	FDR
PHOSPHOLIPID BIOSYNTHESIS	19	2	87.02	7.69	1.61E -07	6.77E -06	4.35E -06
ALANINE METABOLISM	6	3	81.88	7.69	3.10E -07	1.27E -05	4.35E -06
GLUCOSE-ALANINE CYCLE	12	3	81.88	7.69	3.10E -07	1.27E -05	4.35E -06
SELENOAMINO ACID METABOLISM	15	1	87.71	7.69	8.20E -07	3.20E -05	7.47E -06
UREA CYCLE	20	6	50.68	7.69	8.89E -07	3.38E -05	7.47E -06
METHIONINE METABOLISM	24	5	75.80	7.69	4.38E -06	1.62E -04	3.07E -05
VALINE, LEUCINE AND ISOLEUCINE DEGRADATION	36	6	72.32	7.69	7.04E -06	2.53E -04	4.22E -05
BETA OXIDATION OF VERY LONG CHAIN FATTY ACIDS	14	1	82.01	7.69	8.32E -06	2.91E -04	4.37E -05
BUTYRATE METABOLISM	9	1	80.15	7.69	1.51E -05	5.15E -04	7.06E -05
BETAINE METABOLISM	10	3	63.01	7.69	1.73E -05	5.72E -04	7.06E -05
SPHINGOLIPID METABOLISM	15	1	79.49	7.69	1.85E -05	5.92E -04	7.06E -05
AMMONIA RECYCLING	18	9	72.22	7.69	2.14E -05	6.63E -04	7.49E -05
PHENYLALANINE AND TYROSINE METABOLISM	13	3	76.50	7.69	3.35E -05	1.01E -03	1.08E -04
GLYCINE, SERINE AND THREONINE METABOLISM	26	7	53.87	7.69	4.69E -05	1.36E -03	1.41E -04
ARGININE AND PROLINE METABOLISM	26	4	59.90	7.69	8.80E -05	2.46E -03	2.46E -04
HISTIDINE METABOLISM	11	2	71.10	7.69	1.21E -04	3.26E -03	3.17E - 04
GLYCOLYSIS	21	3	60.29	7.69	1.02E -03	2.64E -02	2.46E - 03
NUCLEOTIDE SUGARS METABOLISM	9	2	59.42	7.69	1.06E -03	2.65E -02	2.46E - 03
GALACTOSE METABOLISM	25	1	59.22	7.69	1.29E -03	3.10E -02	2.46E - 03
STARCH AND SUCROSE METABOLISM	14	1	59.22	7.69	1.29E -03	3.10E -02	2.46E - 03
FRUCTOSE AND MANNOSE DEGRADATION	18	1	59.22	7.69	1.29E -03	3.10E -02	2.46E - 03
RETINOL METABOLISM	18	1	59.22	7.69	1.29E -03	3.10E -02	2.46E - 03
GLUTATHIONE METABOLISM	10	1	56.92	7.69	1.82E -03	3.64E -02	3.18E - 03
PORPHYRIN METABOLISM	22	1	56.92	7.69	1.82E -03	3.64E -02	3.18E - 03
MALATE-ASPARTATE SHUTTLE	8	2	35.24	7.69	2.23E -03	4.02E -02	3.75E - 03
PYRUVATE METABOLISM	20	3	34.00	7.69	8.31E -03	1.41E -01	1.34E - 02
PROTEIN BIOSYNTHESIS	19	13	33.79	7.69	1.08E -02	1.74E -01	1.68E - 02
BETA-ALANINE METABOLISM	13	2	41.52	7.69	1.12E -02	1.74E -01	1.68E - 02
GLUCONEOGENESIS	27	5	30.23	7.69	1.48E -02	2.07E -01	2.14E - 02
ASPARTATE METABOLISM	12	4	35.51	7.69	1.97E -02	2.55E -01	2.75E - 02
CYSTEINE METABOLISM	8	1	36.39	7.69	2.24E -02	2.69E -01	2.94E - 02
INSULIN SIGNALLING	19	1	36.39	7.69	2.24E -02	2.69E -01	2.94E - 02
