Supporting Information

Materials and Methods

Non-targeted metabolomics analysis of cecal contents

The extract of cecal contents was detected using an ultra-high performance liquid chromatography-electrospray tandem mass spectrometry (UHPLC–MS/MS) system (Thermo Fisher Scientific, USA). The Chromatography was carried out with an ACQUITY UPLC ® HSS T3 (150 mm × 2.1 mm, 1.8 μm) (Waters, Milford, MA, USA). The column was maintained at 40℃. The flow rate and injection volume were set at 0.25 mL/min and 2 μL, respectively. For LC-electrospray ionization (ESI) (+)-MS analysis, the mobile phases consisted of (C) 0.1% formic acid in acetonitrile (v/v) and (D) 0.1% formic acid in water (v/v). Separation was conducted under the following gradient: 0–1 min, 2% C; 1–9 min, 2–50% C; 9–12 min, 50–98% C; 12–13.5 min, 98% C; 13.5–14 min, 98–2% C; 14–20 min, 2% C. For LC-ESI (−)-MS analysis, the analytes were carried out with (A) acetonitrile and (B) ammonium formate (5 mM). Separation was conducted under the following gradient: 0–1 min, 2%A; 1–9 min, 2–50%A; 9–12 min, 50–98%A; 12–13.5 min, 98%A; 13.5–14 min, 98–2%A; 14–17 min, 2%A. MS detection of metabolites was performed on a Q Exactive Focus (Thermo Fisher Scientific, USA) with an ESI ion source. Simultaneous MS1 and MS/MS (full MS-ddMS2 mode, data-dependent MS/MS) acquisition were used. The parameters were as follows: the ESI-MSn experiments were performed with a spray voltage of 3.50 kV and -2.50 kV for ESI (+) and ESI (−), respectively. Sheath gas and auxiliary gas were set at 30 and 10 arbitrary units, respectively. The capillary temperature was 325℃. MS1

range and MS1 resolving power were m/z 81–1,000 and 70,000 full widths at half maximum (FWHM), respectively. The data-dependent scans per cycle were three. MS/MS resolving power and the normalized collision energy was 17,500 FWHM and 30 eV, respectively. Dynamic exclusion was implemented to remove unnecessary information in MS/MS spectra.

Data preprocessing is followed: unprocessed MS files were converted into mzXML format by soft ProteinWizard (v3.0.8789). The metabolic features detection, chromatographic matching and the alignment of all the metabolite peaks in the LC/MS data were handled by XCMS software (Mialon, Roig, Capodanno, & Cadiere, 2023). The metabolites were identified by accuracy mass (< 30 ppm) and MS/MS data which were matched with HMDB (http://www.hmdb.ca), massbank (http://www.massbank.jp/), LipidMaps (http://www.lipidmaps.org), mzclound (https://www.mzcloud.org) and KEGG (http://www.genome.jp/kegg/). The robust LOESS signal correction (QC-RLSC) was applied for data normalization to correct for any systematic bias (Gagnebin et al., 2017). Ion peaks with relative standard deviations (RSDs) less than 30 % in QC were reserved that ensure proper metabolite identification. Finally, all the peak areas were normalized and used for statistical analysis.