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Corresponding author(s): Jin-Fu Xu

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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	The immunohistochemistry staining analysis: Image-Pro Plus 6.0; The flow cytometry data: FlowJo software (v10.7.2); The western blot data: Tanon 5200 Imaging System; The airway hyperresponsiveness measurement data: eDacq; The ELISA data: Gen5 TS 2.06; The RT-PCR data: Roche LightCycler Ⅱ 480 software 1.5.0.
Data analysis	GraphPad Prism 9.0

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 data that support the findings of this study are available within the article and its supplementary information or from the corresponding authors on request. Key resources are shown in Supplementary Table 4. 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	Given strict inclusion and exclusion criteria as well as low sample size of the current study, the sex of participants was determined based on self-report instead of assigned in the present study. 20 healthy controls (HC), 31 bronchiectasis patients, 30 asthmatics, and 31 patients with bronchiectasis-asthma overlap (BAO) were enrolled in our study, among which 12 HC, 19 bronchiectasis patients, 19 asthmatics and 26 patients with BAO were all females as shown in Supplementary Table 1. And there was no significance concerning the sex distribution across the group (p=0.1643). The majority of participants being female during recruitment corresponds to high prevalence rate among women.
Reporting on race, ethnicity, or other socially relevant groupings	Participants in our study were recruited in Shanghai Pulmonary Hospital and were Asia Chinese Han population.
Population characteristics	The detailed baseline information including age, sex, smoking history, duration of symptoms and P. aeruginosa isolation rates as well as clinical characteristics of participants were presented in Supplementary Table 1 and Table 2 respectively. There was no obvious significance concerning the sex distribution and the percentages of participants with smoking history across the groups (P=0.1643, P=0.4304). Patients with BAO had worse lung function, as indicated by lower FEV1, FVC, FVC% pred values, lower scores on Asthma Control Test (ACT), lower levels of eosinophils and higher percentages of IgE to be below 100 compared to asthmatic patients, but there was no significance of FEV1% pred, FEV1/FVC, fractional exhaled nitric oxide (FeNO) values in patients with BAO (Supplementary Table 2). These characteristics suggested that BAO may tend to be type 2-low asthma with poor control.
Recruitment	The diagnosis of bronchial asthma was based on the Global Initiative for Asthma (GINA) guidelines. The diagnosis of idiopathic bronchiectasis was referred to a guiding principle titled “non-cystic fibrosis bronchiectasis guideline” published by British Thoracic Society in 2019. Patients with BAO met one of the following diagnostic criteria:(1) Bronchiectasis was clinically reported prior to asthma; (2) Asthma was newly diagnosed according to bronchodilator reversibility test on the basis of primary diagnosis of bronchiectasis. Patients with cystic fibrosis or allergic bronchopulmonary aspergillosis (ABPA) were excluded from the study. Participants lacking respiratory symptoms together with chest imaging evidence of acute, active and chronic pulmonary lesions were recruited as healthy controls. The diagnosis of BAO relied on HRCT and bronchodilator reversibility test, so there may be no bias present in the enrollment process.
Ethics oversight	Study protocols for research related to human samples including informed consent, publication of demographic data, and associated corresponding source data were approved by the ethics committees of Shanghai Pulmonary Hospital (approval number K21-318). This study was conducted according to the Declaration of Helsinki principles and signed informed consent was obtained from all participants. We acknowledged that if there is any adverse event related to sample collection, the participant would be treated instantly and extra fees were not provided in the study.

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 general, no statistical methods were used to determine sample sizes. Sample size was based on similar studies in this field and empirical data from pilot experiments. The details on the sample size were included in each figure legend.
Data exclusions	Recovery of more than 1000 colony-forming unit (CFU) of bacteria from lung cultures is a gold indicator of building chronic infection, so data of animals with recovery of less than 1000 colony-forming unit (CFU) of bacteria from lung cultures at indicated time point were excluded.

Replication	Unless otherwise indicated, almost all of experiments involved in our study were performed in three independent batches and similar results were concluded. The details including the numbers of data points and independent experiments were stated in the corresponding figure legends. In addition, as indicated in the figure legends, the experiments related to human samples and protein level of IL-17C secreted into mouse BALF haven't been repeated independently, but their data points have met the request of a minimum 5-10 biological replicates (Fig. 5g-k and Supplementary Fig. 2h-j).
Randomization	For mouse experiment, mice were randomly allocated into each experimental group. For in vitro experiments, cells were randomly cultured in the plate and infection or drug treatments were randomly applied to the cells. For clinical sample analysis, randomization wasn't involved in the study due to the lack of intervention.
Blinding	Only semiquantified analysis including airway inflammation, protein quantification was assigned to an individual blinded to experimental conditions. Other experiments including ELISA, flow cytometry, qRT-PCR, western blotting, binding assay, epithelial permeability measurement, CFU counting have been performed by the investigators de novo in the absence of blinding. These data were collected by the software and may not be impacted by the investigators.

