

Supplementary Materials

Supplemental Figure 1: QC of UPLC-MS/MS. (A) Total ions current of one QC sample by MS; (B) Multi-peak detection plot of metabolites in the multiple reaction monitoring mode; (C) Total ions current overlaps of the QC samples by MS detection.

Supplemental Figure 2: (A) Venn diagrams of unique and shared DEMs between six comparison groups, L-norleucine is the only one overlapped DEMs in six comparison. (B) For 4 of the 27 shared DEMs (overlapped in A vs B, B vs C, and C vs D), their abundances trends in the 4 groups are as follows: $C > D > B > A$. (C) For 16 of the 27 shared DEMs (overlapped in A vs B, B vs C, and C vs D), their abundances trends in the 4 groups are as follows: $C > D > A > B$. (D) For 2 of the 27 shared DEMs (overlapped in A vs B, B vs C, and C vs D).

Supplemental Figure 3: Sample clustering generated by WGCNA software. The closer the distance, the higher the similarity.

Supplemental Table 1: Detail of each individual subjects.

Supplemental Table 2: A total of 683 metabolites were detected.

Supplemental Table 3: Statistical table of DEMs.

Supplemental Table 4: Detail of each DEMs in six comparisons groups. The Excell table contains six sheets, each of which is a group of DEMs.

Supplemental Table 5: Classification of the DEMs of the A vs B, B vs C, and C vs D comparison groups. The results showed that a total of 75 amino acids and its metabolomics, 114 lipids, 31 carboxylic acids and its derivatives, 34 organic acid and

its derivatives, etc. were obtained.