SUPPLEMENTARY METHODS

Study exclusion criteria:

The following exclusion criteria were established: Smokers (including nicotine, marijuana and other narcotics), currently ill or were ill in last one week, history of any chronic medical condition (including skin and food allergies or diagnosed mental health disorder), taking regularly prescribed or over-the-counter medication, taken any oral corticosteroids or other immunosuppressive agents within the last 3 months, recent vaccination (within 3 months) or take recreational drugs, enrolled in another research study, abnormal blood tests during screening (**full blood count:** haemoglobin, platelet count, total white count and differential, **urea and electrolytes:** urea, creatinine, potassium, sodium, chloride, calcium, **liver function tests:** total protein, albumin, bilirubin, alkaline phosphatase, alanine aminotransferase), abnormal findings on physical examination during screening, screening blood pressure >160/100 mmHg or <90/60 mmHg, screening heart rate >100 beats per minute (bpm) or <45 bpm, body mass index (BMI) >30 kg/m^2.

Flow cytometry

Blister cells were suspended in 100µl of cell staining buffer (PBS with 5% FCS, 0.1% sodium azide) and were incubated for 30 min on ice with following antibodies: CD3: FITC, CD19: FITC, CD20: FITC, CD56: FITC, CD14: Brilliant violet (BV) 605, CD16: APC, CD163: BV421, HLA-DR: BV510. All antibodies were sourced from Biolegend. Stained cell sample was washed with PBS and then fixed in 0.5% paraformaldehyde. Fixed sample was acquired on LSR II Fortessa (Becton Dickinson) flow cytometer within 4h. Flow cytometry data was analysed by Flowjo software (Treestar Inc.). Flow cytometric gating strategy employed to identify neutrophils and monocytes/macrophages was as described in [13].

Multiplex ELISA

Human pro-inflammatory panel-1 mutiplex ELISA kit (Meso Scale Delivery, USA) was used to measure cytokines. The assay was performed as per manufacturer's instructions.

Lipidomics

Liquid chromatography–tandem mass spectrometry-based metabololipidomics were performed with samples obtained from human blister supernatants**.** Blister fluid supernatants were anonymized and prior to sample extraction, ice-cold methanol containing deuterium-labelled d4-LTB_4, d4-5S-HETE, d4-PGE_2, and d5-RvD2 internal standards (500 pg each) were added for calculating recoveries. All samples were kept at −20°C for 45 min for protein precipitation and then subjected to solid-phase extraction as recently described in [41]. Extracted samples were analysed by a liquid chromatography–tandem mass spectrometry system (QTRAP 5500; AB Sciex) equipped with an LC-20AD HPLC (Shimadzu, Tokyo, Japan). A Poroshell 120 EC-18 column (100 mm × 4.6 mm × 2.7 μm; Agilent Technologies, Santa Clara, CA) was kept in a column oven maintained at 50°C, and LM were eluted with a gradient of methanol/water/acetic acid from 55:45:0.01 (v/v/v) to 100:0:0.01 at 0.5 ml/min flow rate. To quantify the levels of targeted LM, a multiple reaction monitoring (MRM) method was devised with signature ion fragments for each molecule. Identification was conducted using published criteria including retention times and at least six diagnostic ions. Calibration curves were obtained using authentic LM and SPM mixtures, including d4-LTB_4, d5-LXA_4, d4-PGE_2, d5-RvD2, RvD1, RvD2, RvD3, RvD4, RvD5, PD1, MaR1, RvE1, RvE2, LXA_4, LXB_4, PGE_2, PGD_2, PGF2α, thromboxane TxB_2, and LTB4 at 1.56, 3.12, 6.25, 12.5, 25, 50, and 100 pg. Linear calibration curves for each compound were obtained daily with r^2 values of 0.98–0.99. Quantification was carried out based on peak areas from multiple reaction monitoring (MRM) transitions.

Peripheral blood count

Circulating neutrophil and monocyte count, and systemic CRP concentration were used as surrogates of systemic immune response and were measured by an external pathology lab (The Doctor's Laboratory, UK).

Nitric oxide measurements

Blister exudate was analysed for nitrite (NO_2^-) and nitrate (NO_3^-), as an index of endogenous NO production, using chemiluminescence as described previously [36]. Oxidation of nitric oxide in aqueous solution to nitrite but not nitrate: comparison with enzymatically formed nitric oxide from L-arginine. Briefly, samples and standards containing NO_2^- and NO_3^- were first reduced to NO, which was then quantified after reaction with ozone using a nitric oxide analyzer (NOA 280; Analytix, Boldon, UK). To determine total NO_2^- and NO_3^- concentrations, collectively termed 'NOx', samples were added to 0.1M vanadium (III) chloride in 1M hydrochloric acid refluxing at 90^{o}C under nitrogen.