TYROSINE METABOLISM	38	2	33.29	7.69	3.01E -02	3.01E -01	3.80E - 02
CATECHOLAMINE BIOSYNTHESIS	5	1	33.28	7.69	3.08E -02	3.01E -01	3.80E - 02
BILE ACID BIOSYNTHESIS	49	2	29.41	7.69	3.62E-02	3.01E-01	4.35E - 02
PROPANOATE METABOLISM	18	2	20.73	7.69	9.73E-02	6.81E-01	1.14E - 01
TAURINE AND HYPOTAURNE METABOLISM	7	1	16.53	7.69	1.49E-01	8.94E-01	1.69E - 01
CITRIC ACID CYCLE	23	4	5.20	7.69	4.34E-01	1.00E+00	4.69E - 01
MITOCHONDRIAL ELECTRON TRANSPORT CHAIN	15	2	4.98	7.69	4.43E-01	1.00E+00	4.69E - 01
GLUTAMATE METABOLISM	18	3	5.00	7.69	4.47E-01	1.00E+00	4.69E - 01
PURINE METABOLISM	45	2	3.09	7.69	5.55E-01	1.00E+00	5.68E - 01
PYRIMIDINE METABOLISM	36	2	2.17	7.69	6.21E-01	1.00E+00	6.21E - 01

Table S4. Result from Pathway Analysis for faeces on day 7.

	Total Cmpd	Hits	Rawp	-log(p)	Holm adjust	FDR	Impact
Valine, leucine and isoleucine biosynthesis	11	5	9.21E-08	1.62E+01	3.22E-06	1.79E-06	0.67
Valine, leucine and isoleucine degradation	38	4	1.02E-07	1.61E+01	3.48E-06	1.79E-06	0.02
Glycerophospholipid metabolism	30	2	1.61E-07	1.56E+01	5.32E-06	1.88E-06	0.02
Butanoate metabolism	20	3	1.02E-05	1.15E+01	3.26E-04	8.69E-05	0.00
Sphingolipid metabolism	21	1	1.85E-05	1.09E+01	5.73E-04	8.69E-05	0.00
Cysteine and methionine metabolism	28	3	1.90E-05	1.09E+01	5.73E-04	8.69E-05	0.14
Methane metabolism	9	3	1.95E-05	1.08E+01	5.73E-04	8.69E-05	0.40
Cyanoamino acid metabolism	6	2	1.99E-05	1.08E+01	5.73E-04	8.69E-05	0.00
Phenylalanine metabolism	9	3	3.13E-05	1.04E+01	8.46E-04	1.17E-04	0.41
Phenylalanine, tyrosine and tryptophan biosynthesis	4	2	3.35E-05	1.03E+01	8.72E-04	1.17E-04	1.00
Glycine, serine and threonine metabolism	32	8	3.79E-05	1.02E+01	9.47E-04	1.21E-04	0.60
Pantothenate and CoA biosynthesis	15	3	8.49E-05	9.37E+00	2.04E-03	2.48E-04	0.00
Aminoacyl-tRNA biosynthesis	67	13	1.47E-04	8.83E+00	3.38E-03	3.95E-04	0.14
Starch and sucrose metabolism	23	1	1.29E-03	6.65E+00	2.84E-02	2.66E-03	0.19
Galactose metabolism	26	1	1.29E-03	6.65E+00	2.84E-02	2.66E-03	0.00
Fructose and mannose metabolism	19	1	1.29E-03	6.65E+00	2.84E-02	2.66E-03	0.00
Amino sugar and nucleotide sugar metabolism	37	1	1.29E-03	6.65E+00	2.84E-02	2.66E-03	0.00
Histidine metabolism	15	3	1.40E-03	6.57E+00	2.84E-02	2.72E-03	0.39