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

1.Anti-mouse CD45 APC-Cy7 (Clone 30-F11) Biolegend Cat#103116
2.Anti-mouse Lineage Pacific Blue (Clone 17A2; RB6-8C5; RA3-6B2; Ter-119; M1/70) Biolegend Cat#133310
3.Anti-mouse CD90.2 FITC (Clone 30-H12) Biolegend Cat#105305
4.Anti-mouse RORγt PE (Clone AFKJS-9) eBioscience Cat#12-6988-82
5.Anti-mouse GATA3 APC (Clone 16E10A23) Biolegend Cat#653806
6.Anti-Mouse T-bet PerCP-Cy5.5 (Clone 4B10) Biolegend Cat#644806
7.Anti-mouse EOMES APC (Clone W17001A) Biolegend Cat#157703
8.Anti-mouse CD127 PerCP-Cy5.5 (Clone A7R34) Biolegend Cat#135022
9.Anti-mouse CD3 PerCP-Cy5.5 (Clone 17A2) Biolegend Cat#100218
10.Anti-mouse CD4 BV421 (Clone GK1.5) Biolegend Cat#100443
11.Anti-mouse IL-5 APC (Clone TRFK5) Biolegend Cat#504306
12.Anti-mouse IL-13 PE (Clone W17010B) Biolegend Cat#159403
13.Anti-mouse IL-17A BV650 (CloneTC11-18H10.1) Biolegend Cat#506930
14.Anti-mouse IFN-γ FITC (Clone XMG1.2) Biolegend Cat#505806
15.Anti-mouse IL-17RE Alexa Fluor647 (Clone 944904) R&D Systems Cat#FAB7997R
16.Anti-His Tag APC (Clone J095G46) Biolegend Cat#362605
17.Anti-mouse IL-17C Alexa Fluor647 (Clone 311522) R&D Systems Cat#IC23061R
18.Anti-human CD45 APC/Cyanine7 (Clone HI30) Biolegend Cat#304014
19.Anti-human CD127 BV510 (Clone A019D5) Biolegend Cat#351332
20.Anti-human CD117 (c-kit) BV421 (Clone 104D2) Biolegend Cat#313216
21.Zombie Aqua Fixable Viability Kit Biolegend Cat#423101
22.Zombie Red Fixable Viability Kit PE-Texas Red Biolegend Cat#423109
23.Anti-human CD294 (CRTH2) APC (Clone BM16) Biolegend Cat#350110
24.FITC anti-human Lineage Cocktail (Clone UCHT1; HCD14; 3G8; HIB19; 2H7; HCD56) Biolegend Cat#348801
25.E-cadherin Antibody (Clone G-10) SANTA CRUZ Cat#sc-8426
26.ZO-2 Antibody (Clone E-3) SANTA CRUZ Cat#sc-515115
27.ZO-3 Antibody (Clone 1E8) SANTA CRUZ Cat#sc-293313
28.Anti-Claudin18 Antibody (Clone 34H14L15) Abcam Cat#Ab203563
29.Beta actin antibody (Ag14521) Proteintech Cat#20536-1-AP
30.Anti-IL17RE antibody bioss Cat#bs-18414R
31.ZO-3 Antibody Invitrogen Cat#36-4000
32.Human IL-17C Antibody (Clone 177114) R&D Systems Cat#MAB1234

