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Reporting Summary

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When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure logand, table logand, main

Statistical parameters

		Methods section).
n/a	Cor	nfirmed
	\boxtimes	The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
	\boxtimes	An indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
		The statistical test(s) used AND whether they are one- or two-sided Only common tests should be described solely by name; describe more complex techniques in the Methods section.
X		A description of all covariates tested
\times		A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
	\boxtimes	A full description of the statistics including <u>central tendency</u> (e.g. means) or other basic estimates (e.g. regression coefficient) AND <u>variation</u> (e.g. standard deviation) or associated <u>estimates of uncertainty</u> (e.g. confidence intervals)
	\boxtimes	For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
\times		For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
\times		For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
\boxtimes		Estimates of effect sizes (e.g. Cohen's d, Pearson's r), indicating how they were calculated
	\boxtimes	Clearly defined error bars State explicitly what error bars represent (e.g. SD, SE, CI)
	1	

Our web collection on <u>statistics for biologists</u> may be useful.

Software and code

Policy information about availability of computer code

Data collection No software was used.

Data analysis GraphPad Prism 7

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about <u>availability of data</u>

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

The authors declare that the main data supporting the findings of this study are available within the article and its Supplementary Figures. Additional data are available from the corresponding authors upon request.

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Please select the b	est fit for your research. If you are not sure, read the appropriate sections before making your selection.
Life sciences	Behavioural & social sciences Ecological, evolutionary & environmental sciences
For a reference copy of	the document with all sections, see <u>nature.com/authors/policies/ReportingSummary-flat.pdf</u>
Life scier	nces study design
All studies must dis	sclose on these points even when the disclosure is negative.
Sample size	No sample size calculation was performed. In vitro experiments were repeated a minimum of three independent times with three different batches of primary cells. Based on our many years of experience with the experimental models used in our study, we estimated the use of the following numbers of animals: -For CLP: a minimum of 5 animals/time point for inflammation and morbidity assessment, and 15 animals for the 7d morbidity/mortality assessment time point. -For LPS-induced endotoxemia: 5 mice/group were utilized to analyze the inflammatory process after injection of a sub-lethal dose of LPS.
Data exclusions	Data were excluded only if a value was determined as an outlier by using the Grubbs' test.
Replication	Attempts at replication were successful once the conditions of the experiment were carefully optimized with pilot experiments.
Randomization	Samples or mice were allocated into experimental groups according to treatment (type of stimulation or in vivo model, respectively) and genotype for specific mouse work.
Blinding	Investigators were blinded to group allocation during sample processing and data collection, including histology assessments.

Reporting for specific materials, systems and methods

Mat	terials & experimental systems	Methods					
n/a	Involved in the study	n/a	Involved in the study				
\boxtimes	Unique biological materials	\boxtimes	ChIP-seq				
	Antibodies		Flow cytometry				
	Eukaryotic cell lines	\boxtimes	MRI-based neuroimaging				
\boxtimes	Palaeontology						
	Animals and other organisms						
\boxtimes	Human research participants						

Antibodies

Antibodies used

The list of the antibodies used is as follows: Histology: HRP-conjugated goat anti–rat IgG (catalog number sc-2065, Santa Cruz Biotechnology, Dallas, TX), rat IgG2a anti-mouse Mcpt8 antibody (clone TUG8, catalog number 647401, BioLegend), rat isotype control antibody of irrelevant antigen specificity (clone RA3-6B2, catalog number 103201, BioLegend). FACS, surface staining: Alexa Fluor 700-conjugated mAb to Ly-6G/Ly-6C (clone RB6-8C5, catalog number 108421), allophycocyanin (APC)-conjugated mAb to F4/80 (clone BM8, catalog number 123115), APC-conjugated mAb to CD49b (clone DX5, catalog number 108909), phycoerythrin (PE)-conjugated mAb to FceRIa (clone MAR-1, catalog number 134307), and APC/Cy7-conjugated mAb to c-kit (clone 2B8, catalog number 105825), all from Biolegend, San Diego, CA; and eFluor 450-conjugated mAb to CD11b (clone M1/70, catalog number 48-0112-82), perCP-eFluor 710 (PE-Cy5.5)-conjugated mAb to CD200R (clone OX110, catalog number 46-5201-82), from eBioscience, San Diego, CA). FACS, intracellular staining: PE/Cy7-conjugated mAb to TNF (clone MP6-XT22, catalog number 5063232) and PE-conjugated mAb to IL-6 (clone MP5-20f3, catalog number 504503) from BioLegend.

Validation

We used well-validated commercial antibody reagents for histology and flow cytometry panels. All commercial antibodies have been authenticated by the commercial provider and we have datasheets showing the degree of non-specific binding as measured in cells that do not express the epitope.

Eukaryotic cell lines	
Policy information about <u>cell lines</u>	
Cell line source(s)	No eukariotic cell lines were used
Authentication	Not applicable
Mycoplasma contamination	Not applicable
Commonly misidentified lines	Not applicable

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals

(See ICLAC register)

C57BL/6 mice were purchase from Jackson Laboratories. Mice with transgenic Basoph8-Cre expression on the C57BL/6 background were kindly provided by Dr. R. Locksley (UCSF). Basoph8-Cre mice were crossed with mice containing loxP-flanked Tnf alleles. Basophl-8-Cre mice were also crossed with Rosa-DTa mice purchased from Jackson Laboratories to generate basophil-deficient mice. All of the mice were bred and maintained in the Seattle Children's Research Institute animal facility. All of the experiments were performed using male mice that were 12 weeks old at the beginning of the experiment.

Wild animals

Not applicable

Not applicable

Field-collected samples

Not applicable

Flow Cytometry

Plots

Confirm that:

The axis	labels	state	the	marker	and	fluoroc	hrome	used	(e.g.	CD4-FITC).

- The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).
- All plots are contour plots with outliers or pseudocolor plots.
- A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation

Single peritoneal cell suspensions were stained with a combination of antibodies to assess the expression of cell surface markers. For intracellular cytokine expression measurements, peritoneal cells were maintained in media alone in the presence of GolgiPlug (catalog number BDB555029, FisherScientific) (1:1,000) at 37 C for 4h. The cells were surface-stained with a combination of the antibodies listed above, fixed and permeabilized using a commercially available kit (catalog number 554722, BD Biosciences), and then stained with antibodies against TNF or IL-6.

Instrument

The cells were acquired on a BD LSR II.

Software

The cells were acquired with the FACSDiva software and analyzed with the FlowJo software (version 8.8.7, Tree Star).

Cell population abundance

Describe the abundance of the relevant cell populations within post-sort fractions, providing details on the purity of the samples and how it was determined.

Gating strategy

Representative flow cytometry plots and frequencies used to identify basophils amongst peritoneal cells obtained from mice 24 h after induction of moderate CLP. Cell population considered for analysis using FSC and SSC. Doublets were removed using FSC-A and FSC-W gating. Dead cells were removed from the analysis using DAPI dead cell stain. FceRIa+ c-Kit- CD49b+ cells were gated and defined as basophils. The same gating strategy was used to identify basophils amongst peritoneal cells obtained from CLP-treated basophil deficient mice, which shows a significant reduction in the basophil percentage. Peritoneal mast cells from naïve mice were used to establish gates for FceRla+ and c-Kit- cells.

Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.