Text S1. Metabolomics instrument parameters

The Agilent LC system and AB Sciex 5600 Q-TOF-MS were used for LC-MS/MS analysis. The chromatography was performed on Thermo Hypersil GOLD C18 (100 mm×2.1 mm, 1.9 μm) column. The parameters of the negative ion mode are as follows: the mobile phase is ultra-pure water (containing 0.1% formic acid) in phase A and acetonitrile (containing 0.1% formic acid) in phase B; Gradient elution conditions: 0~1 min, 5% B; 1~11 min, 5~95% B; 11~13 min, 95% B; 13~14 min, 95~5% B; 14~15 min, 5% B; Flow rate: 0.4mL /min; Column temperature: 30℃; Injection volume: 1μL. Mass spectrum conditions: Using an electrospray ionization source (ESI), capillary voltage: 3 kV, capillary temperature: 350°C; Heater temperature: 50℃; Injection voltage: 3.00 kV; Both the solvent removal and the cone gas are nitrogen, the flow rate of the solvent removal gas is 600 L/h, and the scanning range is 80~1000 m/z. The parameters of the positive ion mode are as follows: the mobile phase is ultra-pure water (containing 0.1% formic acid) in phase A and acetonitrile (containing 0.1% formic acid) in phase B; Gradient elution conditions: 0~1 min, 5% B; 1~11 min, 5~95% B; 11~13 min, 95% B; 13~14 min, 95~5% B; 14~15 min, 5% B; Flow rate: 0.4mL /min; Column temperature: 30℃; Sample size: 1 μL. Mass spectrum conditions: Using an electrospray ionization source (ESI), capillary voltage: 3 kV, capillary temperature: 350°C; Heater temperature: 50℃; Injection voltage: 3.00 kV; Both the solvent removal and the cone gas are nitrogen, the flow rate of the solvent removal gas is 600 L/h, and the scanning range is 80~1000 m/z.

Raw LC–MS data were processed using MS-DIAL software for peak detection, deconvolution, peak alignment, and metabolite annotation. Data acquired in positive and negative ion modes were processed separately, and the exported results included metabolite name, molecular formula, mass-to-charge ratio, retention time, and peak

area, among other information. The annotation results from the two ion modes were then integrated. Metabolite annotation was performed using the metabolomics MSP-format MS/MS spectral database provided on the official MS-DIAL website. Specifically, the spectral libraries used were the MS/MS databases established by integrating experimentally measured spectra of authentic standards and biological samples with in silico simulated spectra, under both ESI positive and negative ion modes. For database matching, the mass tolerance was set to 0.02 Da for MS1 precursor ions and 0.025 Da for MS2 fragment ions. Annotation scores were calculated by integrating accurate mass and MS/MS spectral similarity, and only candidate metabolites with a score greater than 0.80 were retained. Metabolites were classified as Level 2 according to the metabolomics reporting standards. For data preprocessing, the peak area of each annotated metabolite was normalized to the peak area of the internal standard compound. Missing values were imputed using half of the minimum non-zero value in the corresponding data matrix. Differential metabolites were screened based on the criteria of $VIP > 1$ and $p < 0.05$.