Validation	1.https://www.biolegend.com/en-us/products/apc-cyanine7-anti-mouse-cd45-antibody-2530. 2.https://www.biolegend.com/en-us/products/pacific-blue-anti-mouse-lineage-cocktail-7765. 3.https://www.biolegend.com/en-us/products/fitc-anti-mouse-cd90-2-thy1-2-antibody-104. 4.https://www.thermofisher.cn/cn/zh/antibody/product/ROR-gamma-t-Antibody-clone-AFKJS-9-Monoclonal/12-6988-82. 5.https://www.biolegend.com/en-us/products/apc-anti-gata3-antibody-9104. 6.https://www.biolegend.com/en-us/products/percp-cyanine5-5-anti-t-bet-antibody-5760. 7.https://www.biolegend.com/en-us/products/alexa-fluor-647-anti-mouse-eomes-antibody-18078. 8.https://www.biolegend.com/en-us/products/percp-cyanine5-5-anti-mouse-cd127-il-7ralpha-antibody-6196. 9.https://www.biolegend.com/en-us/products/percp-cyanine5-5-anti-mouse-cd3-antibody-5596. 10.https://www.biolegend.com/en-us/products/brilliant-violet-421-anti-mouse-cd4-antibody-7142. 11.https://www.biolegend.com/en-us/products/apc-anti-mouse-human-il-5-antibody-989. 12.https://www.biolegend.com/en-us/products/pe-anti-mouse-il-13-antibody-19159. 13.https://www.biolegend.com/en-us/products/brilliant-violet-650-anti-mouse-il-17a-antibody-7684. 14.https://www.biolegend.com/en-us/products/fitc-anti-mouse-ifn-gamma-antibody-995. 15.https://www.rndsystems.com/cn/products/mouse-il-17re-alexa-fluor-647-conjugated-antibody-944904_fab7997r. 16.https://www.biolegend.com/en-us/products/apc-anti-his-tag-antibody-14783. 17.https://www.rndsystems.com/cn/products/mouse-il-17c-alexa-fluor-647-conjugated-antibody-311522_ic23061r. 18.https://www.biolegend.com/en-us/products/apc-cyanine7-anti-human-cd45-antibody-1914. 19.https://www.biolegend.com/en-us/products/brilliant-violet-510-anti-human-cd127-il-7ralpha-antibody-8439. 20.https://www.biolegend.com/en-us/products/brilliant-violet-421-anti-human-cd117-c-kit-antibody-7348. 21.https://www.biolegend.com/en-us/products/zombie-aqua-fixable-viability-kit-8444 22.https://www.biolegend.com/en-us/products/zombie-red-fixable-viability-kit-9338. 23.https://www.biolegend.com/en-us/products/apc-anti-human-cd294-crth2-antibody-7837. 24.https://www.biolegend.com/en-us/products/fitc-anti-human-lineage-cocktail-cd3-cd14-cd16-cd19-cd20-cd56-6689. 25.https://www.scbt.com/zh/p/e-cadherin-antibody-g-10. 26.https://www.scbt.com/zh/p/zo-2-antibody-e-3. 27.https://www.scbt.com/zh/p/zo-3-antibody-1e8. 28.https://www.abcam.cn/products/primary-antibodies/claudin18-antibody-34h14l15-ab203563.html. 29.https://www.ptgcn.com/products/ACTB-Antibody-20536-1-AP.htm. 30.https://www.biosschina.com/#/productDetail?goods_id=7405. 31.https://www.thermofisher.cn/cn/zh/antibody/product/ZO-3-Antibody-Polyclonal/36-4000. 32.https://www.rndsystems.com/cn/products/human-il-17c-antibody-177114_mab1234.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	The A549 lung epithelial cell line (SCSP-503, Chinese Academy of Sciences) and BEAS-2B bronchial epithelial cells (SCSP-5067, Chinese Academy of Sciences) were obtained from Chinese Academy of Sciences.
Authentication	The cell lines were purchased from the commercial vendors and them have been authenticated for scientific researches.
Mycoplasma contamination	The cell lines used in our study have been confirmed negative for mycoplasma contamination before conducting in vitro study.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used in the study.

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	Il17re-/- mice (Il17retm1Lex/Mmucd) on B6N.129S5 background were provided by Prof. Youcun Qian, Chinese Academy of Sciences. C57BL/6 mice were bought from Shanghai SLRC Laboratory Animal Co., Ltd. (Shanghai, China). All mice were maintained in specific pathogen-free (SPF) animal facilities with a 12-h light and dark circle, temperature of 20-25 ℃ and relative humidity of 50% at Laboratory Animal Center of Tongji University. All animals were age-matched and sex-matched, and then randomized into different groups. The age for all strains of mice was 6-8 weeks.
Wild animals	Wild animals weren't involved in the study.
Reporting on sex	Both male and female mice were involved in our study. All animals were age-matched and sex-matched, and then randomized into different groups. In general, we didn't observe difference across the sex.
Field-collected samples	The study didn't involve samples collected from the field.
Ethics oversight	Experiments were conducted according to the Declaration of Helsinki conventions for the use and care of animals and were approved by the Institutional Animal Care and Use Committee of Tongji University (approval number TJBE00120101).

