## SUPPLEMENTARY MATERIALS

### Cardiolipin measurement

Lipids were extracted from 6 mg of tissue with methanol and methyl tert-butyl ether. Water was subsequently added for phase separation. After concentrating extracts to complete dryness, samples were reconstituted prior to LC-MS analysis in 110 µL of methanol:toluene (90:10, v/v) with 50 ng/mL CUDA standard.

All measurements were carried out on an Agilent 6530a Q-TOF instrument [1]. For positive mode, 10 µL of diluted samples were injected. For negative mode, 1uL of diluted samples were injected. Samples were separated on a Waters Acquity UPLC CSH C18 column (100 × 2.1 mm; 1.7 µm) coupled to an Acquity UPLC CSH C18 VanGuard precolumn (5 × 2.1 mm; 1.7 µm). The column was maintained at 65° C with a flow rate of 0.6 mL/min. The positive ionization mobile phases consisted of (A) acetonitrile:water (60:40, v/v) with ammonium formate (10 mM) and formic acid (0.1%) and (B) 2-propanol:acetonitrile (90:10, v/v) with ammonium formate (10 mM) and formic acid (0.1%). The negative ionization mobile phases consisted of (A) acetonitrile:water (60:40, v/v) with ammonium formate (10 mM) and (B) 2-propnol:acetonitrile (90:10, v/v) with ammonium formate (10 mM). The separation was conducted under the following gradient: 0 min 15% B; 0−2 min 30% B; 2−2.5 min 48% B; 2.5−11 min 82% B; 11−11.5 min 99% B; 11.5−12 min 99% B; 12−12.1 min 15% B; 12.1−15 min 15% B.

The Agilent 6530a QTOF instrument was operated using positive mode electrospray ionization using the following parameters. Acquisition parameters: Mass range, 120-1700 m/z; Acquisition rate, 2 spectra/second; Acquisition time, 500 ms/spectrum; Mode, MS(Seg). Source Parameters: Gas Temp, 325° C; Drying Gas, 8L/min; Nebulizer, 35psig; Sheath Gas Temp, 350° C; Sheath gas flow, 11L/min; VCap, 3500V; Spectrum data type, Centroid. MS TOF parameters: Fragmentor, 120V; Skimmer, 65V; OCT 1 RP Vpp, 750V, Collision Energy, 0V. MSMS were acquired in a separate injection using the following acquisition parameters: MS1 Mass range, 65-1700m/z; MS/MS mass range, 35-1700; MS1 acquisition rate, 4 spectra/second; MS1 acquisition time, 250 ms/spectrum; MS/MS acquisition rate, 8 sepctra/s; MS/MS acquisition time, 125 ms/spectrum. Collision energy depended on m/z and was calculated using the following formula: 3×((m/z)/100)+2.5. Source parameters for MS/MS injections were the same as MS injections.

The Agilent 6530a QTOF instrument was operated using negative mode electrospray ionization using the following parameters. Acquisition parameters: Mass range, 60-1700 m/z; Acquisition rate, 2 spectra/second; Acquisition time, 500 ms/spectrum; Mode, MS(Seg). Source Parameters: Gas Temp, 325° C; Drying Gas, 8L/min; Nebulizer, 35psig; Sheath Gas Temp, 350° C; Sheath gas flow, 11L/min; VCap, 3500V; Spectrum data type, Centroid. MS TOF parameters: Fragmentor, 120V; Skimmer, 65V; OCT 1 RP Vpp, 750V, Collision Energy, 0V. MSMS were acquired in a separate injection using the following acquisition parameters: MS1 Mass range, 65-1700m/z; MS/MS mass range, 35-1700; MS1 acquisition rate, 4 spectra/second; MS1 acquisition time, 250 ms/spectrum; MS/MS acquisition rate, 8 sepctra/s; MS/MS acquisition time, 125 ms/spectrum. Collision energy depended on m/z and was calculated using the following formula: 3×((m/z)/100)+2.5. Source parameters for MS/MS injections were the same as MS injections.

A calibration curve was run for cardiolipin quantification using CL 72:8. The curve was run at the following concentrations: 0.001µg/mL, 0.01µg/mL, 0.1µg/mL, 1µg/mL, 10µg/mL, 20µg/mL, 50µg/mL, 100µg/mL. The LC-MS/MS data was analyzed by MS-DIAL software.

## REFERENCE


1. Tsugawa H, Ikeda K, Takahashi M, Satoh A, Mori Y, Uchino H, Okahashi N, Yamada Y, Tada I, Bonini P, Higashi Y, Okazaki Y, Zhou Z, et al. A lipidome atlas in MS-DIAL 4. Nat Biotechnol. 2020; 38:1159–63. https://doi.org/10.1038/s41587-020-0531-2 PMID: 32541957