nature portfolio

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Last updated by author(s): 07/03/2026

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	FACSDiva v9
Data analysis	FlowJo v10.4 Seurat v4 scRepertoire v1.7 Harmony v0.1 10X Genomics CellRanger v6 GraphPad Prism v9

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 newly generated scRNAseq data are available at GSE333232.

Human research participants

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

Reporting on sex and gender	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

Life sciences study design

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

Sample size	No sample size calculation were performed for single cell RNA sequencing analysis as all available studies were included and this was a hypothesis-generating experiment. All data points in a given figure panel represent biological replicates. Numbers of mice were similar to other single cell studies in asthma models published in Nature (volume 638, pages 490–498 (2025)).
Data exclusions	No data were excluded from analysis.
Replication	All reported findings were statistically significant and represent reproducible, consistent data obtained from multiple different tissue samples. The number of individual replicates for each experiments is indicated in each figure legend and individual data points are always shown for each panel where appropriate.
Randomization	There were no experiments with prospective interventions that would require randomization. Inbred mouse strains were used for all experiments and additional covariates, e.g. age or housing conditions, were not present and/or were consistent.
Blinding	Histology was scored by a blinded reader. For other experiments, all data reported is quantitative and no blinding was performed..

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

Please see Supplementary Table 14 for information on antibodies used, including dilutions.

Validation

All antibodies were obtained from commercial sources, with validation performed by the manufacturer. No additional in-house validation was performed. Please see links for additional validation information:

CD4 GK1.5 BUV496 BD Biosciences 612952 https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/buv496-rat-anti-mouse-cd4.612952
CD4 GK1.5 BV605 Biolegend 100451 https://www.biolegend.com/en-gb/products/brilliant-violet-605-anti-mouse-cd4-antibody-10708?GroupID=BLG4745

CD4 GK1.5 BUV496 BD Biosciences 612952 https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/buv496-rat-anti-mouse-cd4.612952
CD4 GK1.5 BV605 Biolegend 100451 https://www.biolegend.com/en-gb/products/brilliant-violet-605-anti-mouse-cd4-antibody-10708?GroupID=BLG4745
CD4 RM4-5 BV510 Biolegend 100559 https://www.biolegend.com/fr-ch/products/brilliant-violet-510-anti-mouse-cd4-antibody-7991?GroupID=BLG4745
CD8a 53-6.7 APC-Cy7 Biolegend 100714 https://www.biolegend.com/en-us/products/apc-cyanine7-anti-mouse-cd8a-antibody-2269?GroupID=BLG279
CD8a 53-6.7 PE-Cy7 Biolegend 100721 https://www.biolegend.com/en-us/products/pe-cyanine7-anti-mouse-cd8a-antibody-1906
CD11c N418 PE-Cy7 Biolegend 117317 https://www.biolegend.com/en-us/products/pe-cyanine7-anti-mouse-cd11c-antibody-3086?GroupID=BLG11937
CD19 6D5 APC-Cy7 Biolegend 115530 https://www.biolegend.com/en-us/products/apc-cyanine7-anti-mouse-cd19-antibody-3903
CD19 6D5 PE/Dazzle™ 594 Biolegend 115553 https://www.biolegend.com/ja-jp/products/pe-dazzle-594-anti-mouse-cd19-antibody-10071
CD44 IM7 PerCP/Cy5 Biolegend 103032 https://www.biolegend.com/ja-jp/products/percp-cyanine5-5-anti-mouse-human-cd44-antibody-5605
CD44 IM7 PE-Cy7 Biolegend 103030 https://www.biolegend.com/en-us/products/pe-cyanine7-anti-mouse-human-cd44-antibody-3932
CD45 30-F11 FITC Biolegend 103108 https://www.biolegend.com/en-us/products/fitc-anti-mouse-cd45-antibody-99
CD45 30-F11 BV510 Biolegend 103138 https://www.biolegend.com/en-us/products/brilliant-violet-510-anti-mouse-cd45-antibody-7995
CD45 30-F11 BV785 Biolegend 103149 https://www.biolegend.com/en-us/products/brilliant-violet-785-anti-mouse-cd45-antibody-10636?GroupID=BLG1932
CD45 30-F11 BUV737 BD Biosciences 568344 https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/buv737-rat-anti-mouse-cd45.568344
CD45 30-F11 Biotin Biolegend 103104 https://www.biolegend.com/en-us/products/biotin-anti-mouse-cd45-antibody-98
CD45.1 A20 BUV737 BD Biosciences 812811 https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/buv737-mouse-anti-mouse-cd45-1.612811
CD45.2 104 BV421 Biolegend 109832 https://www.biolegend.com/en-us/products/brilliant-violet-421-anti-mouse-cd45-2-antibody-7328
CD62L MEL-14 BV421 Biolegend 104436 https://www.biolegend.com/en-us/products/brilliant-violet-421-anti-mouse-cd62l-antibody-7164
CD69 H1.2F3 BV421 Biolegend 104545 https://www.biolegend.com/en-us/products/brilliant-violet-421-anti-mouse-cd69-antibody-7358
CD69 H1.2F3 PE-Cy7 Biolegend 104512 https://www.biolegend.com/en-us/products/pe-cyanine7-anti-mouse-cd69-antibody-3168
Ly108 330-AJ APC Biolegend 134609 https://www.biolegend.com/en-us/products/apc-anti-mouse-ly108-antibody-15660
TCRb H57-597 BV421 Biolegend 109230 https://www.biolegend.com/en-us/products/brilliant-violet-421-anti-mouse-tcr-beta-chain-antibody-7251
TCRb H57-597 BV785 Biolegend 109249 https://www.biolegend.com/en-us/products/brilliant-violet-785-anti-mouse-tcr-b-chain-antibody-17614
TCRb H57-597 PerCP/Cy5 Biolegend 109228 https://www.biolegend.com/en-us/products/percp-cyanine5-5-anti-mouse-tcr-beta-chain-antibody-5603
TCRb H57-597 PE-Cy7 Biolegend 109222 https://www.biolegend.com/en-us/products/pe-cyanine7-anti-mouse-tcr-beta-chain-antibody-4144
ST2 U29-93 PE BD Biosciences 566311 https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/pe-rat-anti-mouse-il-33r-st2.566311
Ly-6G 1A8 APC Biolegend 127613 https://www.biolegend.com/en-us/products/apc-anti-mouse-ly-6g-antibody-6115
CXCR5 L138D7 BV711 Biolegend 145529 https://www.biolegend.com/en-us/products/brilliant-violet-711-anti-mouse-cd185-cxcr5-antibody-15717

