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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	SpectroFlow (v3.0.3) was used for flow cytometry data collection on Cytek® Aurora; ZEN3.1 (blue edition) was used for PPFE-immunofluorescence staining image data collection on ZEISS Axioscan 7; Aperio Console DX (v102.0.4.46) was used for histology & immunhistochemistry staining image data collection on Aperio AT2 DX digital slide scanner. LAS X (5.3.0) was used for immunofluorescence staining image data collection on Leica Stellaris 8. Imaris (v10.1, Oxford Instruments) was used for whole-mount tissue immunofluorescence staining image data collection and analysis.
Data analysis	Flow cytometry data analysis: FlowJo 10 (v10.5.3); Statistic: GraphPad Prism (v10); Immunofluoresence/Immunochemistry image analysis & histology tumor burden analysis: QuPath (v0.2.3); scRNA-seq analysis: R (v4.4.2), Cell Ranger (v6.0), Seurat R package (v4.3.0); survival package in R (v3.6-4); The R scripts that support the findings of this study are available from https://github.com/KWhh666/Manuscript_2024, and https://doi.org/10.5281/zenodo.17841956.

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

Raw and fully processed scRNA-seq data reported in this study have been deposited in the Gene Expression Omnibus and are publicly available under accession numbers GSE275770. For human survival analysis, RNA-seq gene expression profiles and associated clinical data from 518 lung adenocarcinoma (LUAD) patients were obtained from The Cancer Genome Atlas (TCGA) (https://portal.gdc.cancer.gov/). For analysis of lung-innervating VSN populations previously described by Zhao et al, the dataset is publicly available under the accession number GSE192987.

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	The sample sizes used in this paper were selected based on those used in previous publications (Jin et al. Cell 2019). Exact sample sizes are described in each figure legends or Methods.
Data exclusions	Data from mice with technical failure in procedures (such as VNG injection, brain injection or tumor induction) were excluded.
Replication	All the experimental findings were reproduced and validated by at least three biological replicates in at least two independent experiments.
Randomization	Tumors were initiated in age- and sex-matched mice and assigned randomly to experimental and control groups before treatment.
Blinding	The investigators were not blinded to group allocation during treatments but were blinded during mice harvest and data collection.

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. For CD8 and Arg1 FFPE-IF staining: anti-CD8 (4SM15, 1:250, 14-0808-82, eBioscience); anti-Arg1 (D4E3M, 1:250, 93668, Cell Signaling Technology).

2. For in vivo mice experiments: anti-CD4 (GK1.5, BP0003-1, BioXCell), anti-CD8 (2.43, BE0061, BioXCell). Rat IgG2b (LTF-2, BE0090, BioXCell) was used as the isotype control.

3. For immunofluorescence staining: anti-TH (1:250, AB1542, Abcam), anti-cFOS (1:300, 2250, Cell Signaling Technology), anti-TUBB3 (1:1000, ab190575, Abcam), anti-RFP (1:1000, 600-401-379, Rockland), anti-HB-EGF (1:800, AF-259-NA, R&D system), anti-TRPV1 (1:1000, ACC-030, Alomone Labs), and anti-cFOS (1:1000, ab222699, Abcam), anti-RFP (1:200, 200-101-379, Rockland), anti-RFP (1:200, 200-301-379, Rockland), anti-GFP (1:200, GFP-1020, Aves labs), anti-VAChT (1:250, 139103, Synaptic Systems).

