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Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see Authors & Referees and the Editorial Policy Checklist.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, main text, or Methods section).

n/a	Confirmed	
☐	☒	The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	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.*
☒	☐	A description of all covariates tested
☒	☐	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistics including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. F, t, r) with confidence intervals, effect sizes, degrees of freedom and P value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐	Estimates of effect sizes (e.g. Cohen's d, Pearson's r), indicating how they were calculated
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	FACS Diva v8.0, Attune Nxt Software v2.7, Volocity v6.3, Proteome Discoverer v2.1.1.21, Mascot v 2.5.1, StepOnePlus v2.3 andNeqtSeq System Suite for the Illumina NextSeq v500.
Data analysis	GraphPad Prism v.6 and v.7, ImageLab v6.0, R v3.3.2, FlowJo v.8 Mac, Volocity v6.3, ImageJ v1.440, Proteome Discoverer v2.1.1.21, Mascot v 2.5.1.

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 availability of data

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 data that support the findings from this study, including the R code used for bioinformatics analysis and heatmap generation, are available from the corresponding authors upon reasonable request. Sequencing data have been deposited in the GEO database under the accession number GSE122412.

Field-specific reporting

Please select the best 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 nature.com/authors/policies/ReportingSummary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	No statistical tests were used to predetermine sample size. For in vivo experiments, sample sizes were determined based on the numbers required to achieve statistical significance using non-parametric statistics.
Data exclusions	Statistical tests for outliers are routinely performed, however no data was excluded in this manuscript.
Replication	Consistent results obtained from at least two or three biological replicates per experiment were used in the manuscript. All attempts at replication were successful.
Randomization	Allocation of mice was random in all in vivo experiments, taken from littermates.
Blinding	The investigators were blinded to allocation during all in vivo experiments and outcome assessments.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☒	☐ Unique biological materials
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology
☐	☒ Animals and other organisms
☒	☐ Human research participants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☐	☒ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used	Antibodies used for flow cytometry were anti-CD45 (eBioscience clone 30-F11), anti-CD11b (eBioscience clone M1/70), anti-Ly6G (BD Pharmingen clone 1A8), anti-CD88/C5aR1 (eBioscience clone S5/1), anti-Ly6C-FITC (BD Biosciences clone AL-21), anti-CD16 (eBioscience clone 3G8), anti-CD62L (mouse-specific, eBioscience clone MEL-14), and anti-CD62L (human-specific, BioLegend clone DREG-56), anti-CD90.2 (eBioscience clone 53-2.1), anti-VCAM1 (eBioscience clone 429), anti-CXCR2 (BioLegend clone SA045E1), anti-FcgRIII (R&D Systems clone # 275003), and anti-FcgRIV (Sino Biological, clone #012). All flow cytometry antibodies were used following the manufacturer's instructions. Antibodies used for immunoblotting were anti-ELMO1 rabbit polyclonal antibody (made in-house, 1:1,000 dilution), anti-ERK2 (Santa Cruz, goat polyclonal, 1:3,000 dilution), anti-GAPDH-HRP (Sigma clone GAPDH-71.1, 1:10,000 dilution), anti-beta-ACTIN-HRP (Sigma clone AC-15, 1:10,000 dilution), anti-FcgRI (Santa Cruz goat polyclonal sc-7642, 1:1,000 dilution) or anti-Syk (Santa Cruz, rabbit polyclonal sc-1077, 1:1,000 dilution). Antibody used for

immunoprecipitation was anti-ELMO1 mouse monoclonal antibody (made in-house, used at 5 micrograms per milligram of total protein extract).

Validation — Common antibodies used for flow cytometry are routinely checked for quality. Any new antibody used for flow cytometry or western blotting were tested with appropriate isotype control or protein-deficient cells.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	HL-60 and L929 cell lines were acquired from the ATCC and are available upon request.
Authentication	Morphological shape of cell lines and expression of specific cell surface markers used was regularly monitored via microscopic examination and flow cytometry.
Mycoplasma contamination	All cell lines used in the laboratory are regularly tested for mycoplasma contamination. Additionally, all media and serum lots used are regularly tested as well. All materials used in this study tested negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used.

Animals and other organisms

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

Laboratory animals	All animals and animal-derived materials are reported in the Methods section. Animals were maintained according to IACUC and UVa animal facility standards, including ad libitum feeding. C57BL/6J, DBA/1J, NOD, Mrp8-Cre, Cx3cr1-Cre, Lyz2-Cre, and Ubc-CreERt2 mice were obtained from Jackson Laboratories. Elmo1fl/fl and Elmo1–/– mice have been generated in our laboratory and were described previously (see Methods).
Wild animals	This study did not involve any wild animals.
Field-collected samples	This study did not involve field-collected samples.

Flow Cytometry

Plots

Confirm that:

☒ The axis labels state the marker and fluorochrome 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	All sample preparation is reported in the Methods section. Bone marrow cells for neutrophils and macrophages was obtained by flushing femur and tibia using serum-complete media. Peritoneal exudates were obtained via cold PBS flush. Fibroblast like synovioctes were prepared by dissection and enzymatic digestion. All samples were filtered prior to staining. Samples were kept on ice during staining and collection. All fluorescent antibodies were aliquotted in a sterile hood with minimal light exposure. Staining of samples were protected from light throughout.
Instrument	Data were collected on a FACS Canto I (Becton Dickinson) or the Attune Nxt (Thermo Fisher) flow cytometers.
Software	Data were collected analyzed with FlowJo v8 and v10 (Treestar, Inc).
Cell population abundance	Purity of isolated samples was obtained by antibody stain and FACS. Sample purity was greater than 95% in all experiments.
Gating strategy	Standard lymphocyte gates were applied, following by doublet exclusion using FSC-AxW and SSC-AxW. In our studies, neutrophils were gated using a combination of CD11b and Ly6G, while macrophages were gated based on CD11b and F4/80.

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