Arginine and proline metabolism	44	5	1.64E-03	6.41E+00	2.84E-02	3.02E-03	0.08
Porphyrin and chlorophyll metabolism	27	1	1.82E-03	6.31E+00	2.91E-02	3.18E-03	0.00
Glycolysis or Gluconeogenesis	26	4	3.46E-03	5.67E+00	5.19E-02	5.77E-03	0.14
D-Glutamine and D-glutamate metabolism	5	2	5.81E-03	5.15E+00	8.13E-02	9.24E-03	0.00
Pyruvate metabolism	22	3	8.31E-03	4.79E+00	1.08E-01	1.26E-02	0.24
betaAlanine metabolism	19	2	1.12E-02	4.49E+00	1.35E-01	1.64E-02	0.00
Tyrosine metabolism	42	2	3.01E-02	3.50E+00	3.32E-01	4.14E-02	0.14
Ubiquinone and other terpenoidquinone biosynthesis	3	1	3.08E-02	3.48E+00	3.32E-01	4.14E-02	0.00
Primary bile acid biosynthesis	46	2	3.62E-02	3.32E+00	3.32E-01	4.70E-02	0.06
Glutathione metabolism	26	2	8.01E-02	2.52E+00	6.41E-01	9.96E-02	0.01
Nitrogen metabolism	9	3	8.25E-02	2.49E+00	6.41E-01	9.96E-02	0.00
Taurine and hypotaurine metabolism	8	1	1.49E-01	1.90E+00	8.94E-01	1.74E-01	0.43
Propanoate metabolism	20	2	3.96E-01	9.25E-01	1.00E+00	4.48E-01	0.00
Alanine, aspartate and glutamate metabolism	24	6	4.36E-01	8.29E-01	1.00E+00	4.69E-01	0.35

Table S5. Result from Quantitative Enrichment Analysis for urine on day 7.

	Total Cmpd	Hits	Statistic Q	Expected Q	Raw p	Holm p	FDR
VITAMIN B6 METABOLISM	10	1	67.76	7.69	2.98E -04	1.40E -02	1.08E-02
OXIDATION OF BRANCHED CHAINFATTY ACIDS	14	2	60.35	7.69	1.02E -03	4.71E -02	1.08E-02
BETA OXIDATION OF VERY LONG CHAIN FATTY ACIDS	14	2	60.35	7.69	1.02E -03	4.71E -02	1.08E-02
PROTEIN BIOSYNTHESIS	19	12	34.74	7.69	1.08E -03	4.76E -02	1.08E-02
PHOSPHOLIPID BIOSYNTHESIS	19	2	57.08	7.69	1.15E -03	4.94E -02	1.08E-02
TRYPTOPHAN METABOLISM	34	2	56.57	7.69	1.84E -03	7.74E -02	1.44E-02
STARCH AND SUCROSE METABOLISM	14	2	53.41	7.69	2.86E -03	1.17E -01	1.92E-02
BETA-ALANINEMETABOLISM	13	2	42.52	7.69	4.73E -03	1.89E -01	2.78E-02
ARGININE AND PROLINE METABOLISM	26	7	28.18	7.69	9.47E -03	3.69E -01	4.87E-02
PURINE METABOLISM	45	2	43.22	7.69	1.04E -02	3.94E -01	4.87E-02
PROPANOATE METABOLISM	18	1	40.28	7.69	1.48E -02	5.46E -01	5.78E-02
PYRIMIDINE METABOLISM	36	2	34.72	7.69	1.51E -02	5.46E -01	5.78E-02
UREA CYCLE	20	8	26.76	7.69	1.60E -02	5.60E -01	5.78E-02
SELENOAMINO ACID METABOLISM	15	1	34.35	7.69	2.76E -02	9.39E -01	8.08E-02
GLUTAMATE METABOLISM	18	3	33.05	7.69	2.82E -02	9.39E -01	8.08E-02
