**Supporting Information for ORIGINAL ARTICLE**

**Materials and Methods**

**2. Materials and methods**

*2.7.2 Data acquisition for* *untargeted metabolomics*

The UHPLC system (Ultimate 3000, Thermo Fisher Scientific, USA) was used to perform chromatographic separation. For the separations of polar metabolites, the solvent A was composed of 0.1% formic acid in water and solvent B was composed of 0.1% formic acid in acetonitrile. The gradient was generated with solvents A and B as follows: 0 min, 3% A and 97% B; 1 min, 3% A and 97% B; 5 min, 8% A and 92% B; 10 min, 20% A and 80% B; 15 min, 40% A and 60% B; 16 min, 50% A and 50% B; 16.1 min, 3% A and 97% B. The flow rate was 0.2 mL/min and the injection volume was 5 µL. The column temperature was maintained at 25 ℃. For the separations of non-polar metabolites, the gradient was generated with solvents A (0.1% formic acid in water) and B (acetonitrile) as follows: 0.00 min, 95% A and 5%B; 2.00 min, 45% A and 55% B; 10.00 min, 5% A and 95%B; 15.00 min, 5% A and 95%B; 15.50 min, 95% A and 5%B. The flow rate was 0.3 mL/min and the injection volume was 3 µL. The column temperature was maintained at 35 ℃.

The LTQ Orbitrap Velos Pro was combined with UHPLC *via* an ESI interface. Mass spectrometry analysis was performed in both positive and negative ion modes. The acquisition software (Xcalibur 3.0, Thermo) continuously evaluated the full scan survey MS data as it collected and triggered the acquisition of MS/MS spectra depending on preselected criteria. Mass spectrum conditions were as follows: ion spray voltage, 3.4 kV; sheath gas flow rate, 35 arb; aux gas flow rate, 10 arb; capillary temperature, 350 °C; auxiliary gas heater temperature: 350 °C. The full mass resolution as 30000 and the MS2 experiments were set as data-dependent scan.