4. For flow cytometry: LIVE/DEAD™ Fixable Blue dye (1:1000, L23105, Invitrogen), Alexa Fluor 532-I-A/I-E (M5/114.15.2, 1:800, 58-5321-82, invitrogen), Alexa Fluor 647-SiglecF (E50-2440, 1:600, 562680, BD), Alexa Fluor 647-TCF1 (C63D9, 1:600, 6709S, Cell Signaling Technology), Alexa Fluor 700-Ki67 (B56,1:600, 561277, BD), APC/Cy7-I-A/I-E (M5/114.15.2, 1:2500, 107628, BioLegend), APC/Fire810-B220 (RA3-6B2, 1:800, 103278, BioLegend), APC-IRF8 (V3GYWCH, 1:600, 17-9852-80, Invitrogen), BUV395-CD45.1 (A20, 1:300, 565212, BD), BUV563-CD11c (N418, 1:800, 749040, BD), BUV615-CD44 (IM7, 1:1500, 751414, BD), BUV661-CCR7 (4B12,1:400, 741677, BD), BUV737-Ly6G (1A8, 1:800, 741813, BD), BUV805-CD11b (M1/70, 1:800, 741934, BD), BV421-CD86 (GL-1, 1:600, 105005, BioLegend), eFlour450-TCRd (GL3, 1:300, 48-5711-80, Invitrogen), BV570-CD8a (53-6.7, 1:600, 100740, BioLegend), BV570-CD90.2 (30-H12, 1:600, 105329, BioLegend), BV605-CD45.1 (A20, 1:1000, 110736, BioLegend), BV605-CD45.2 (104, 1:400, 109841, BioLegend), BV605-CD45.2 (104, 1:600, 109836, BioLegend), BV605-Tim-3 (RMT3-23, 1:400, 119721, BioLegend), BV605-TNFα (MP6-XT22, 1:1000, 506329, BioLegend), PE-TNFα (MP6-XT22, 1:1500, 506306, BioLegend), BV650-IL-17A (TC11-18H10.1, 1:600, 506930, BioLegend), BV650-XCR1 (ZET, 1:600, 148220, BioLegend), BV711- I-A/I-E (M5/114.15.2, 1:2500, 107643, BioLegend), BV711-KLRG1 (2F1/KLRG1, 1:800, 138427, BioLegend), BV711-NK1.1 (PK136, 1:600, 108745, BioLegend), BV711-Tim-3 (RMT3-23, 1:300, 119727, BioLegend), BV750-CD11b (M1/70, 1:3000, 101267, BioLegend), BV750-CD4 (GK1.5, 1:600, 100467, BioLegend), BV750-CD45.2 (104, 1:600, 109857, BioLegend), BV785-CD4 (GK1.5, 1:800, 100467, BioLegend), BV785-PD-1 (29F.1A12, 1:800, 135225, BioLegend), BV786-SiglecF (E50-2440, 1:500, 740956, BD), PE-Cy7-CD101 (Moushi101, 1:800, 25-1011-82, Invitrogen), APC-RORγt (B2D, 1:600, 17-6981-82, Invitrogen), eFluor450-Arg1 (A1exF5, 1:1200, 48-3697-82, Invitrogen), PE-Arg1(A1exF5, 1: 2000,12-3697-82, Invitrogen), FITC-CD103 (2E7, 1:500, 121419, BioLegend), FITC-IFNγ (XMG1.2, 1:500, 505806, BioLegend), FITC-Ly6C (AL-2T, 1:1000, 127645, BioLegend), Alexa Fluor 488-TCF1 (C63D9, 1:600, 2203S, Cell Signaling Technology), PE/CF594-CD45 (30-F11, 1:200, 562420, BD), PE/Cy5-PD-L1 (10F.9G2, 1:2400, 124344, BioLegend), PE/Cy7-PD-1 (RMP1-30, 1:600, 109110, BioLegend), PE-CD80 (16-10A1, 1:1500, 555769, BD), PE-IL-12p40 (C15.6, 1:600, 554479, BD), PerCP/eFluor710-CD172a (P84, 1:1000, 46-1721-82, eBioscience), PerCP/eFluor710-Eomes (Dan11mag, 1:700, 46-4875-82, eBioscience), PerCP-Ly6C (HK1.4, 1:800, 128028, BioLegend), Spark Blue 550-CD8 (53-6.7, 1:600, 100780, BioLegend), PE/Cy5-CD127(A7R34, 1:400, 15-1271-81, Invitrogen).

5. For Ce3D imaging,
CD11c N418 eFluor450 Armenian hamster / IgG eBioscience 48-0114-82 1:50
MHC-II M5/114.15.2 Brilliant Violet 510 Rat IgG2b, κ BioLegend 107636 1:200
TUBB3 TUJ1 AF488 Mouse IgG2a, κ BioLegend 801203 1:100
CD3 17A2 SparkRed718 Rat IgG2b, κ BioLegend 100282 1:50
CD45 30-F11 DyLight 755 Rat IgG2b, κ Novus NB100-77417IR 1:50
CD103 Goat polyclonal Unconjugated Goat IgG R&D AF1990 1:200
Donkey anti Goat IgG Donkey polyclonal Alexa Fluor Plus 800 Donkey IgG Thermo A32930 1:200

Validation

These antibodies have been validated for the specificity and application by the manufactures and numerous citations (see detailed reference on the website). All antibodies used for flow cytometry are commercially available.

