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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	Bulk RNA Seq Data
Data analysis	Conventional flow cytometry data were acquired using BD Diva v9.0. Flow Cytometry data were analyzed using FlowJo v10.8.1 (Treestar). GraphPad Prism (10) was used for graphical and statistical analyses. Images were processed and analyzed using Fiji ImageJ v2.3.0/1.53f51 and QuPath v0.4.3 softwares. 500 ng of lung RNA/sample were used to prepare libraries for sequencing by using KAPA RNA HyperPrep Kits (Roche). Libraries generated with IAV-infected samples were sequenced by Macrogen, while libraries generated from SARS-CoV2 infected samples were sequenced at the Genomic facility of the CIML. All libraries were sequenced using Illumina platforms. Alignments of fastq files obtained after sequencing were generated with STAR 2.7.9a software using the GRCm38 reference genome. The number of reads mapped to each gene was determined with featureCounts v2.0.1 using Mus_musculus.GRCm38.100.gtf annotation file. Gene models (gene symbols of the type "Gmxxxx") were then removed from the feature count file and TPM normalization was applied using the Scuttle package of R 1.0.34.

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

Bulk RNA-Seq data have been deposited into GEO database and will be available for the scientific community as soon as the paper will be accepted for publication. Bulk RNA-seq data have been deposited in the GEO repository under accession no. GSE302271 for IAV-infected samples and GSE302124 for SARS-CoV2-infected samples

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 methods were used to pre-determine sample sizes but our sample sizes are similar to those reported in previous publications (Abbas et al. Nat Immunol 2020 PMID: 32690951; Valente et al. Nat. Immunol. PMID: 36928414).
Data exclusions	No animals or data points were excluded from the analyses
Replication	The number of experiments have been specified in each legend of figure. All experiments, except the Bulk RNA Seq, the lung integrity analysis (EpCAM staining) by immunofluorescence and the qPCR and LegendPLEX experiments on CTR, Irf7KO and pDC-less SBMC, were reproduced at least twice.
Randomization	No randomization was performed in this study.
Blinding	No blinding was performed in this study, excep for anatomopathological analysis

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
☒	☐ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

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

Antibodies

Antibodies used

FACS
anti-BST2 BV786 927 BD biosciences cat# 747603 ; RRID:AB_2744171 1/200
anti-CD11b BUV395 clone M1/70 BD biosciences cat# 565976 ; RRID:AB_2738276 1/400
anti-CD11c BUV737 N418 BD biosciences cat# 749039 ; RRID:AB_2873433 1/200
anti-CD11c BV421 HL3 BD biosciences cat# 562782 ; RRID:AB_2737789 1/500
anti-CD11c BV786 HL3 BD biosciences cat# 563735 ; RRID:AB_2738394 1/200
anti-CD19 PE 1D3 BD biosciences cat# 557399 ; RRID:AB_395050 1/400
anti-CD19 BV711 1D3 BD biosciences cat# 563157 ; RRID:AB_2738035 1/800

