**Bile-acid targeted metabolomics**

Each sample was homogenized in LC-MS grade water at a ratio of 150 μL per 10 mg raw material and with the aid of 5-mm stainless steel metal balls. Bile acids were extracted by addition of acetonitrile at a ratio of 350 μL per 10 mg raw material followed by vortexing and sonication (1 min) in an ice-water ultrasonic bath. The samples were centrifuged. 20 μL of the supernatants were precisely taken out and mixed with a predefined mix of 14 deuterium-labeled bile acids as the internal standards. The mixtures were subjected to phospholipid-depletion solid-phase extraction according to a validated protocol for sample cleanup and bile acid enrichment. The flow-through fractions were collected and then dried under a gentle nitrogen flow. The dried residues were dissolved in 200 μL of 50% methonal. 10 μL were injected for quantitation by UPLC-MRM/MS. A Dionex UPLC system was connected to an AB Sciex 4000 QTRAP mass spectrometer which was operated in the negative ion multiple-reaction monitoring (MRM) mode and with electrospray ionization. UPLC separation was carried out on a 15 cm long C-18 UPLC column with water-acetonitrile-formic acid as the mobile phase for binary gradient elution using a developed and validated protocol for comprehensive analysis of bile acids in biological samples (Han, etc. manuscript submitted to Analytical Chemistry). The column temperature was 45 oC and the flow rate was 0.35 mL/min. 45 bile acids (including the 19 targeted bile acids) were involved in the quantitation by UPLC/scheduled MRM/MS. Concentrations of the detected bile acids were calculated with internal standard calibration from the linearly regressed standard calibration curves of individual bile acids. The lower limits of quantitation were 0.08 nmoles/mg for all the bile acids.