Sample processing and metabolite extraction: Samples were extracted in ice cold methanol, prior to dilution 1:1 (v/v) with 10 mM ammonium acetate for analysis by ultra-high pressure liquid chromatography coupled to mass spectrometry (UHPLC-MS).

Ultra-High-Pressure Liquid Chromatography-Mass Spectrometry (MS): The analytical platform employed a Vanquish UHPLC system (Thermo Fisher Scientific, San Jose, CA, USA) coupled online to a Q Exactive mass spectrometer (Thermo Fisher Scientific, San Jose, CA, USA). Lipidomics analyses were performed as described in previous method papers and application notes. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7640979/ https://www.haematologica.org/article/view/9990, https://www.haematologica.org/article/view/9990 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7640979/, https://pubmed.ncbi.nlm.nih.gov/31119660/

Lipidomics: Samples were resolved over an ACQUITY HSS T3 column (2.1 x 150 mm, 1.8 µm particle size (Waters, MA, USA) using an aqueous phase (A) of 25% acetonitrile and 5 mM ammonium acetate and a mobile phase (B) of 50% isopropanol, 45% acetonitrile and 5 mM ammonium acetate. Samples were eluted from the column using either the solvent gradient: 0-1 min 25% B and 0.3 mL/min; 1-2 min 25-50% B and 0.3 mL/min, 2-8 min 50-90% B and 0.3 mL/min, 8-10 min 90-99% B and 0.3 mL/min, 10-14 min hold at 99% B and 0.3 mL/min, 14-14.1 min 99-25% B 1and 0.3 mL/min, 14.1-16.9 min hold at 25% B and 0.4 mL/min, 16.9-17 min hold at 25% B and resume flow of 0.3 mL/min. isocratic elution of 5% B flowed at 250 µl/min and 25ºC or a gradient from 0-5% B over 0.5 min; 5-95% B over 0.6 min, hold at 95% B for 1.65 min; 95-5% B over 0.25 min; hold at 5% B for 2 min, flowed at 450 µl/min and 35ºC4. The Q Exactive mass spectrometer (Thermo Fisher Scientific, San Jose, CA, USA) was operated independently in positive or negative ion mode, scanning in Full MS mode (2 µscans) from 150 to 1500 m/z at 70,000 resolution, with 4 kV spray voltage, 45 shealth gas, 15 auxiliary gas. dd-MS2 was performed at 17,500 resolution, AGC target = 1e5, maximum IT = 50 ms, and stepped NCE of 25, 35 for positive mode, and 20, 24, and 28 for negative mode.

Quality control and data processing: Calibration was performed prior to analysis using the PierceTM Positive and Negative Ion Calibration Solutions (Thermo Fisher Scientific). Acquired data was then converted from .raw to .mzXML file format using Mass Matrix (Cleveland, OH, USA). Samples were analyzed in randomized order with a technical mixture injected incrementally to qualify instrument performance. This technical mixture was also injected three times per polarity mode and analyzed with the parameters above, except CID fragmentation was included for unknown compound identification.

Lipid assignment and relative quantitation: Lipid assignments were performed using Lipid Search (Thermo Fisher); spectral libraries generated in LipidSearch for this dataset were then imported into Compound Discoverer (Thermo Fisher Scientific, San Jose, CA). Spectral libraries were generated from high-resolution accurate intact mass, isotopic pattern, and MS2 fragmentation spectra against the LipidMaps databases. Graphs and statistical analyses (either t-test or repeated measures ANOVA) were prepared with GraphPad Prism 5.0 (GraphPad Software, Inc, La Jolla, CA), and MetaboAnalyst 5.0.