Live Died Blue (1:1000, L23105, Invitrogen): https://www.thermofisher.com/order/catalog/product/L23105;
Alexa Fluor 488-TCF1 (C63D9, 1:600, 2203S, Cell Signaling Technology): https://www.cellsignal.com/products/antibody-conjugates/tcf1-tcf7-c63d9-rabbit-mab-alexa-fluor-488-conjugate/6444;
Alexa Fluor 532-I-A/I-E (M5/114.15.2, 1:800, 58-5321-82, invitrogen): https://www.thermofisher.com/antibody/product/MHC-Class-II-I-A-I-E-Antibody-clone-M5-114-15-2-Monoclonal/58-5321-82;
Alexa Fluor 647-SiglecF (E50-2440, 1:600, 562680, BD): https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/alexa-fluor-647-rat-anti-mouse-siglec-f.562680;
Alexa Fluor 647-TCF1 (C63D9, 1:600, 6709S, Cell Signaling Technology): https://www.cellsignal.com/products/antibody-conjugates/tcf1-tcf7-c63d9-rabbit-mab-alexa-fluor-647-conjugate/6709;

Alexa Fluor 700-Ki67 (B56,1:600, 561277, BD): https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/alexa-fluor-700-mouse-anti-ki-67.561277;
APC/Cy7-I-A/I-E (M5/114.15.2, 1:2500, 107628, BioLegend): https://www.biolegend.com/en-us/lyophilized-control-cells/apc-cyanine7-anti-mouse-i-a-i-e-antibody-5966?GroupID=BLG11931;
APC/Fire810-B220 (RA3-6B2, 1:800, 103278, BioLegend): https://www.biolegend.com/fr-lu/products/apcfire-810-anti-mouse-human-cd45r-b220-antibody-19557?GroupID=GROUP658;
APC-IRF8 (V3GYWCH, 1:600, 17-9852-80, Invitrogen): https://www.thermofisher.com/antibody/product/IRF8-Antibody-clone-V3GYWCH-Monoclonal/17-9852-82;
BUV395-CD45.1 (A20, 1:300, 565212, BD): https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/buv395-mouse-anti-mouse-cd45-1.565212;
BUV563-CD11c (N418, 1:800, 749040, BD): https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/buv563-hamster-anti-mouse-cd11c.749040;
BUV615-CD44 (IM7, 1:1500, 751414, BD): https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/BUV615-Rat-Anti-Mouse-CD44.751414/;
BUV615-CD44 (IM7, 1:800, 751414, BD): https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/BUV615-Rat-Anti-Mouse-CD44.751414/;
BUV661-CCR7 (4B12,1:400, 741677, BD): https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/buv661-mouse-anti-human-ccr7-cd197.749824;
BUV737-Ly6G (1A8, 1:800, 741813, BD): https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/buv737-rat-anti-mouse-ly-6g.741813;
BUV805-CD11b (M1/70, 1:800, 741934, BD): https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/buv805-rat-anti-cd11b.741934;
BV421-CD44 (IM7, 1:1500, 103040, BioLegend): https://www.biolegend.com/en-us/explore-new-products/brilliant-violet-421-anti-mouse-human-cd44-antibody-7225;
BV421-CD86 (GL-1, 1:600, 105005, BioLegend): https://www.biolegend.com/en-us/products/brilliant-violet-421-anti-mouse-cd86-antibody-20728?GroupID=BLG10719;
eFlour450-TCRd (GL3, 1:300, 48-5711-80, Invitrogen): https://www.thermofisher.com/antibody/product/TCR-gamma-delta-Antibody-clone-eBioGL3-GL-3-GL3-Monoclonal/48-5711-82;
BV570-CD8a (53-6.7, 1:600, 100740, BioLegend): https://www.biolegend.com/en-us/products/brilliant-violet-570-anti-mouse-cd8a-antibody-7377?GroupID=BLG2559;
BV570-CD90.2 (30-H12, 1:600, 105329, BioLegend): https://www.biolegend.com/en-us/products/brilliant-violet-570-anti-mouse-cd90-2-thy1-2-antibody-7514?lang=de;
