

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 (<i>n</i>) 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. <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>
☒	☐ 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 <i>d</i> , Pearson's <i>r</i>), 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	Sequencing (10X Chromium; CellRanger (10X Genomics); SpectroFlo® and FACS Diva software (Flow cytometry); FX6 Edge, Vilber (Cytokine array), EVOS™ M5000 Invitrogen imaging system (Light microscopy); Slideview VS200 research slide scanner system (Olympus); Stellaris 5 microscope (Leica)
Data analysis	FIJI (NIH); HALO v3.6.4134.396; FlowJo (v10), FIJI, R packages (decoupleR, enrichr, scran, presto, scater, complexHeatmap), GraphPad Prism (v10)

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](#)

The previously published data are available online at Gene Expression Omnibus (GSE76925: <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE76925>). Bulk RNA seq (GSE303772) scRNA seq (GSE303713) data have been deposited at GEO. Source data are provided.

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	No human participants
Reporting on race, ethnicity, or other socially relevant groupings	No human participants
Population characteristics	No human participants
Recruitment	No human participants
Ethics oversight	No human participants

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	Per experiment sample sizes were determined to be big enough to give statistically valid results. Results were always confirmed in repeats of the experiments with comparable sample sizes. No formal statistical methods were used to predetermine sample sizes; our sample sizes are similar to those reported in previous publications.
Data exclusions	No data was excluded.
Replication	Per experiment (with the same settings) the same results were obtained. All experiments were repeated at least twice with sufficient replicates to ensure reproducibility of the results.
Randomization	Allocation was random in that mice were randomly selected to be exposed to room air or cigarette smoke. We did not use a randomization protocol for the rest of the experiments.
Blinding	Data collection and analysis were not performed blind to the conditions of the experiments, because investigators who planned the experiments also performed them.

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

CD45 (BD Biosciences, #564279, 30-F11; 1:800), CD11b (BD Biosciences, #612800, M1/70; 1:800), Ly6C (BD Biosciences, #755195, HK1.4.rMAb; 1:800), SiglecF (BD Biosciences, #747316, E50-2440; 1:800), Ly6G (BioLegend, #127672, 1A8; 1:800), CD64 (BioLegend, #139309, X54-5/7.1; 1:200), CD11c (BioLegend, #117320, N418; 1:800), Spp1 (ThermoFisherScientific, #CL48822952; polyclonal; 1:200), iNOS (ThermoFisherScientific, #35-5920-82, CXNFT; 1:200), Gpnmb (ThermoFisherScientific, #50-5708-82, CTSREVL; 1:200), Ly6G (BioLegend, #612921, 1A8; 1:800), Ly6C (BioLegend, #128041, HK1.4; 1:800), MHCII (BioLegend, #107630, M5/114.15.2; 1:800), CD163 (Cytex, #62-1631-80, TNKUPJ; 1:200), CD45 (BioLegend, #103174, 30-F11; 1:800), CD36 (ThermoFisherScientific, #63-0362-82, HM36; 1:400), Mmp12 (ThermoFisherScientific, #PA5-13181), SPC (SevenHillsBioReagents, #76694; 1:200), E-Cadherin (BioLegend, #147304; 1:400), JAM-1 (BioLegend, #158506; 1:400), Ki-67 (BioLegend, #652406; 1:200), anti-CD68, FA-11, Bio-Rad; anti-living Colors® DsRed Polyclonal Antibody, TaKaRa; CD11c, CL1831, Novus Biologicals; anti-CD31, R&D systems; all 1:500). CD45 (BioLegend, #304026, HI30; 1:400), CD11b (BioLegend, #101216, M1/70, 1:400), CD14 (BioLegend, #301842, M5E2, 1:400), CD16 (BD Biosciences, #746199, RUO, 1:400), CD68 (BioLegend, #333822, Y1/82A, 1:400), CD163 (BioLegend, #333612, GHI/61, 1:400), CD321 (BioLegend, #353504, OV-5B8, 1:400) and Ki-67 (BioLegend, #350504, RUO, 1:400).

Validation

Antibodies used in this study were suggested by the manufacturer's for the species used (mouse) and validated in each experiment. Gates were set against FMO (fluorescence minus one) or unstimulated negative controls.

Eukaryotic cell lines

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

Cell line source(s)

MLE-12 (obtained from ATCC; #CRL-2110)

Authentication

None were authenticated.

Mycoplasma contamination

Cell lines were tested negative mycoplasma contamination.

Commonly misidentified lines
(See [ICLAC](#) register)

n/a

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

Animal experiments were conducted in AAALAC certified facilities of F. Hoffmann-La Roche in Basel. Throughout the studies, mice were kept under specific-pathogen-free conditions with continuous health monitoring. The WT and Ms4a3tdTom mice were purchased from Charles River Laboratories (JAX stock #036382 bred to ROSA26-tdTomato (Ai14) mice (#007914), resulting in Ms4a3-Cre-RosaTdT mice)⁴⁶. The mice were housed in a 12h-on (6 am–6pm), 12h-off light cycle with room temperature of 20–24°C and humidity of 30–70%. We used female and age-matched mice (8–10 week-old upon experiment start) for each individual experiment. The sample collection and processing were not performed in a blinded manner.

Wild animals

n/a

Reporting on sex

Female mice were used. Based on preliminary findings, we proceeded with female mice exclusively for this study, in order to limit animal use, to avoid fighting behavior and for their greater availability during the ordering process.

Field-collected samples

n/a

Ethics oversight

Permission for animal studies was obtained from the local regulatory agencies (BS Kantonales Veterinäramt BS, cantonal approval number #3090; national number #35788), and all study protocols were in compliance with federal and cantonal guidelines.

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

Plants

Seed stocks

n/a

Novel plant genotypes

n/a

Authentication

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

Single-cell suspensions were generated using cell strainers and syringes and Fc receptors were blocked for at least 15 minutes with Ultra-LEAF™ Purified anti-mouse CD16/32 antibody in PBS supplemented with 1% FBS (FACS buffer) to prevent nonspecific antibody binding. For surface antigen staining, cells were incubated in FACS buffer with fluorophore-conjugated antibodies for at least 30 minutes on ice. Live/DEAD Fixable Dead Cell Stain kits were used to exclude the dead cells. When only surface antigens were stained, fixation buffer containing 4% paraformaldehyde was used. For staining of intracellular antigens, cells were fixed and permeabilized on ice for at least 30 minutes, and intracellular antigens were stained directly or via primary and secondary antibodies. Samples were washed and run on BD Symphony or Cytex Aurora flow cytometers and analyzed in FlowJo software (v10, FlowJo).

Instrument

We used BD Symphony or Cytex Aurora flow cytometers/sorters.

Software

We used FACS Diva Software/SpecroFlow to collect and FlowJo (v10) to analyze data.

Cell population abundance

Purity of sorted cells was confirmed by measuring a small fraction of the cells after each FACS-sort.

Gating strategy

Gates were first set based on FSC-A/SSC-A and doublets were excluded using FSC-H and FSC-A. Live/death dye was used to exclude dead cells. Myeloid cells were then gated for further analysis. More detailed gating strategies are shown as part of the main and supplementary figure set. All gating strategies are shown as illustrations in the figures.

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