

Analytical Platform 10 (non-targeted CE-ESI-MS) was conducted by the Shulaev group at the Virginia Bioinformatics Institute. Frozen tissue in 1.5 mL microcentrifuge tubes, with two 2.3 mm stainless steel balls added, was ground 2 times with a Retsch mixer mill for 30 s each at 30 cycles/s. Aliquots of 300  $\mu$ L each of ice-cooled LC-MS grade methanol and ice-cooled water (with 50  $\mu$ M methionine sulfone and 3-Fluoro-DL-phenylalanine as cationic internal standards and 50  $\mu$ M of thiourea, DMSO, and mesityl oxide as neutral electroosmotic flow markers) were added to each sample. Samples were ground again and centrifuged 10 min at 14,000 rpm. Supernatant was decanted and spun with 10 kDa MW cut-off filters as before to remove protein and debris and to degass the sample. Aliquots of 20  $\mu$ L were transferred daily for analysis by CE-ESI-MS. Samples were stored at  $-80^{\circ}\text{C}$ .

All CE-ESI-MS experiments were performed using a Beckman Coulter P/ACE MDQ capillary electrophoresis system with a Thermo Finnigan LCQ DECA XP plus mass spectrometer. All system control, data acquisition, and data evaluation were performed with Xcalibur v1.3 software. The CE-MS adapter kit was used to couple the CE system with the MS system equipped with an electrospray ionization (ESI) source.

Separations were carried out on bare fused-silica capillaries with 75  $\mu$ m i.d. X 360  $\mu$ m o.d. X 80 cm total length. All solvents were degassed prior to use. The electrolyte for the CE separation (running buffer) was 1M solution of formic acid. Prior to first use, a new capillary was flushed with  $\text{H}_2\text{O}$  (5 min), 0.1 N NaOH (5 min), and running buffer (10 min). Before each injection, the capillary was preconditioned for 4 min by flushing with running buffer. Samples were pressure injected for 10s at 4psi. The applied voltage for separation was set at 25 kV, and the capillary temperature was maintained at  $20^{\circ}\text{C}$ . The syringe pump built in the DECA was used to deliver sheath liquid (5  $\mu$ L/min 0.5% acetonitrile in 50% (V/V) methanol-water) to the interface between CE and MS to provide a stable electrical connection between the tip of the capillary and ground. ESI-MS was conducted in the positive ion mode with full scan from 50 to 206 m/z, and the capillary voltage was set at 4 kV. A flow rate of heated dry nitrogen gas (heater temperature  $180^{\circ}\text{C}$ ) was maintained at 10  $\mu$ L/min.