BV605-CD45.1 (A20, 1:1000, 110736, BioLegend): https://www.biolegend.com/en-us/products/brilliant-violet-650-anti-mouse-cd45-1-antibody-7644?GroupID=BLG1933;
BV605-CD45.2 (104, 1:400, 109841, BioLegend): https://www.biolegend.com/nl-nl/products/brilliant-violet-605-anti-mouse-cd45-2-antibody-9695?GroupID=BLG7009;
BV605-CD45.2 (104, 1:600, 109836, BioLegend): https://www.biolegend.com/en-us/products/brilliant-violet-605-anti-mouse-cd45-antibody-8721?GroupID=BLG6831;
BV605-TIM3 (RMT3-23, 1:400, 119721, BioLegend): https://www.biolegend.com/en-us/products/pe-anti-mouse-cd366-tim-3-antibody-2657?GroupID=BLG10656;
BV605-TNFα (MP6-XT22, 1:1000, 506329, BioLegend): https://www.biolegend.com/nl-nl/products/brilliant-violet-605-anti-mouse-tnf-alpha-antibody-7682?GroupID=GROUP24;
PE-TNFα (MP6-XT22, 1:1500, 506306, BioLegend): https://www.biolegend.com/nl-nl/products/pe-anti-mouse-tnf-alpha-antibody-978;
BV650-IL-17A (TC11-18H10.1, 1:600, 506930, BioLegend): https://www.biolegend.com/en-ie/products/brilliant-violet-650-anti-mouse-il-17a-antibody-7684;
BV650-XCR1 (ZET, 1:600, 148220, BioLegend): https://www.biolegend.com/en-ie/explore-new-products/brilliant-violet-650-anti-mouse-rat-xcr1-antibody-12421?GroupID=GROUP20;
BV711-I-A/I-E (M5/114.15.2, 1:2500, 107643, BioLegend): https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/bv711-rat-anti-mouse-i-a-i-e.563414;
BV711-KLRG1 (2F1/KLRG1, 1:800, 138427, BioLegend): https://www.biolegend.com/nl-be/products/brilliant-violet-711-anti-mouse-human-klrg1-mafa-antibody-13583;
BV711-NK1.1 (PK136, 1:600, 108745, BioLegend): https://www.biolegend.com/en-us/search-results/brilliant-violet-711-anti-mouse-nk-1-1-antibody-9576?GroupID=GROUP20;
BV711-Tim-3 (RMT3-23, 1:300, 119727, BioLegend): https://www.biolegend.com/en-us/soluble-mhc/brilliant-violet-711-anti-mouse-cd366-tim-3-antibody-14918?GroupID=BLG10656;
BV750-CD11b (M1/70, 1:3000, 101267, BioLegend): https://www.biolegend.com/en-us/products/purified-anti-mouse-human-cd11b-antibody-351?GroupID=BLG10660;
BV750-CD4 (GK1.5, 1:600, 100467, BioLegend): https://www.biolegend.com/en-us/punchout/search-results/brilliant-violet-750-anti-mouse-cd4-antibody-15756;
BV750-CD45.2 (104, 1:600, 109857, BioLegend): https://www.biolegend.com/en-us/products/brilliant-violet-750-anti-mouse-cd45-2-antibody-18842;
BV785-CD4 (GK1.5, 1:800, 100467, BioLegend): https://www.biolegend.com/en-us/productstab/brilliant-violet-785-anti-mouse-cd4-antibody-11948;
BV785-PD-1 (29F.1A12, 1:800, 135225, BioLegend): https://www.biolegend.com/en-us/search-results/brilliant-violet-785-anti-mouse-cd279-pd-1-antibody-9874;
BV785-PD-L1 (10F.9G2, 1:800, 124331, BioLegend): https://www.biolegend.com/en-us/products/brilliant-violet-785-anti-mouse-cd274-b7-h1-pd-l1-antibody-13497;
BV786-SiglecF (E50-2440, 1:500, 740956, BD): https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/bv786-rat-anti-mouse-siglec-f.740956;
PE-Cy7-CD101 (Moushi101, 1:800, 25-1011-82, Invitrogen): https://www.thermofisher.com/antibody/product/CD101-Antibody-clone-Moushi101-Monoclonal/25-1011-82
PE-Cy5.5-iNOS (CXNFT, 1:800, 35-5920-82, Invitrogen): https://www.thermofisher.com/antibody/product/iNOS-Antibody-clone-CXNFT-Monoclonal/35-5920-82
APC-RORγt (B2D, 1:600, 17-6981-82, Invitrogen): https://www.thermofisher.com/antibody/product/ROR-gamma-t-Antibody-clone-B2D-Monoclonal/17-6981-82

