**Analysis protocol:**

*MS Analysis:* Compounds were separated using an Ultimate3000 (ThermoFisher Scientific), fitted with a Waters Acquity UPLC BEH HILIC column (2.1 x 75 mm, 1.7 µm particle size). The compounds were eluted with the following gradient: 95:5 10 mM ammonium acetate with ~0.014% ammonium hydroxide: acetonitrile (mobile phase A) and acetonitrile with ~0.014% ammonium hydroxide (mobile phase B) using the following gradient program: 0 min 5% A; 3 min 63% A; 7 min 63% A; 7.1 min 5% A; 9.9 min 5%. The flow rate was set at 0.30 mL min-1 for 0-7.1 min; increased to 0.5 mL min-1 from 7.1-7,2 min; 7.2-9.5 min at 0.5 mL min-1; and decreased to 0.30 mL min-1 from 9.5 – 10.0 min. The column temperature was set to 50 °C, and the injection volume was 2 µL. The compounds were analyzed with a high-resolution accurate mass Q Exactive HF mass spectrometry system (ThermoFisher Scientific). The heated electrospray ionization (HESI) source was operated at a capillary temperature of 275 ⁰C, a spray voltage of 3.5 kV, and sheath, auxiliary, and sweep gas flows of 48, 11, and 2, respectively. The instrument acquired MS data in the 70-1050 m/z range in positive and negative ionization modes. MS/MS experiments were performed by acquiring mass spectra in a data-dependent acquisition fashion. Survey MS were collected with a resolution of 120,000 and the top 10 dd-MS2 were collected at a resolution of 30,000 and an isolation window of 0.4 m/z. Stepped normalized collision energies of 10, 30, and 50 fragmented selected precursors in the HCD cell prior to combination of ion for analysis in the orbitrap. Dynamic exclusion was set at 10 s and ions with charges greater than 2 were omitted.

Data acquisition and processing were carried out using Xcaliber V4.0 (ThermoFisher Scientific) and Compound Discoverer V3.0 (ThermoFisher Scientific), respectively. The pooled QC injection were used to adjusted for instrument drift using a loess algorithm. Background peaks were removed from the dataset using sample blank injections. The features were filtered to be greater than 50% present in the QC injections and relative standard deviation of less than 30%.

For metabolite identification, UPLC-MS/MS experiments were done for the panel of best discriminant features. Compounds were separated with a Waters Acquity UPLC BEH Amide column (2.1 x 150mm, 1.7 µm particle size) using the following gradient: 80:20 10mM ammonium formate with 0.1% formic acid: acetonitrile (mobile phase A) and acetonitrile with 0.1% formic acid (mobile phase B), and the gradient program: 0 min 5% A; 0.5 min 5% A; 8 min 60% A; 9.4 min 60% A; 11 min 5% A. The flow rate was set to 0.40 mL min-1, the column temperature was set to 40 °C, and the injection volume was 2 µL. Compounds were analyzed on an Orbitrap ID-X Tribrid mass spectrometer (ThermoFisher Scientific) using data dependent acquisition methods. An inclusion list of precursors was created and MS/MS spectra of ions above the intensity threshold of 6.0E3 were collected with an isolation window of 0.8 m/z. Survey MS were collected with a resolution of 60,000. Stepped normalized collision energy of 15, 30, and 45 fragmented the precursors in the HCD cell and ions were analyzed in the orbitrap at a resolution of 30,000. Sequentially, precursors were fragmented with CID collision energy of 45 and were analyzed in the ion trap.

Data were processed using Compound Discoverer v3.0 (ThermoFisher Scientific) and elemental formulas of the features were generated based on exact masses and isotope patterns. Some features with no predicted elemental formulas in Compound Discoverer were analyzed using Xcaliber v3.0 to assign elemental formulas. Tentative identities were searched against literature, and MS databases such as human metabolome database (HMDB), Metlin, mzCloud, and MassBank using elemental formulas and exact masses with a mass error of 10mDa. Fragmentation patterns were analyzed and matched using tandem MS databases to confirm the metabolite identity of the features for which MS/MS spectra were successfully acquired.

*NMR Analysis:* NMR spectra were acquired using an Avance III HD 600 MHz Bruker NMR spectrometer with a Bruker SampleJet cooled to 5.6 0C.

*NMR Data Acquisition:* The following experiments were carried out: One-dimensional nuclear Overhauser effect pulse sequence with pre-saturation of water resonance (NOESYPR1D), two-dimensional (2D) 1H-13C heteronuclear single quantum correlation (HSQC) and HSQC–TOCSY (HSQC–total correlation spectroscopy).

*NMR Data Processing:* For 1D 1H NMR metabolomics spectra, phase and baseline correction and referencing were carried out with the Bruker’s TopSpin software. Using the Edison laboratory in-house MATLAB scripts (<https://github.com/artedison/Edison_Lab_Shared_Metabolomics_UGA>), referencing of DSS compound was confirmed. In addition, the ends of NMR spectra (less than 0.50ppm, greater than 10.0ppm) and water regions (between 4.89ppm and 4.68ppm) were removed from all sample. Urine NMR spectra were aligned using constrained correlation optimized warping (CCOW), and normalized using probabilistic quotient normalization (PQN). 2D NMR Data (HSQC, and HSQC-TOCSY) pre-processing was carried out using NMR Pipe. Metabolites were identified using Bruker AssureNMR software (Bruker Biospin, USA) with BBiorefcode metabolite database and COLMARm. Metabolites were assigned a confidence score from 1 to 5, with 5 as the highest confidence score. The scores are defined as the following: (1) putatively characterized compound classes or annotated compounds, (2) matches from 1D NMR to literature and/or 1D BBiorefcode compound (AssureNMR) or other database libraries such as BMRB and HMDB, (3) matched to HSQC, (4) matched to HSQC and validated by HSQC–TOCSY (COLMARm), and (5) validated by spiking the authentic compound into sample.

*NMR Extraction of Peak Intensity:* The metabolites and their confidence scores are reported in our paper (Table S4). Metabolic features in the aligned and normalized 1D 1H NMR spectra were quantified by taking spectral areas for integration.