anti-CD19 Alexa Fluor 700 1D3 BD biosciences cat# 557958 ; RRID:AB_396958 1/200
anti-CD26 PE H194-112 biolegend cat# 137803 ; RRID:AB_2093729 1/200
anti-CD3 Alexa Fluor 700 500A2 Thermofisher cat# 56-0033-82 ; RRID:AB_837094 1/200
anti-CD3 BV786 145-2C11 BD biosciences cat# 564379 ; RRID:AB_2738780 1/200
anti-CD3 FITC 145-2C11 BD biosciences cat# 553061 ; RRID:AB_394595 1/200
anti-CD4 FITC RM4-5 BD biosciences cat# 553047 ; RRID:AB_394582 1/200
anti-CD45.2 BV605 104 biolegend cat# 109841 ; RRID:AB_2563485 1/200
anti-CD45.2 BUV737 104 BD biosciences cat# 612778 ; RRID:AB_2870107 1/300
anti-CD45.1 Pe-Cy7 A20 BD biosciences cat# 560578 ; RRID:AB_1727488 1/400
anti-CD45.1 BV605 A20 BD biosciences cat# 747743 ; RRID:AB_2872215 1/200
anti-CD64 A647 X54-5/7.1 BD biosciences cat# 558539 ; RRID:AB_647120 1/400
anti-CD69 PE H1.2F3 BD biosciences cat# 561932 ; RRID:AB_394726 1/400
anti-CD69 APC H1.2F3 BD biosciences cat# 560689 ; RRID:AB_1727506 1/400
anti-CD8a BV711 53-6.7 BD biosciences cat# 563046 ; RRID:AB_2737972 1/200
anti-CD86 Pe-Cy7 GL1 BD biosciences cat# 560582 ; RRID:AB_1727518 1/400
anti-CX3CR1 BV711 SA011F11 biolegend cat# 149031 ; RRID:AB_2565939 1/100
anti-human/mouse Granzyme B A647 GB11 biolegend cat# 515406 ; RRID:AB_2566333 1/100
anti-I-A/I-E APC/Cy7 M5/114.15.2 biolegend cat# 107628 ; RRID:AB_2069377 1/200
anti-IFNg A700 XMG1.2 BD biosciences cat# 557998 ; RRID:AB_396979 1/200
anti-IFNg APC XMG1.2 BD biosciences cat# 554413 ; RRID:AB_398551 1/200
anti-Ly6C Alexa Fluor 700 AL-21 BD biosciences cat# 561237 ; RRID:AB_10612017 1/200
anti-Ly6C PE-Cy7 AL-21 BD biosciences cat# 560593 ; RRID:AB_1727557 1/400
anti-Ly6D EF450 49-H4 thermofisher cat# 48-5974-80 ; RRID:AB_2574089 1/400
anti-Ly6D FITC 49-H4 biolegend cat# 138606 ; RRID:AB_11203888 1/600
anti-Ly6G Alexa Fluor 700 1A8 biolegend cat# 561236 ; RRID:AB_10611860 1/200
anti-Ly-6G APC-Cy7 1A8 biolegend cat# 127624 ; RRID:AB_10640819 1/400
anti-NK1.1 Alexa Fluor 700 PK136 BD biosciences cat# 560515 ; RRID:AB_10612564 1/200
anti-NK-1.1 Pe-Cy7 PK136 BD biosciences cat# 552878 ; RRID:AB_394507 1/200
anti-Siglec-F A647 E50-2440 BD biosciences cat# 562680 ; RRID:AB_2687570 1/400
anti-XCR1 antibody BV650 ZET biolegend cat# 148220 ; RRID:AB_2566410 1/800
anti-mouse CD326 A647 G8.8 biolegend cat# 118212 ; RRID:AB_1134101 1/200

IF
Anti-Influenza A NP Monoclonal Antibody (D67J) mouse purified Thermofisher Scientific #cat MA1-7057 ; RRID AB_559682 1/50. D67J
Anti-mouse NeuN rat purified Biolegend #cat 608451 ; RRID AB_2927957 1/200 W18230A
Anti-mouse cFos rabbit purified Synaptic system #cat 226 008 1/200 " Rb108B5"
Anti-mouse Iba1 goat purified Novus biologicals #cat NB100-1028 1/200 Polyclonal
Anti-mouse GFAP chicken purified Novus biologicals #cat NBP1-05198 1/200 Polyclonal
anti-mouse GFP Alexa Fluor rabbit A488 Thermofisher #cat A-21311 ; RRID AB_221477 1/500 Polyclonal
anti-mouse CD45 rat Ef450 Invitrogen #cat 14-0451-82 ; RRID AB_467251 1/300 "30-F11"
Anti-mouse CD326 (Ep-CAM) rat A647 Biolegend #cat 118211 ; RRID AB_1134104 1/200 G8.8
Anti-RFP pre-absorbed rabbit purified Rockland cat# 600-401-379 1/1000 Polyclonal
anti-IAV Hemagglutinin rabbit purified Invitrogen cat# PA5-34930 ; RRID:AB_2552279 1/1000 Polyclonal
Anti-mouse Goat A633 Invitrogen #cat A-21136 ; RRID AB_2535775 1/500 Polyclonal
Anti-rat Goat A568 Invitrogen #cat A-11077 ; RRID AB_2534121 1/500 Polyclonal
Anti-rabbit Goat A488 Invitrogen #cat A-11008 ; RRID AB_143165 1/500 Polyclonal
Anti-goat Donkey A488 Thermofisher #cat A-11055 ; RRID AB_2534102 1/500 Polyclonal
Anti-chicken Donkey Cy3 Merck #cat AP194C 1/500 Polyclonal
Anti-rabbit Donkey A647 Invitrogen #cat A-31573 ; RRID AB_2536183 1/500 Polyclonal

