## Supplementary information

### Supplementary Table S1 NMR data for metabolites detected in urine extracts

| Key | Metabolites                      | δ1 H (ppm)                                      | δ13 C (ppm) |
|-----|----------------------------------|------------------------------------------------|-------------|
| 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), 1.292(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   | Isovalerylglucine                | 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), 1.703(m), 3.725(d)           | 23.39, 24.3, 26.62, 56.88 |
| 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), 2.385(d)                               | 30.2, 51.6  |
| 14  | Threonine                        | 1.330(d), 1.357(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 |
| 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), 3.929(m), 4.147(t) | 25.78, 32.11, 48.71, 48.71, 63.51 |
| 25  | N-Acetylglutamic acid            | 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-Acetycholine                   | 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  | Levulinic acid                   | 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  |
|    | Compound                        | δ Values (ppm)                      | J Values (Hz) | Multiplicity | Assignments       |
|----|---------------------------------|------------------------------------|--------------|--------------|-------------------|
| 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 | Creatine                        | 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 | N6,N6,N6-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 | Phenyll alanine                 | 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-Hydroxyphenylaceta            | 3.437(s), 6.850(d), 7.154(d)       |              | —            |                   |
| 70 | p-Hydroxyphenylaceta            | 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-Hydroxyphenylacetate          | 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-Phenylacetylglucose           | 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 | Phenylacetylglucose             | 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         |                   |
| Metabolites               | δ1 H (ppm)                     | δ13 C (ppm)       |
|--------------------------|--------------------------------|-------------------|
| Glycolate                | 3.932(s)                       | 64.19             |
| Hippurate                | 3.975(d), 7.553(t), 7.642(t), 7.837(d), 8.508(s) | 46.1, 131.5, 134.9, 129.9 |
| 4-Hydroxyhippurate       | 3.978(s), 6.976(d), 7.765(d)    | —                 |
| Tartrate                 | 4.329(s)                       | 77.38             |
| 1-Methyl nicotinamide    | 4.476(s), 8.181(t), 8.894(d), 8.960(d), 9.272(s) | 50.85, 131.14, —, —, — |
| Allantion                | 5.39(s)                        | —                 |
| Fumarate                 | 6.524(s)                       | 137.5             |
| p-Hydroxybenzoate        | 6.970(m), 7.759(m)              | 117.2, 133.68     |
| Benzoate                 | 7.474(t), 7.546(t), 7.863(d)    | —                 |
| Xanthine                 | 7.909(s)                       | 141.77            |
| Hypoxanthine             | 8.22(s), 8.20(s)               | 145.2, 147.5      |
| Oxypurinol               | 8.209(s)                       | 129.09            |
| Formate                  | 8.467(s)                       | 172.4             |

Note: a indicates the displacement value of $^{1}H/^{13}C$ 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)       |
|-----|--------------------------|--------------------------------|-------------------|
| 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 |
|   | Compound                  | ¹H/¹³C Peaks                             |   |
|---|---------------------------|------------------------------------------|--|
| 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, 39.3, 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: a indicates the displacement value of ¹H/¹³C is based on the HSQC spectra. “—” indicates the corresponding displacement value of ¹³C 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 ¹H-NMR-based metabonomic analysis of urine samples. PCA (A) and PLS-DA (B) score plots derived from the ¹H-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 ¹H-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.