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

Plants

Seed stocks

Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.

Novel plant genotypes

Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.

Authentication

Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.

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

Lung tissues of the indicated mice were prepared into single cell suspension with the digestion buffer (sterile PBS supplemented with 2.5 mg/mL type 2 collagenase, 1% DNase Ⅰ). After red blood cell lysis and filtering, cells were centrifuged and subsequently pellets were suspended with 30% (v/v) Percoll solution (GE healthcare). After centrifuging, cell pellets were washed and re-suspended in sterile PBS containing 3% (v/v) FBS, 0.05 mM EDTA, 100 U/ml penicillin and streptomycin. An aliquot of suspension was used for cell number counts and the remaining cells was stimulated with cell activation cocktail with Brefeldin A (Biolegend) for 4 h prior to staining for flow cytometry analysis.

Instrument

Flow cytometry analysis was performed by CytoFLEX LX (BECKMAN COULTER). Flow cytometry sorting was performed by FACSAria III (BD).

Software

FlowJo software was used for data analysis of flow cytometry.

Cell population abundance

1.If aiming at live BALF cells, the cell counts of eosinophils, neutrophils and alveolar macrophages would be equal to the product of total cell numbers and the corresponding percentages among single cells;

2.If aiming at leukocytes in mice lung tissue, the cell population abundance was equal to the product of total numbers of leukocytes and the corresponding percentages among live CD45 positive leukocytes as indicated by statistics in FlowJo;

3.If aiming at lymphocytes in mice lung tissue, the cell population abundance was equal to the product of total numbers of lymphocytes and the corresponding percentages among live CD45 positive lymphocytes as indicated by statistics in FlowJo.

Gating strategy

1. Eosinophils(SiglecF+ CD11c-); Alveolar macrophages (SiglecF+ CD11c+); Neutrophils (SiglecF-CD11c-CD11b+Ly6G+): FSC-A/SSC-A (cell populations)---FSC-A/FSC-H (Single cells)---SiglecF-PERCPEF710/CD11c-FITC---Ly6G-PE/CD11b-APC;

2. ILC2 (Live/CD45+/Lineage-/CD90.2+/GATA3+/PE-);ILC3(Live/CD45+/Lineage-/CD90.2+/GATA3-/PE+): FSC-A/SSC-A (cell populations)---FSC-A/FSC-H (Single cells)---Live-dead-FVK510/SSC-A---CD45-APCCY7/SSC-A---Lineage-Pacific blue/CD90.2-FITC---GATA3-APC/RORγt-PE;

3 ILC2 (Live/CD45+/Lineage-/CD90.2+/ST2+/CD25+): FSC-A/SSC-A (cell populations)---FSC-A/FSC-H (Single cells)---Live-dead-FVK510/SSC-A---CD45-APCCY7/SSC-A---Lineage-Pacific blue/CD90.2-FITC---ST2-APC/CD25-PE;

4. ILC2 (Live/CD45+/Lineage-/CD127+/IL-5+/IL-13+); ILC3 (Live/CD45+/Lineage-/CD127+/IL-17A+): FSC-A/SSC-A (cell populations)---FSC-A/FSC-H (Single cells)---Live-dead-FVK510/SSC-A---CD45-APCCY7/SSC-A---Lineage-Pacific blue/CD127-PERCPCY5.5----IFNγ-FITC/SSC-A---IL-5-APC/IL-13-PE---IL-17A-Bv650/SSC-A.

5. ILC3 (CD45low/CD3-/CD90.2high): FSC-A/SSC-A (cell populations)---FSC-A/FSC-H (Single cells)---CD45-APCCY7/SSC-A---CD90.2-FITC/CD3-PERCPCY5.5;

6. Th1 (Live/CD45+/CD3+/CD4+/IFNγ+); Th2 (Live/CD45+/CD3+CD4+/IL-5+IL-13+); Th17 (Live/CD45+/CD3+/CD4+/IL-17A+): FSC-A/SSC-A (cell populations)---FSC-A/FSC-H (Single cells)---Live-dead-FVK510/SSC-A---CD45-APCCY7/SSC-A---CD4-Bv421/CD3-PERCPCY5.5----IFNγ-FITC/SSC-A---IL-5-APC/IL-13-PE---IL-17A-Bv650/SSC-A.

For noncontinuous indicators, positive-negative division was referred to single-staining tube. For continuous indicators, positive-negative division was referred to FMO tubes. .

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