METHIONINE METABOLISM	24	3	25.83	7.69	2.92E -02	9.39E -01	8.08E-02
BETAINE METABOLISM	10	3	25.83	7.69	2.92E -02	9.39E -01	8.08E-02
BUTYRATE METABOLISM	9	1	32.45	7.69	3.35E -02	1.00E+00	8.73E-02
GLYCINE, SERINE AND THREONINE METABOLISM	26	6	22.07	7.69	3.56E -02	1.00E+00	8.81E-02
GALACTOSE METABOLISM	25	3	25.87	7.69	3.91E -02	1.00E+00	9.20E-02
ALANINE METABOLISM	6	3	20.99	7.69	6.70E -02	1.00E+00	1.43E-01
GLUCOSE-ALANINE CYCLE	12	3	20.99	7.69	6.70E -02	1.00E+00	1.43E-01
AMMONIA RECYCLING	18	6	19.43	7.69	7.14E -02	1.00E+00	1.46E-01
FRUCTOSE AND MANNOSE DEGRADATION	18	2	21.88	7.69	8.16E -02	1.00E+00	1.60E-01
MALATE-ASPARTATE SHUTTLE	8	2	20.22	7.69	1.03E -01	1.00E+00	1.93E-01
CYSTEINE METABOLISM	8	1	19.68	7.69	1.12E -01	1.00E+00	1.95E-01
INSULIN SIGNALLING	19	1	19.68	7.69	1.12E -01	1.00E+00	1.95E-01
VALINE, LEUCINE AND ISOLEUCINE DEGRADATION	36	5	15.37	7.69	1.21E -01	1.00E+00	2.02E-01
TAURINE AND HYPOTAURINE METABOLISM	7	1	14.93	7.69	1.72E -01	1.00E+00	2.70E-01
BILE ACID BIOSYNTHESIS	49	1	14.93	7.69	1.72E -01	1.00E+00	2.70E-01
GLYCOLYSIS	21	3	13.59	7.69	1.88E -01	1.00E+00	2.85E-01
GLUCONEOGENESIS	27	5	12.04	7.69	2.05E -01	1.00E+00	3.02E-01
PYRUVATE METABOLISM	20	3	10.72	7.69	2.52E -01	1.00E+00	3.42E-01
KETONE BODY METABOLISM	10	2	10.39	7.69	2.59E -01	1.00E+00	3.42E-01
GLYCEROLIPID METABOLISM	13	1	10.41	7.69	2.61E -01	1.00E+00	3.42E-01
NICOTINATE AND NICOTINAMIDE METABOLISM	13	1	10.34	7.69	2.62E -01	1.00E+00	3.42E-01
NUCLEOTIDE SUGARS METABOLISM	9	1	8.75	7.69	3.05E -01	1.00E+00	3.77E-01
RETINOL METABOLISM	18	1	8.75	7.69	3.05E -01	1.00E+00	3.77E-01
LYSINE DEGRADATION	13	1	7.08	7.69	3.58E -01	1.00E+00	4.21E-01
BIOTIN METABOLISM	4	1	7.08	7.69	3.58E -01	1.00E+00	4.21E-01
CITRIC ACID CYCLE	23	6	5.58	7.69	4.50E -01	1.00E+00	5.15E-01
MITOCHONDRIAL ELECTRON TRANSPORT CHAIN	15	2	4.41	7.69	4.89E -01	1.00E+00	5.47E-01
TYROSINE METABOLISM	38	3	3.50	7.69	5.58E -01	1.00E+00	6.09E-01
ASPARTATE METABOLISM	12	5	0.68	7.69	8.37E -01	1.00E+00	8.89E-01
HISTIDINE METABOLISM	11	2	0.33	7.69	8.51E -01	1.00E+00	8.89E-01
PHENYLALANINE AND TYROSINE METABOLISM	13	3	0.20	7.69	8.83E -01	1.00E+00	9.02E-01
UBIQUINONE BIOSYNTHESIS	10	1	0.08	7.69	9.21E -01	1.00E+00	9.21E-01

Table S6. Result from Pathway Analysis for urine on day 7.

