

Reporting Summary

Nature Portfolio 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 Portfolio policies, see our [Editorial Policies](#) and the [Editorial Policy Checklist](#).

Statistics

For all statistical analyses, confirm that the following items are present in the 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 |
| ☐ | ☒ | A statement on 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
<i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i> |
| ☒ | ☐ | 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 statistical parameters 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
<i>Give P values as exact values whenever suitable.</i> |
| ☒ | ☐ | 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 |

Our web collection on [statistics for biologists](#) contains articles on many of the points above.

Software and code

Policy information about [availability of computer code](#)

Data collection

N/A

Data analysis

GraphPad Prism graphing and statistical software (ver. 8; GraphPad Software)

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 and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio [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 description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our [policy](#)

All data are included in the Supplementary Information or available from the authors, as are unique reagents used in this Article. The raw numbers for charts and graphs are available in the Source Data file whenever possible.

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender	N/A
Reporting on race, ethnicity, or other socially relevant groupings	N/A
Population characteristics	N/A
Recruitment	N/A
Ethics oversight	N/A

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is 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/documents/nr-reporting-summary-flat.pdf](https://www.nature.com/documents/nr-reporting-summary-flat.pdf)

Life sciences study design

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

Sample size	The sample sizes were originally calculated using a power analysis with the following parameters: an effect size of 0.35, statistical power of 80%, and a significance level of 5%. We did not perform a specific sample size estimation for each experiment because we have extensive experience with the in vivo and in vitro models used in this study.
Data exclusions	No data were excluded.
Replication	Most experiments were performed in three independent experiments; however, in accordance with the principle of minimizing animal use, some experiments were stopped after two trials due to clear and unambiguous results.
Randomization	Animals/cells were randomly assigned to groups.
Blinding	The investigators were blinded to group allocation during data collection and/or analysis.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☐	☒ Antibodies
☐	☐ Eukaryotic cell lines
☐	☐ Palaeontology and archaeology
☐	☒ Animals and other organisms
☐	☐ Clinical data
☐	☐ Dual use research of concern
☐	☐ Plants

Methods

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

Antibodies

Antibodies used	APC anti-Ly6G (clone: 1A8; cat: 127614; lot: B448088; BioLegend), PerCP-Cy5.5 anti-CD11b (clone: M1/70; cat: 101228; lot: B423267; BioLegend), FITC anti-MPO (clone: 2D4; cat: ab90812; lot: 110654-1; Abcam), anti-Histone H3 (citrulline R2 + R8 + R 17; cit-H3; cat: ab5103; lot: 1116477-2; Abcam), PE anti-rabbit IgG (clone: Poly4064; cat: 406421; lot: B440363; BioLegend), APC anti-F4/80 (clone: BM8; cat: 123116; lot: B422785; BioLegend), PE anti-iNOS (clone: C-11; cat: sc-7271; lot: C2125; Santa Cruz Biotechnology), BV421 anti-CD112 (clone: 828038; cat: 748046; lot: 2151227; BD Biosciences), anti-CD112 (cat: MAB3869; lot: CHTE0123041; R&D Systems)
Validation	We only used commercially available antibodies. Validation of antibodies is provided on the manufacturers' website and/or datasheets.

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)	N/A
Authentication	N/A
Mycoplasma contamination	N/A
Commonly misidentified lines (See ICLAC register)	N/A

Palaeontology and Archaeology

Specimen provenance	N/A
Specimen deposition	N/A
Dating methods	N/A
☐ Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.	
Ethics oversight	N/A

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Animals and other research organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research, and [Sex and Gender in Research](#)