PD-1 29F.1A12 BV605 Biolegend 135220 https://www.biolegend.com/en-us/products/brilliant-violet-605-anti-mouse-cd279-pd-1-antibody-7648
Siglec-F S17007L PE Biolegend 155505 https://www.biolegend.com/en-us/products/pe-anti-mouse-cd170-siglec-f-antibody-16372
KLRG1 2F1/KLRG1 BV711 Biolegend 138427 https://www.biolegend.com/en-us/products/brilliant-violet-711-anti-mouse-human-klrg1-mafa-antibody-13583
Streptavidin PE Biolegend 405203 https://www.biolegend.com/en-us/products/pe-streptavidin-1475
Streptavidin PE BD Biosciences 554061 https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/pe-streptavidin.554061
Streptavidin BV711 BD Biosciences 563262 https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/bv711-streptavidin.563262
Streptavidin APC-Cy7 Biolegend 405208 https://www.biolegend.com/en-us/products/apc-cyanine7-streptavidin-1471
Gata3 L50-823 R718 BD Biosciences 567633 https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/R718-Mouse-Anti-GATA3.567633
Gata3 16E10A23 PE Biolegend 653804 https://www.biolegend.com/de-de/products/pe-anti-gata3-antibody-9076?GroupID=GROUP26
TCF1 C63D9 AF647 CST 6709S https://www.cellsignal.com/products/antibody-conjugates/tcf1-tcf7-c63d9-rabbit-mab-alexa-fluor-647-conjugate/6709

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	All mice were 8-12 weeks of age and obtained from the Jackson Laboratory. Strains used include: - C56BL/6 - B6.SJL-Ptprca Pepcb/BoyJ - B6.129P2-Tcrbtm1Mom/J - B6(Cg)-Tcf7tm1Hhx/J - B6(129X1)-Tg(Cd4-cre/ERT2)11Gnri/J
Wild animals	N/A
Reporting on sex	Female and male B6 mice were used in a matched manner but not separately analyzed.
Field-collected samples	N/A
Ethics oversight	Brigham & Women's Hospital IACUC

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	Single cell suspensions were obtained from indicated tissues as described in Methods section.
Instrument	BD Fortessa
Software	FlowJo v10.4
Cell population abundance	Sort purity was not assessed as all cells were loaded for scRNAseq. Contaminating populations were identified by transcriptional profile and clustered separately.
Gating strategy	1.) FSC/SSC gating was used to identify lymphocytes. 2.) Live/dead exclusion was performed using fixable Live/Dead Blue dye (Invitrogen) 3.) Key populations were identified as shown in representative plots in each figure.

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