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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	All flow cytometric data were acquired on BD LSR Fortessa X20 or FACSAria III with FACS Diva software (version 9.0). Single cell sequencing data were collected by Illumina Novaseq 6000.
Data analysis	For whole gene expression, target gene expression and TCR sequencing, reads were processed with BD Multiplex Rhapsody Analysis Pipeline Version 1.9 following manufacturer's instructions. Software used in the study: FlowJo software (version 10.8.1), GraphPad Prism (version 9.5.0), R (version 4.4.0), Python (version 3.9.11), Adobe Illustrator (version 24.2). Packages used in the study: Seurat (version 4.0.1), iSMNN (version 1.20), vegan (version 2.6.4), entropy (version 1.3.1), ggplot2 (version 3.5.1), scVelo (version 0.2.5). A tool used in the study: samtools (version 1.15.1).

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 generated or analysed in this study are provided in the article and its Supplementary Information/Source Data file. RNA and TCR sequencing data first reported in this study are deposited in the NGDC (https://ngdc.cncb.ac.cn/gsa/) under accession number CRA023351 (https://ngdc.cncb.ac.cn/gsa/browse/CRA023351). Source Data are provided with this paper.

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

Life sciences study design

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

Sample size	No statistical method was used to predetermine the sample size for our experiments, but our sample sizes are similar to or larger than those reported in previous publications in the field. All experiments performed in at least two independent batches, or have at a minimum 5 independent biological replicates. All sample sizes are clearly indicated in the manuscript.
Data exclusions	No data have been excluded for statistical analysis.
Replication	All experiments were performed with a minimum of two independent replicates and replication was successful.
Randomization	Mice were randomly assigned to all experiments.
Blinding	Mice were allocated to groups according to genotype and/or treatment, and WT/mutant genotypes were blinded to investigators before analysis. Age-matched and only male mice were used for the experiment to minimize biological variables.

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

The following antibodies were used at a 1:100 dilution:
APC anti-mouse CD3ε antibody clone 145-2C11, 100312, Biolegend.
PE anti-mouse CD4 antibody clone GK1.5, 100408, Biolegend.
eFluor 450 anti-mouse CD8a monoclonal antibody clone 53-6.7, 47-0081-82, eBioscience.
BV650 Anti-mouse CD45R/B220 clone RA3-6B2, 563893, BD Biosciences.
APC-Cy™7 anti-mouse CD4 clone GK1.5, 552051, BD Biosciences.

CD90.2 (Thy-1.2) Monoclonal Antibody (53-2.1), APC-eFluor™ 780, 47-0902-82, eBioscience, 0.5mg per mouse.
Brilliant Violet 510™ anti-mouse CD45 Antibody Clone 30-F11, 103138, Biolegend, 0.25mg per mouse.
InVivoMAb anti-mouse TCR γ/δ Clone UC7, BE0070, Bioxcell, 10µg per milliliter.
InVivoPlus anti-mouse IFNγ, Clone XMG1.2, BP0055, Bioxcell, 10µg per milliliter.

Validation

All antibodies used are commercial antibodies reported by the manufacturer to be validated for use.

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

Wild-type mice (C57BL/6 background) were purchased from GemPharmatech Co. Ltd. C57BL/6J.129P2-Tcrdtm1Mom/J (Tcrd-/-) and C57BL/6-Il17atm1Bcgen/J (IL17-GFP) mice were provided by Zhinan Yin from the Institute of Biomedical Translational Research, Jinan University. At the beginning of the experiments, all mice were 6-8 weeks old and sex-matched.

Wild animals

No wild animals were used.

Reporting on sex

In order to minimize technical variabilities and batch effects, only males were used in all the experiments.

Field-collected samples

No field-collected samples were used in this study.

Ethics oversight

All mice in this study were maintained under specific pathogen-free conditions, 12 light/12 dark cycle, temperatures of ~18-24°C with 40-60% humidity. All mice experiments described here complied with the guidelines of the Committee on the Use and Care of Animals of Guangzhou Medical University (Guangzhou, China), and were approved by the Animal Subjects Committee of Guangzhou Medical University.

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	Bronchoalveolar lavage fluid (BALF) in mice was acquired by inflating lungs with 1 mL of complete RPMI 1640 medium via tracheal cannulation, followed by three lavages. BALF samples were centrifuged at 500 g, 4°C for 5 minutes to separate supernatant and cell pellets. The lungs were washed in PBS and minced into small pieces with scissors. The lung tissue was digested for 30 min at 37 °C in HBSS containing 2% heat-inactivated FBS, 100×Pen Strep, 2mM L-glutamine, 25 mM HEPES, 1mg/mL Collagenase D, and 0.1mg/mL DNase I. The spleen was dissected, and splenocytes were isolated using mechanical dissociation protocol. Cell suspension was filtered through a 70 µm strainer. Red blood cells were lysed as required. Induced sputum mononuclear cells (ISMCs) were isolated from induced sputum cell pellet by density-gradient sedimentation using Ficoll-Paque according to the manufacturer's instructions (GE Healthcare, 17-1440-02). ISMCs were seeded at up to 10,000 cells per well in 200 µl of complete RPMI medium. Cells were stimulated with PMA (50 ng/ml) and ionomycin (1 µg/ml) and 1 GolgiPlug (1 µM). Plates were incubated at 37 °C and 5% CO2 for 4 h. For flow cytometry, filtered cell suspension was stained with antibodies as described below. Single - cell suspensions were stained in 96 -well round-bottom plates at 0.5 million lymphocytes per well. For surface staining, cells were stained with the indicated antibodies at room temperature (20 - 25°C) for 30 minutes, and then labeled with Fixable Viability Dye eFluor™ 450 at room temperature (20 - 25°C) in the dark for another 15 minutes. Then cells were washed with FACS buffer twice and resuspended in FACS buffer for flow cytometer detection. For scRNA-seq and TCR-seq assays, the cell suspension was filtered through a 70 µm filter to remove debris and stained with sample tags (BD Mouse Single-Cell Sample Multiplexing Kit) and CD3-APC antibody for 30 min at 4 °C. Fixable Viability Dye eFluor™ 450 was used to exclude dead cells. Live CD3+ T cells were sorted from the airway (CD45+ CD90.2- cells in BALF), the airway-parenchyma interface (air-par, CD45+ cells in lungs), the parenchyma (CD45- CD90.2- cells in lungs), and the spleen into cold buffer (BD Rhapsody™ Cartridge Reagent Kit) using a BD FACSAria III cell sorter, with the samples kept at 4 °C throughout acquisition.
Instrument	LSR Fortessa and FACS-sort Arialll
Software	BD Diva software v9.0 and Flowjo v10.8.1
Cell population abundance	Frequencies of cell populations are stated in dot plots and graphs.
Gating strategy	Gating strategies are stated in the according Fig.1 and Supplementary Fig. 7. In brief, all cells were gated on SSC-A/FSC-A and FSC-H/FSC-A to identify as singlet, then as live (FVD 520-), T cells (CD3+ B220-), and further subdivided into CD4+ and CD8+ T cells. T cells from the airway were identified as CD45+ CD90.2- cells in BALF, T cells from the airway-parenchyma interface (air-par) were identified as CD45+ cells in lungs, T cells from the parenchyma were identified as CD45-CD90.2- cells in lungs and T cells from spleen were identified as CD90.2- cells in spleen.

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