eFluor450-Arg1 (A1exF5, 1:1200, 48-3697-82, Invitrogen): https://www.thermofisher.com/antibody/product/Arginase-1-Antibody-clone-A1exF5-Monoclonal/48-3697-82;
PE-Arg1(A1exF5, 1: 2000,12-3697-82, Invitrogen): https://www.thermofisher.com/antibody/product/Arginase-1-Antibody-clone-A1exF5-Monoclonal/12-3697-82;
FITC-CD103 (2E7, 1:500, 121419, BioLegend): https://www.biolegend.com/en-us/explore-new-products/fitc-anti-mouse-cd103-antibody-7053;
FITC-IFNγ (XMG1.2, 1:500, 505806, BioLegend): https://www.biolegend.com/en-us/products/fitc-anti-mouse-ifn-gamma-antibody-995?GroupID=GROUP24;
FITC-Ly6C (AL-2T, 1:1000, 127645, BioLegend): https://www.biolegend.com/en-us/explore-new-products/fitc-anti-mouse-ly-6c-antibody-4896;
Pacific Blue -Granzyme B (GB11, 1:500, 515408, BioLegend): https://www.biolegend.com/en-us/products/pacific-blue-anti-human-mouse-granzyme-b-antibody-8612?GroupID=BLG15670;
PE/CF594-CD45 (30-F11, 1:200, 562420, BD): https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/pe-cf594-rat-anti-mouse-cd45.562420;
PE/Cy5-PD-L1 (10F.9G2, 1:2400, 124344, BioLegend): https://www.biolegend.com/ja-jp/products/percp-cyanine5-5-anti-mouse-cd274-b7-h1-pd-l1-antibody-13667;
PE/Cy7-PD-1 (RMP1-30, 1:600, 109110, BioLegend): https://www.biolegend.com/en-us/cell-separation/pe-cyanine7-anti-mouse-cd279-pd-1-antibody-3612;
PE-CD80 (16-10A1, 1:1500, 555769, BD): https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/pe-hamster-anti-mouse-cd80.553769;
PE-IL-12(p40/p70) (C15.6, 1:600, 554479, BD): https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/pe-rat-anti-mouse-il-12-p40-p70.562038;
PerCP/Cy5.5-CD4 (RM4-5, 1:600, 100540, BioLegend): https://www.biolegend.com/en-us/products/percp-cyanine5-5-anti-mouse-cd4-antibody-4230?GroupID=BLG4211;
PerCP/eFluor710-CD172a (P84, 1:1000, 46-1721-82, eBioscience): https://www.thermofisher.com/antibody/product/CD172a-SIRP-alpha-Antibody-clone-P84-Monoclonal/46-1721-82;
PerCP/eFluor710-Eomes (Dan11mag, 1:700, 46-4875-82, eBioscience): https://www.thermofisher.com/antibody/product/EOMES-Antibody-clone-Dan11mag-Monoclonal/46-4875-82;
PerCP-Ly6C (HK1.4, 1:800, 128028, BioLegend): https://www.biolegend.com/en-us/search-results/percp-anti-mouse-ly-6c-antibody-7166?GroupID=BLG7242;
Spark Blue 550-CD8 (53-6.7, 1:600, 100780, BioLegend): https://www.biolegend.com/de-de/products/spark-blue-550-anti-mouse-cd8a-antibody-18489?GroupID=BLG6765;
PE/Cy5-CD127(A7R34, 1:400, 15-1271-81, Invitrogen): https://www.thermofisher.com/antibody/product/CD127-Antibody-clone-A7R34-Monoclonal/15-1271-82.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	KP tumor cell line was derived from autochthonous lung tumors grown in Kras-G12D/+; p53-fl/fl; Rosa26-lsl-tdTomato mice infected with Ad-SPC-Cre in the lab. NGF knockout tumor cell line was generated by transducing KP cell line with lentivirus expressing cas9 and sgRNA targeting the Rosa26 locus (control) or sgRNA targeting NGF.
Authentication	The KP tumor cell line identity was confirmed by PCR genotyping and characteristic morphology. NGF knockout was verified by Western Blot.
Mycoplasma contamination	The cell lines were treated with MycoZap™ Plus-CL (Lonza, 195262) and tested for no mycoplasma containmination with Universal Mycoplasma Detection kit (ATCC, 30-1012K).
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	In vivo experiments were performed using mice on a C57BL/6 background unless otherwise specified. The following mouse strains were used in the study: KrasLSL-G12D/+; p53fl/fl (KP), KP; lsl-tdTomato, Wild type C57BL/6J (000664, JAX), B6.129-Trpv1tm1(cre)Bbm/J (Trpv1-cre, 017769, JAX), C57BL/6-Gt(ROSA)26Sortm1(HBEGF)Awai/J (lsl-DTR, 007900, JAX), Slc17a6tm2(cre)Lowl/J (Vglut2-Cre, 016963, JAX), Tg(Actl6b-Cre)4092Jiwu/J (Baf53b-Cre, 027826, JAX), B6.129-Ppargtm2Rev/J (Pparγfl/fl, 004584, JAX) and B6.Cg-Tg(Itgax-cre)1-1Reiz/J (CD11c-cre, 008068, JAX), Npy2r-ires-Cre, P2ry1-ires-Cre, Trpv1-dtr, Adrβ2-/- and Batf3-/-. Mice were 6–12 weeks of age at the start of experiments.
Wild animals	Study did not involve wild animals.
Reporting on sex	Both male and female mice were included in all experiments reported in this manuscirpt, as there were no differences between sexes observed in any of our biological or functional assays.
Field-collected samples	Study did not involve samples collected from the field.
Ethics oversight	All animal procedures were performed in accordance with institutional guidelines and approved by the Institutional Animal Care and