Laboratory animals	8-12-week-old male wild type (WT) C57BL/6J mice (stock no. 000664) and PAD4 ^{-/-} (B6.Cg-Padi4tm1.1Kmw/J) mice (stock no. 030315) were both purchased from The Jackson Laboratory.
Wild animals	The study did not involve wild animals.
Reporting on sex	Only male mice were used to minimize deviations based on sex, which could have required an inhumane number of animals. However, this does not necessarily mean that our findings are only applicable to males.
Field-collected samples	Mice were housed in a temperature-controlled room (20–26°C), with a humidity level of 30–70%, under 12-h intermittent light and dark cycles and fed a standard mouse chow diet with water. All moribund animals were euthanized humanely when they met two of the following humane criteria: body condition score of 2 or less; failure to eat or drink; grimace score of 2; hunched posture; immobility (activity level minimal or absent); labored breathing; reduced response to human touch; weight loss greater than 20%; and tumor burden.
Ethics oversight	All animal experiments were performed following the National Institutes of Health guidelines for the care and use of laboratory animals. The present studies using live animals were reviewed and approved by the Feinstein Institutes for Medical Research's Institutional Animal Care and Use Committee (IACUC) in Manhasset, NY.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Clinical data

Policy information about [clinical studies](#)

All manuscripts should comply with the ICMJE [guidelines for publication of clinical research](#) and a completed [CONSORT checklist](#) must be included with all submissions.

Clinical trial registration	N/A
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Study protocol	N/A
Data collection	N/A
Outcomes	N/A

Dual use research of concern

Policy information about [dual use research of concern](#)

Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No	Yes
☒	☐ Public health
☒	☐ National security
☒	☐ Crops and/or livestock
☒	☐ Ecosystems
☒	☐ Any other significant area

Experiments of concern

Does the work involve any of these experiments of concern:

No	Yes
☒	☐ Demonstrate how to render a vaccine ineffective
☒	☐ Confer resistance to therapeutically useful antibiotics or antiviral agents
☒	☐ Enhance the virulence of a pathogen or render a nonpathogen virulent
☒	☐ Increase transmissibility of a pathogen
☒	☐ Alter the host range of a pathogen
☒	☐ Enable evasion of diagnostic/detection modalities
☒	☐ Enable the weaponization of a biological agent or toxin
☒	☐ Any other potentially harmful combination of experiments and agents

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A

ChIP-seq

Data deposition

- ☐ Confirm that both raw and final processed data have been deposited in a public database such as [GEO](#).
- ☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links <i>May remain private before publication.</i>	N/A
Files in database submission	N/A
Genome browser session (e.g. UCSC)	N/A

Methodology

Replicates	N/A
Sequencing depth	N/A
Antibodies	N/A
Peak calling parameters	N/A
Data quality	N/A
Software	N/A

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	Blood samples were RBC-lysed. Liver samples were digested using collagenase type 4. Bone marrow-derived cells were isolated by flushing out the femurs and tibias.
Instrument	BD LSR Fortessa (BD Biosciences)
Software	FlowJo software (ver. 10; Tree Star)
Cell population abundance	Cell population abundance varies depending on target cells and experiments and is provided in the dot plots.
Gating strategy	Leukocyte area was gated in FSC/SSC, followed by single cell gating in FSC-A/FSC-H. Neutrophils were identified as Ly6G +CD11b+ cells, and NETs were determined as CitH3+MPO+ neutrophils. Kupffer cells were defined as F4/80+CD11b+ cells within the negative population in the Live/Dead gating. Gating was determined using Fluorescence Minus One controls.
☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.	

Magnetic resonance imaging

Experimental design

Design type	N/A
Design specifications	N/A
Behavioral performance measures	N/A

Acquisition

Imaging type(s)	N/A
Field strength	N/A
Sequence & imaging parameters	N/A
Area of acquisition	N/A
Diffusion MRI	☐ Used ☐ Not used

Preprocessing

Preprocessing software	N/A
Normalization	N/A

Normalization template	N/A
Noise and artifact removal	N/A
Volume censoring	N/A

Statistical modeling & inference

Model type and settings	N/A
Effect(s) tested	N/A
Specify type of analysis:	☐ Whole brain ☐ ROI-based ☐ Both
Statistic type for inference	N/A
(See Eklund et al. 2016)	
Correction	N/A

Models & analysis

n/a	Involvement in the study
☒	☐ Functional and/or effective connectivity
☒	☐ Graph analysis
☒	☐ Multivariate modeling or predictive analysis