	Total Cmpd	Hits	Raw p	-log(p)	Holm adjust	FDR	Impact
Valine, leucine and isoleucine degradation	38	3	2.28E-05	1.07E+01	9.13E-04	9.13E-04	0.01
Vitamin B6 metabolism	9	1	2.98E-04	8.12E+00	1.16E-02	5.96E-03	0.00
Glutathione metabolism	26	1	4.58E-04	7.69E+00	1.74E-02	6.10E-03	0.00
Lysine degradation	20	1	1.07E-03	6.84E+00	3.97E-02	1.07E-02	0.00
Glycerophospholipid metabolism	30	4	2.51E-03	5.99E+00	9.02E-02	2.00E-02	0.09
beta-Alanine metabolism	19	2	4.73E-03	5.35E+00	1.66E-01	3.15E-02	0.44
Glycine, serine and threonine metabolism	32	7	6.01E-03	5.11E+00	2.04E-01	3.43E-02	0.06
Arginine and proline metabolism	44	8	9.47E-03	4.66E+00	3.12E-01	4.14E-02	0.26
Propanoate metabolism	20	3	9.83E-03	4.62E+00	3.14E-01	4.14E-02	0.00
Purine metabolism	68	2	1.04E-02	4.57E+00	3.21E-01	4.14E-02	0.03
Phenylalanine, tyrosine and tryptophan biosynthesis	4	1	1.34E-02	4.31E+00	4.02E-01	4.31E-02	0.50
Phenylalanine metabolism	9	1	1.34E-02	4.31E+00	4.02E-01	4.31E-02	0.41
Pantothenate and CoA biosynthesis	15	1	1.48E-02	4.22E+00	4.13E-01	4.31E-02	0.00
Pyrimidine metabolism	41	2	1.51E-02	4.19E+00	4.13E-01	4.31E-02	0.00
Valine, leucine and isoleucine biosynthesis	11	3	1.62E-02	4.12E+00	4.22E-01	4.33E-02	0.33
Butanoate metabolism	20	4	2.63E-02	3.64E+00	6.56E-01	6.57E-02	0.10
Aminoacyl tRNA biosynthesis	67	9	2.90E-02	3.54E+00	6.96E-01	6.82E-02	0.00
Synthesis and degradation of ketone bodies	5	1	3.35E-02	3.40E+00	7.69E-01	7.43E-02	0.60
Galactose metabolism	26	3	3.91E-02	3.24E+00	8.61E-01	8.24E-02	0.02
Histidine metabolism	15	2	4.97E-02	3.00E+00	1.00E+00	9.95E-02	0.24
Fructose and mannose metabolism	19	2	8.16E-02	2.51E+00	1.00E+00	1.48E-01	0.00
Amino sugar and nucleotide sugar metabolism	37	2	8.16E-02	2.51E+00	1.00E+00	1.48E-01	0.00
Nitrogen metabolism	9	2	9.98E-02	2.30E+00	1.00E+00	1.74E-01	0.00
Cysteine and methionine metabolism	28	1	1.12E-01	2.19E+00	1.00E+00	1.87E-01	0.02
Taurine and hypotaurine metabolism	8	1	1.72E-01	1.76E+00	1.00E+00	2.65E-01	0.43
Primary bile acid biosynthesis	46	1	1.72E-01	1.76E+00	1.00E+00	2.65E-01	0.03
Starch and sucrose metabolism	23	2	1.95E-01	1.63E+00	1.00E+00	2.80E-01	0.19
Pentose phosphate pathway	19	1	1.96E-01	1.63E+00	1.00E+00	2.80E-01	0.00
Glycolysis or Gluconeogenesis	26	6	2.03E-01	1.60E+00	1.00E+00	2.80E-01	0.14
Pyruvate metabolism	22	3	2.52E-01	1.38E+00	1.00E+00	3.28E-01	0.24
Glycerolipid metabolism	18	1	2.61E-01	1.34E+00	1.00E+00	3.28E-01	0.28
Nicotinate and nicotinamide metabolism	13	1	2.62E-01	1.34E+00	1.00E+00	3.28E-01	0.12
D-Glutamine and D-glutamate metabolism	5	3	3.30E-01	1.11E+00	1.00E+00	3.99E-01	0.00
Biotin metabolism	5	1	3.58E-01	1.03E+00	1.00E+00	4.21E-01	0.00
Alanine, aspartate and glutamate metabolism	24	7	4.19E-01	8.69E-01	1.00E+00	4.79E-01	0.41
Methane metabolism	9	1	4.32E-01	8.39E-01	1.00E+00	4.80E-01	0.00
Citrate cycle (TCA cycle)	20	6	4.50E-01	8.00E-01	1.00E+00	4.86E-01	0.28
Glyoxylate and dicarboxylate metabolism	16	4	5.21E-01	6.51E-01	1.00E+00	5.49E-01	0.59