Other reagents
Nuclease Free water Qiagen Cat# 129114
EDTA Merck Cat# E9884
Bovine Serum albumin VWR Cat# 1010-70
Fetuin, Fetal Bovine Serum Merck Cat# 341506
PBS 10x Thermofisher Cat# 14200067
Triton X100 Sigma Cat# X100
Rabbit serum Jackson Immunoresearch Cat# 011-000-120
Antigen Fix Diapth Cat# P0016
RPMI 1640 medium Thermofisher Cat# 21875034
2-Mercaptoethanol (50 mM) Thermofisher Cat# 31350010
RBC lysis buffer Thermofisher Cat# 00-4333-57
DNAase I gradeII from bovine pancreas Merck Cat# 10104159001
Collagenase IV Worthington Biochemical Corporation Cat# WOLS04189
Sucrose Merck Cat# S9378
Sodium phosphate monobasic dihydrate (NaH2PO4) Merck Cat# S9390
Sodium phosphate dibasic (Na2HPO4) Merck Cat# 71640
Fluorescein isothiocyanate–dextran (10kDa) Merck Cat# FD10S
Absolute ethanol molecular grade Thermofisher BP2818-500
Formalin VWR Chemical #9713.5000
Trizol Invitrogen #15596026
Isopropanol Invitrogen #327272500
Paraffin Fischer Histoplast #6.774060
LIVE/DEAD™ Fixable Aqua Dead Cell Stain Kit Thermofisher Cat# L34957
LEGENDplex™ Mouse Anti-Virus Response Panel (13-plex) with V-bottom Plate Biolegend Cat# 740622
ONEGreen Fast qPCR Premix Ozyme Cat# OZYA008-1000

RNeasy Plus Mini Kit Qiagen Cat# 74134
QuantiTect Rev. Transcription Kit Qiagen Cat# 205311
IFN alpha Mouse ELISA Kit Thermofisher Cat# BMS6027
Pierce™ BCA Protein Assay Kits Thermofisher Cat# 23225
iScript™ cDNA Synthesis Kit BioRad Cat #1708891
Solution de formol, tamponnée à pH neutre (10 %) Merck Cat# HT501128-4L
CountBright Plus Absolute – Counting bead Invitrogen Cat# C36995

Validation

Each antibody has been previously titrated for optimal performance in the used assay, according to manufacturer's instructions

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals

C57BL/6J (B6) mice were purchased from Janvier Labs.
Pacsin1-LSL-DTA, SiglechiCre, SiglecHiCre_Pacsin1-LSL-DTA (abbreviated pDC-less), SiglecHiCre_Pacsin1-LSL-tdT_Ifnb1-eYFP (abbreviated SCRIPT), Ifnar1-KO, Stat1-KO were generated by Ciphe.
IfnbEYFP, BDCA2-hDTR, Ifngr1-KO and K18-hACE C57BL/6J mice were purchased from Jackson Laboratories.
TLR7KO mice were kindly provided by L. Alexopoulou, CIML. Ifnl2/3 KO were provided by A. Broggi, CIML. B6.A2G-Mx1 congenic mice were kindly provided by M. Le Bert, TAAM, Orleans, France. IR7KO mice were kindly provided by C. Svanborg, Lund, Sweden.
All genetically modified mouse lines were under C57BL/6J genetic background. We used 6 to 15-week-old mice that were age- and sex-matched.

Mice were housed under 12h dark/12h light cycle, with a temperature range of 20-22 °C and a humidity range of 40-70%.

Wild animals

This study did not use wild animals

Field-collected samples

This study did not involve field-collected samples

Ethics oversight

All animal experiments were performed in accordance with national and international laws for laboratory animal welfare and experimentation (EEC Council Directive 2010/63/EU, September 2010). Protocols were approved by the Marseille Ethical Committee for Animal Experimentation (registered by the Comité National de Réflexion Ethique sur l'Expérimentation Animale under no. 14; APAFIS no. 21626-2019072606014177 v.4 and APAFIS #35098-2022020215455814 v4, APAFIS#26484-2020062213431976 v6).

