

Supplementary Material and Methods

PMN staining for flow-cytometry analysis

After PMN isolation, cells were stained using anti-human CD66b-BV421 and FVS510 (BD Biosciences, Le Pont de Claix, France). After wash, cells were fixed and used for flow cytometry acquisition with a BD LSRFortessa™ system (BD Biosciences, San Jose, CA). CD66b-BV421 and FVS510 were excited with the 405 nm laser and detected with emission filters 450/50 nm and 525/50 nm, respectively. At the first stage, single cells were selected by a FSC-H/FSC-A gate. On this population, cells were selected by a FSC-A/SSC-A gate excluding subcellular debris and FVS510+ gate excluding dead cells. Ten thousand cells were collected per sample. Data analysis was performed with FlowJo software (Tree Star, Stanford University, USA).

Lactate dehydrogenase quantification

Cytotoxicity was determined by measuring lactate dehydrogenase activity in cell culture supernatant according to the manufacturer's protocol (Roche, Sigma Aldrich, Saint-Quentin Fallavier, France). The absorbance was read at 492 nm corrected at 570 nm on a BMG Labtech Fluostar Optima®.

Supplementary Figure Legends

Figure S1. Chemical structure of compounds 4aa and 4ba.

Figure S2. Lactate dehydrogenase activity in PMN supernatants after 4h of treatment. DMSO (black circle), LPS + DMSO (black square), LPS + Zardaverine at 10 μ M (black triangle), LPS + compound 4aa at 20 μ M (inverted black triangle), LPS + compound 4ba at 20 μ M (black diamond). n=7.

Figure S3. Representative histogram and quantification of initial shifts in CD66b (A), CD63 (B) and CD16 (C) expression for PMNs before (black stars) and after (grey stars) transmigration. n=10.

Figure S4. Representative dot plot of purified blood cells after Polymorphprep™ (left panel) and histogram of CD66b+ cells (right panel).

Figure S5. Pyridazinone scaffold-based compounds concentration dependent-effect on IL-8 secretion quantified by ELISA after 4h of treatment: Zardaverine (A), 4aa (B) and 4ba (C). DMSO (black circle), LPS + DMSO (black square), LPS + Zardaverine at 10 μ M (black triangle), LPS + compound 4aa at 20 μ M (inverted black triangle), LPS + compound 4ba at 20 μ M (black diamond). n=9, * $p < 0.05$ vs DMSO, # $p < 0.05$ vs LPS.