nature portfolio

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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 *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 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 *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

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	In FACS experiment, cells were analysed and sorted using a BD FACS Melody™ Cell Sorter (BD Biosciences, San Jose, CA, USA).
Data analysis	Data were analyzed using R (v4.3.2) and Python (v3.11). For single-cell RNA-seq, reads were processed with Cell Ranger (v7.1) and downstream analyses were performed in Seurat (v4.4); cells with <200 genes or >10% mitochondrial reads were excluded. Differential expression was assessed with a Wilcoxon rank-sum test (two-sided), and p values were adjusted using the Benjamini–Hochberg method. Imaging quantifications were performed in Fiji (ImageJ v2.9) with custom macros (available as described below). Statistical details, including exact n values and test types, are reported in the figure legends and Methods.

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

Single-cell RNA-sequencing data heve been deposited in the NCBI Gene Expression Omnibus (GEO) database under accession number: E-GEAD-882 and ArrayExpress database under accession number: E-MTAB-14315.

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	Not applicable
Reporting on race, ethnicity, or other socially relevant groupings	Not applicable
Population characteristics	Not applicable
Recruitment	Not applicable
Ethics oversight	Not applicable

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

Life sciences study design

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

Sample size	We estimated the required sample sizes by considering variations and means, and sought to reach reliable conclusions using sample sizes that were as small as possible. Previously published results, complexity, the cost of experiments and past experience were used to determine the sample size.
Data exclusions	No data were excluded.
Replication	Experiments included sufficient sample sizes to ensure the reproducibility of the findings. All experiments, except for the single-cell RNA sequencing, were independently repeated at least three times, and all replication attempts were successful. Single-cell RNA sequencing was conducted once using pooled samples from over 10 mice.
Randomization	All mice have similar weight, age and healthy state. Healthy mice were assigned randomly into control and treated groups.
Blinding	All researchers were blinded during data collection and image quantification and 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
[ ]	[x] Antibodies
[ ]	[x] Eukaryotic cell lines
[x]	[ ] Palaeontology and archaeology
[ ]	[x] Animals and other organisms
[x]	[ ] Clinical data
[x]	[ ] Dual use research of concern
[x]	[ ] Plants

Methods

n/a	Involved in the study
[x]	[ ] ChIP-seq
[ ]	[x] Flow cytometry
[x]	[ ] MRI-based neuroimaging

Antibodies

Antibodies used: anti-mouse CD16/CD32 (553141, BD Biosciences, 1:500 dilution), Brilliant Violet 421 anti-mouse CD31 (102424, Biolegend, 1:200 dilution), FITC anti-mouse CD45 antibodies (103107, Biolegend, 1:200 dilution), APC anti-mouse CD157 antibodies (140207, Biolegend, 1:200 dilution), PE anti-mouse CD201 antibodies (141503, Biolegend, 1:200 dilution), APC anti-mouse CD201 antibodies (141505, Biolegend, 1:200 dilution), anti-PECAM1 (553370, BD Biosciences, 1:200 dilution), anti-BST1 (552545, BD Biosciences, 1:200 dilution), anti-EPCR (16-2012-83, Invitrogen, 1:200 dilution), anti-Collagen Type Ⅳ (AB756P, Merck Millipore, 1:200 dilution), Alexa Flour 488 goat anti-rat IgG(H+L) (A11006, Invitrogen, 1:500 dilution), Alexa Flour 594 goat anti-mouse IgG(H+L) (A11005, Invitrogen, 1:500 dilution), Alexa Flour 488 goat anti-rabbit IgG(H+L) (A11008, Invitrogen, 1:500 dilution), Alexa Flour 594 goat anti-rat IgG(H+L) (A11007, Invitrogen, 1:500 dilution), Alexa Flour 647 goat anti-rat IgG(H+L) (A21247, Invitrogen, 1:500 dilution)

Validation: All antibodies used were purchased from commercial sources and reputable vendors. Antibodies were stored as recommended by the manufacturer.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s): The cell line of OP9 (RCB1124) was obtained from the RIKEN BioResource Center (BRC), Japan.

Authentication: Cell lines have been authenticated by RIKEN BRC, the original provider.

Mycoplasma contamination: Cell lines were confirmed to be free of mycoplasma contamination by the RIKEN BioResource Center.

Commonly misidentified lines (See ICLAC register): None.

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: Animals were housed in a specific pathogen–free (SPF) facility under a 12-h light/12-h dark cycle (lights on at 08:00), with temperature maintained at 23 ± 1.5 °C and relative humidity at 45**%**±15**%**. Wild type C57BL/6J mice were obtained from SLC and Charles River Laboratories. Procr::CreERT2-IRES-tdTomato and C57BL/6-Gt(ROSA)26Sor<tm1(HBEGF)Awai>/J mice were obtained from The Jackson Laboratory. Rosa26::CAG-lsl-tdTomato mice were obtained from The Institute of Medical Science, The University of Tokyo. ATF3 LoxP/LoxP (fl/fl) mice were obtained from Tokyo Medical and Dental University.

Wild animals: No wild animals were used in this study.

Reporting on sex: Sex and gender were not considered in study design.

Field-collected samples: No field collected samples were used in this study.

Ethics oversight: Animal studies were approved by the Institutional Review Board of Osaka University.

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

Plants

Seed stocks	Not applicable
Novel plant genotypes	Not applicable
Authentication	Not applicable

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	Tissues were dissected from adult C57BL/6J mice and enzymatically dissociated using Dispase I (Roche, Basel, Switzerland) and 1% Collagenase I and II (Worthington, Lakewood, NJ, USA) to obtain single-cell suspensions. The cell suspensions were filtered through 40 µm nylon mesh filters and stained with fluorophore-conjugated antibodies against target markers relevant to each experimental condition, as described in the corresponding figure legends. Propidium iodide (PI) was added immediately before flow cytometry to exclude dead cells.
Instrument	BD FACS™ Melody cell sorter (BD Biosciences)
Software	FlowJo v10
Cell population abundance	Gating strategies were established using unstained control samples to distinguish positive and negative populations. In some experiments, post-sort fractions were re-analyzed to confirm sorting purity.
Gating strategy	Doublets were excluded by gating on forward and side scatter plots. Single cells were selected based on their linear relationship between height and width parameters. Live cells were gated by exclusion of propidium iodide (PI)-positive events, and endothelial cells were defined as $CD31^{+}CD45^{-}$.

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