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

Samples originated from mouse organs.
For cytometry,
Spleens were incubated with a digestion solution (DMEM (Thermofisher), DNase I (Roche Diagnostics), Collagenase IV (Wortington biochemicals) for 25 minutes at 37°C. After enzymatic digestion, the cells were mechanically dissociated and filtered through a 70µM filter. RBC lysis was performed with RBC lysis buffer (Thermofisher) and the reaction was stopped with a Staining Buffer solution (PBS1X, EDTA 2mM, 2% FCS).
Lungs were harvested in DMEM medium. They were cut and transferred to Gentle MACS type C tubes (Miltenyi), containing a digestion solution (DMEM, DNase I (Roche Diagnostics), Collagenase IV (Wortington biochemicals). The tubes were placed on the Gentle MACS and treated with programme 37_m_LDK_1. After digestion, lung cell suspensions were filtered through a 70µm cell strainer and centrifuged. RBC lysis was performed using RBC lysis buffer (eBioscience) and the reaction was stopped with 10mL of Staining Buffer.
For microscopy of the lungs, mouse lungs were perfused with a mixture of 1:2 of AntigenFix (Diapath, containing 4% paraformaldehyde) and 1:2 of Optimal Cutting Temperature (OCT, Sakura Fineteck), collected and fixed in AntigenFix for 4h at 4°C and then washed several times in phosphate buffer (PB; 0.025 M NaH2PO4 and 0.1 M Na2HPO4). Lungs were incubated in PB solution containing 30% Sucrose overnight at 4°C and then embedded in OCT freezing medium, snap frozen and stored at −80 °C. Cryosections, 30 µm, were performed using a microtome (Leica 3050s Cryostat) at temperatures between −24 °C and −20 °C.

For microscopy of the brains, mice were euthanized with overdose of ketamine-xylazine anesthetic and perfused transcardially with phosphate buffered saline (PBS) for antibody staining. Skull caps and meninges were removed, and following a brief wash in PBS, the brains were sectioned sagittally to keep one left side for microscopic analysis and the other for RNA extraction. The left-brain part was incubated for 2 days in formalin 2,5% (diluted in PBS) (Ref: sigma HT501128-4L) then, overnighted in 30% sucrose (Ref: Sigma S0389-1KG). Brains were embedded in OCT freezing medium (Ref: CellPath KMA-0100-00A), snap frozen and stored at −80 °C. Cryosections, 25 µm, were performed using a microtome (Leica 3050s Cryostat) at temperatures between −23 °C and −20 °C.

Instrument

Canto II, LSRII UV, LSR Fortessa X-20

Software

BD DIVAv9.0, FlowJo v10.8.1

Cell population abundance

Describe the abundance of the relevant cell populations within post-sort fractions, providing details on the purity of the samples and how it was determined.

Gating strategy

The gating strategies have been provided in the Extended Data Figures.
Figure 1a :
CD45-pos/live then for red pulp: macrophages CD64-pos CD11b-neg, for neutrophils: Ly6G-pos while for B cells in CD19-pos; for NK and T cells: Ly6G-neg CD19-neg/CD3-neg NK1.1-pos versus CD3-pos NK1.1-neg, respectively; for pDC: Ly6G-neg CD19-neg/CD3-neg NK1.1-neg/CD11b-neg/CD11c-pos BST2-pos and for cDC: Ly6G-neg CD19-neg/CD3-neg NK1.1-neg/CD11c-pos MHC II-pos.

Figure 1c :
CD45pos/live/Ly6Gneg CD19neg CD3neg NK1.1neg (lineage-) then for cDC: CD11c-pos MHC II- pos/XCR1-pos (for cDC1) versus CD11bpos (for cDC2); for pDC and tDC: Ly6G-neg CD19-neg CD3-neg NK1.1-neg (lineage-)/XCR1-neg CD11b-neg/ CD11c-pos BST2-pos/Ly6D-pos CX3CR1-neg (for pDC) versus Ly6D-neg CX3CR1-pos/Ly6Chigh (for tDChigh) or Ly6Clow (for tDClow).

Figure 6a :
CD45pos/live then for alveolar macrophages: SiglecF-pos CD11b-neg while for eosinophils SiglecF-pos CD11b-pos; for pDC and tDC: SiglecF-neg/Ly6G-neg CD19-neg CD3-neg NK1.1-neg (lineage-neg)/Xcr1-neg CD11b-neg/CD11c-pos Bst2-pos/Ly6D-pos CX3CR1-neg (for pDC) versus Ly6D-neg CX3CR1-pos (for tDC); for cDC: SiglecF-neg/Ly6G-neg CD19-neg CD3-neg NK1.1-neg (lineage-neg)/CD11c-pos MHC II-pos/Xcr1-pos CD11b-neg (for cDC1) versus Xcr1-neg CD11b-pos (for cDC2).

Figure 6b :
CD45-pos/live/SiglecF-neg, then for neutrophils: Ly6G-pos while for B cells CD19-pos; for NK and T cells: Ly6G-neg CD19-neg/ CD3-neg NKp46-pos (for NK) versus CD3-pos NKp46-neg (for T cells); for monocytes: CD3-neg NKp46-neg/CD11b-pos Ly6C-pos.

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