**Cell line sample collection and extraction method**

Extractions were performed on 1 × 107 cells/sample after being scraped off the dish in 4 mL of 50:50 acetonitrile:water and collected into 15 mL tubes. Added 1 mL of an ice-cold chloroform to the tubes and 10 ceramic beads. Tubes were vortexed for 30 seconds on a multi-tube vortexer at 5000 rpm three times to homogenize and centrifuged samples at 4 °C in a swinging bucket centrifuge for 60 min at 3,700 rpm. Majority of aqueous (top) layer was carefully transferred to 5 mL cryotubes. Majority of lipid (bottom) layer was carefully transferred to 7 mL glass vials. Remaining protein layer and residual aqueous & lipid layers were transferred into a 2 mL Lo-Bind tubes. Original tubes were rinsed with 600 µL of 2:1 chloroform:methanol solution and transferred to the 2 mL tubes. Centrifuged tubes at 15,000 rpm at 4 °C for 20 min and transferred remaining aqueous & lipid fractions into respective tubes. Protein pellets were dried for 20 min on Speedvac (no heat) and tubes reweighed for later normalization.

For each study sample, an 800 µL aliquot of the aqueous fractions was transferred to labeled 2.0 mL Lo-Bind tubes. Analytical pooled QC samples were generated by transferring an additional 75 µL aliquot from all study samples into a 10 mL tube. The total pooled sample was vortexed and 800 µL aliquots were transferred to 2.0 mL tubes labeled Pool. All tubes were frozen for 1 hr and lyophilized to dryness overnight. Samples were reconstituted by adding 700 µL of 90:10 D2O:Chenomx ISTD master mix to each, vortexed for 2 mins and centrifuged at 16,000 rcffor 4 min. A 600 µL aliquot of the supernatant was transferred into 5 mm NMR tubes (Bruker-Biospin, Switzerland), and kept on ice until data acquisition.

**Broad spectrum metabolomics**

1H NMR spectra of cellular extracts were acquired on a Bruker Avance III 600 MHz spectrometer (located at the David H. Murdock Research Institute at Kannapolis, NC, USA) using a 5 mm cryogenically cooled ATMA inverse probe and ambient temperature of 25 °C. A noesypr-1d pulse sequence was used for data acquisition. For each sample 256 transients were collected into 32 k data points using a spectral width of 11.00 ppm, 2s relaxation delay, 100 ms mixing time and an acquisition time of 2.482 s per FID. The water resonance was suppressed using resonance irradiation during the relaxation delay. Spectra were zero filled, and Fourier transformed after exponential multiplication with line broadening factor of 0.5. Phase and baseline of the spectra were manually corrected for each spectrum. Spectra were referenced internally to the DSS signal. The quality of each NMR spectrum was assessed for the level of noise and alignment of identified markers. Spectra were assessed for missing data and underwent quality checks.

NMR spectra were pre-processed using ACD 1D NMR Processor 12.0 (ACD Labs, Toronto, CA) for metabolomics analysis. NMR bins (0.14 – 9.35 ppm) were made after excluding water (4.66-4.86 ppm) and imidazole (7.15-7.26 ppm) using intelligent binning width of 0.04 ppm and 50% looseness factor. Integrals of each of the bins were normalized to total integral of each of the spectrum.