Supplementary Material

Table 1 : Primers Quantitect (Qiagen) references

Target Gene	Official Symbol	QIAGEN GeneGlobe ID
NADPH oxidase 2 (Cybb)	*gp91phox*	QT00139797
cytochrome b-245 (Cyba)	*p22phox*	QT00154518
Neutrophil cytosolic factor 4 (Ncf4)	*p40phox*	QT00108619
Neutrophil cytosolic factor 1 (Ncf1)	*p47phox*	QT00097293
Neutrophil cytosolic factor 2 (Ncf2)	*p67phox*	QT00149947
Rac family small GTPase 1	*Rac1*	QT01070146
catalase	*Cat*	QT01058106
superoxide dismutase 1	*Sod1*	QT00165039
superoxide dismutase 2	*Sod2*	QT00161707
Nuclear factor of kappa light polypeptide gene enhancer in B cells 1	*Nfkb1*	QT00154091
nuclear factor of kappa light polypeptide gene enhancer in B cells 2	*Nfkb2*	QT00129864
interleukin 6	*Il6*	QT00098875
C-C motif chemokine ligand 2	*Ccl2*	QT00167832
C-C motif chemokine ligand 5	*Ccl5*	QT01747165
C-C motif chemokine ligand 3	*Ccl3*	QT00248199
C-X-C motif chemokine receptor 5	*Cxcr5*	QT00253449
interleukin 11	*Il11*	QT00122122
platelet/endothelial cell adhesion molecule 1	*Pecam1*	QT01052044
vascular cell adhesion molecule 1	*Vcam1*	QT00128793
intercellular adhesion molecule 1	*Icam1*	QT00155078
nitric oxide synthase 3, endothelial cel	*Nos3 (eNOS)*	QT00152754
claudin 1	*Cldn1*	QT00159278
claudin 5	*Cldn5*	QT00254905
tight junction protein 1	*Tjp1 (ZO-1)*	QT00493899
Occludin	*Ocln*	QT00111055
Angiopoietin 2	*Angpt2*	QT00173026
Angiopoietin 1	*Angpt1*	QT00166859
Fms-like tyrosine kinase 1	*Flt1 (VEGFR1)*	QT00096292
kinase insert domain receptor	*Kdr (VEGFR2)*	QT00097020
Vascular Endothelial Growth Factor	*Vegfa*	QT00160769
Notch3	*Notch3*	QT01051729
hypoxanthine phosphoribosyltransferase	*Hprt1*	QT00166768
glyceraldehyde-3-phosphate dehydrogenase	*Gapdh*	QT01658692

Protocol for untargeted plasma metabolomics analysis

Metabolomic experimentation was carried out by the CRIBIOM platform - CRIblage BIOlogique Marseille at the Centre Cardiovasculaire et Nutrition (C2VN) (Marseille, France).

- **Sample preparation and spectrometry analysis**

Samples of 100 µL of plasma from mice belonging to our different exposure groups (N=12 per group) were sent to the platform. To minimize analytical variability, the samples were processed in a random order and analyzed in continuous batches. Quality control (QC) samples were prepared by mixing an equal volume of each plasma sample across all conditions. Polar and non-polar metabolites were extracted from 100 µL of plasma by protein precipitation with 400 µL of cold methanol (MetOH) at -20°C. Filtered extract was dried under the gentle nitrogen flux ant the dry extracts were dissolved into 125 µL of 10% acetonitrile / 0.1% formic acid solution. After reconstitution, 50 µL of each extracted sample were used for chromatographic analysis. The chromatographic analyses were performed using an ultra-performance liquid chromatography (UPLC) Vanquish Horizon Flex system (Thermo Fisher Scientific), coupled with a high-resolution Orbitrap Exploris 240 mass spectrometer (Thermo Fisher Scientific). For the reverse phase analysis, a Hypersil Gold column (100 × 2.1 mm, 1.9 µm; Thermo Scientific) maintained at 40 °C was used with a flow rate of 0.4 mL/min and an injection volume of 5 µL. The mobile phase consisted of solvent A (water containing 0.1% formic acid) and solvent B (acetonitrile containing 0.1% formic acid). The chromatographic gradient was programmed as follows: 0-1 min, 100% A; 1-11 min, linear gradient to 100% B; 11-13 min, 100% B; 13-14 min, return to 100% A; 14-16 min, re-equilibration to 100% A.

For the analysis of polar compounds, a SeQuant® ZIC®-HILIC PEEK Coated column (150 × 2.1 mm; 5 µm; Merck) maintained at 25 °C was used with a flow rate of 0.25 mL/min and an injection volume of 5 µL. The mobile phase consisted of solvent A (water containing 16

mM ammonium formate) and solvent B (acetonitrile containing 0.1% formic acid). The applied gradient was as follows: 0-2 min, 97% B; 2-10 min, linear decrease to 70% B; 10-15 min, decrease to 10% B; 15-17 min, hold at 10% B; 17-18 min, return to 97% B; 18-27 min, re-equilibration at 97% B. Mass spectrometry analysis was performed in positive and negative ionization modes during a single acquisition ('switching polarity'). Full scan spectra were acquired over a mass range of m/z 60 to 800, with a resolution of 45,000 (FWHM at m/z 200).

For the HILIC analyses, the source parameters were as follows: spray voltage of 3.5 kV, capillary temperature of 320 °C, auxiliary temperature of 310 °C, nebulizer gas flow (sheath gas) of 30 arbitrary units, auxiliary gas flow of 8 arbitrary units, and S-Lens RF level of 60 V. For the C18 analyses, the spray voltage was 4.0 kV, the auxiliary temperature was 320 °C, and the S-Lens RF level was 80 V. In both chromatographic methods, the injection time was set to 200 ms, and a microscan was acquired per spectrum.

- **Data processing**

Samples were analyzed in two independent analytical series for each chromatography mode. After acquisition by LC–MS, the raw data files (MS1 and MS/MS in both ionization modes) were processed using MS-DIAL software (version 5.4; RIKEN Center, Japan).

The preprocessing included peak detection, spectral deconvolution, inter-sample alignment, missing value filling, and removal of signals present in extraction blanks. Features were annotated by comparing them to an in-house spectral database containing approximately 1,300 metabolites, including about 800 entries with validated MS/MS fragmentation spectra. Annotations were validated based on the concordance of m/z values, retention time, and experimentally acquired MS/MS spectra. Following this process, 254 metabolites were reliably annotated or identified and incorporated into a final matrix, which contains their relative intensities across all plasma samples.