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	No software was used.
Data analysis	GraphPad Prism v9.1.1 GraphPad Software Schneider https://www.graphpad.com/scientific- software/prism/ R software 4.1.0 GNU project https://www.r-project.org R Studio RStudio https://www.rstudio.com Bcl2fastq v2.20.0.422 (Illumina https://support.illumina.com/sequencing/sequencing_software/bcl2fastq-conversion-software.html) Seven Bridges Genomics (BD Biosciences, https://www.sevenbridges.com) Seurat v4.03 Hao et al, 2021 https://satijalab.org/seurat/get_ started.html RRID:SCR_016341 Image J Fiji Schindelin et al, 2012 https://imagej.net/Fiji/ FlowJo v10.7.1 (Becton Dickinson & Company) cutadapt, Martin et al 2011 Bowtie2, Langmead et al, 2012 MAgECK, Li et al, 2014 Code is available at https://github.com/Moors-Code/Eosinophils_scRNASeq

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

ScRNAseq data used to illustrate this protocol have been deposited at the Gene Expression Omnibus under the accession number GSE182001.

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	*Use the terms sex (biological attribute) and gender (shaped by social and cultural circumstances) carefully in order to avoid confusing both terms. Indicate if findings apply to only one sex or gender; describe whether sex and gender were considered in study design whether sex and/or gender was determined based on self-reporting or assigned and methods used. Provide in the source data disaggregated sex and gender data where this information has been collected, and consent has been obtained for sharing of individual-level data; provide overall numbers in this Reporting Summary. Please state if this information has not been collected. Report sex- and gender-based analyses where performed, justify reasons for lack of sex- and gender-based analysis.*
Population characteristics	*Describe the covariate-relevant population characteristics of the human research participants (e.g. age, genotypic information, past and current diagnosis and treatment categories). If you filled out the behavioural & social sciences study design questions and have nothing to add here, write "See above."*
Recruitment	*Describe how participants were recruited. Outline any potential self-selection bias or other biases that may be present and how these are likely to impact results.*
Ethics oversight	*Identify the organization(s) that approved the study protocol.*

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	In accordance with the 3Rs, the smallest sample size was chosen that could give a significant difference. Given the robustness of the phenotypes across all methods used (transcriptome and protein level), the minimum sample size assuming no overlap in control versus experimental is three animals per experiment.
Data exclusions	No animals were excluded, unless data acquisition quality was insufficient.
Replication	Data was combined from independent mice, treated on different days and analyzed together.
Randomization	No randomization was used
Blinding	The researcher was blinded to the genotype during the processing and data acquisition.

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

Methods

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

Antibodies

Antibodies used: Cell were stained with fixable viability dye eFluor 780 (1:1000, 65-0865-14 eBioscience) and a combination of the following antibodies (1:200, all from BioLegend unless stated otherwise): anti-mouse CD45 BV650 (30-F11, 103151), CD11b BV510 (M1/70, 101263), MHC-II AF700 (M5/114.15.2, 107622), Ly6G Percp-Cy5.5 (1A8, 127616), CD80 BV605 (16-10A1, 104729), PD-L1 PE-Cy7 (10F.9G2, 124314).Fc block (anti-CD16/CD32, 101302 Affymetrix) was included to minimize nonspecific antibody binding.

Validation: All antibodies have been previously validated by the manufacturer.

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: C57BL/6J (B6J, stock no. 000664) and dCas9-KRAB (stock no.030000) were obtained from The Jackson Laboratory. Il5–transgenic have been previously described.

Wild animals: N/A

Reporting on sex: All experiments were performed on 6-12 week-old male and female mice.

Field-collected samples: N/A

Ethics oversight: All experimental procedures at the University of Zurich and ETH Zurich were performed in accordance with Swiss Federal regulations and approved by the Cantonal Veterinary Office and/or in accordance with the European Communities Council Directive (86/609/EEC).

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

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: Preparation of single-cell suspensions from tissues
Gastrointestinal tissues: stomach, colon and small intestine (SI) were harvested, cleaned of faecal matter and cut longitudinally. Organs were washed in PSB and cut into pieces (1-2cm) and Peyer's patches were removed from the SI. Pieces were washed twice in a shaking incubator with wash buffer (2% BSA, 100U/mL penicillin/streptomycin, 5mM EDTA in HBSS, 25 minutes, 37°C). Tissues were then rinsed in cold PBS and digested for 50 minutes at 37°C in complete medium (10% FBS, 100U/ml, penicillin/streptomycin (P0781 Sigma) in RPMI-1640) containing 15mM Hepes (H0887 Sigma), 0.05mg/ml DNase I (10104159001 Roche) and an equal amount of 250U/mL type IV (C5138 Sigma) and type VIII collagenase (C2139 Sigma) (for colon and SI), or 500U/mL type IV collagenase (for stomach). Cells were passed through a 70µm cell strainer, centrifuged for 8 minutes and layered onto a 40/80% Percoll (17089101 Cytiva) gradient (18 minutes, 2100 g, 20°C, no brake). The interphase was collected and washed in PBS.
Lung: lungs were perfused with PBS, harvested and cut into pieces before digestion in complete medium supplemented with 500U/mL type IV collagenase (Sigma) and 0.05mg/ml DNase I (Roche) for 50minutes at 37°C. Lungs were then passed through a 70µm cell strainer and mesh with syringe plungers.

Blood: blood was sampled by post-mortem cardiac puncture in 2% BSA 5mM EDTA PBS. The suspension was layered over Histopaque 1119 (density of 1.119 g/mL; 11191 Sigma-Aldrich) and centrifuged at 800g for 20 minutes. The interphase was washed in PBS and red blood cells were lysed in ice-cold distilled water for 30 seconds.
Bone marrow (BM): femur and tibia were flushed through a 23-gauge needle and collected in complete RPMI medium. Suspensions were filtered through a 40µm cell strainer and red blood cells were lysed in ice-cold distilled water for 30 seconds.
Spleen: spleen were harvested, meshed through a 40µm cell strainer using a syringe plunger, and red blood cells were lysed in ice-cold distilled water for 30 seconds.
Unless specified, all centrifugation steps were performed at 500 g for 8 minutes at 10°C.
For surface staining, cells were stained in PBS at 4°C for 30 minutes with the fixable viability dye eFluor 780 (1:1000, 65-0865-14 eBioscience) and a combination of the following antibodies (1:200, all from BioLegend unless stated otherwise): anti-mouse CD45 BV650 (30-F11, 103151), CD11b BV510 (M1/70, 101263), MHC-II AF700 (M5/114.15.2, 107622), Ly6G Percp-Cy5.5 (1A8, 127616), CD80 BV605 (16-10A1, 104729), PD-L1 PE-Cy7 (10F.9G2, 124314), Siglec F BV421 (E50-2440, 552126 BD Biosciences).

Instrument

LSRII Fortessa or FACS AriaIII 5L (BD Biosciences)

Software

Aquired data were analyzed using FlowJo software.

Cell population abundance

Absolute numbers of cells are outlined in relevant Figures.

Gating strategy

Events were initially gated by FSC-A and SSC-A, then by FSC-A and FSC-H (to exclude doublets). Live CD45+ cells were then gated using a fixable viability dye. Subsequent gating depends on the population of interest and is outlined in Supplementary Information.

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