Ethics oversight	Use Committee (IACUC) and the Institutional Biosafety Committee of the University of Pennsylvania, Yale University, or St. Jude's Children's Research Hospital.

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	As described in the Methods section, mice were injected retro-orbitally with PE-CF594 conjugated anti-CD45 antibody (30-F11, BD Bioscience) 2 min prior to euthanasia to exclude the circulating immune cells from analysis. Lungs were collected, dissociated with the gentleMACS dissociator system (Miltenyibiotec), and digested with 125U/mL Collagenase IV (Worthington Biochemical) and 100U/mL DNase I (Roche) at 37C,100 rpm for 30 min. Digested lung tissue was then filtered with a 100 µm cell strainer. Lymph node samples were grinded up and passed through a 70 µm cell strainer. Red blood cells were lysed with ammonium chloride–potassium bicarbonate (ACK) lysis buffer. After blocking FcR with the Fc-block reagent (2.4G2, BD Bioscience), single-cell suspensions were stained with antibodies. Dead cells were stained with LIVE/DEAD™ Fixable Blue dye. For intracellular cytokine staining, cells were pre-incubated with the Cell Stimulation Cocktail (eBioscience) and the Protein Transport Inhibitor Cocktail (eBioscience) for 4 hours at 37 °C before surface staining. Transcription factor staining was performed using the Foxp3 Fixation/Permeabilization Solution Kit (eBioscience).
Instrument	Cytek® Aurora (Cytek Bioscience)
Software	Flow data collection: SpectroFlow (v3.0.3) Flow data analysis: FlowJo 10 (v10.5.3)
Cell population abundance	For flow cytometry, live cell abundance was determined by Live/dead staining. For FACS, cell purity was confirmed to be >98%.
Gating strategy	Gating strategies are provided in Extended Data 5d-e 1). SSC vs. FSC gating to exclude debris. 2). FSC-H vs. FSC-A gating to exclude doublets. 3). Live/Dead Blue vs. FSC-A to exclude dead cells. 4). CD45 vs. CD11b gating to exclude non-immune cells. 5). ivCD45 vs. FSC-A gating to distinguish tissue-resident vs. circulating cells. 6). CD8 or CD90.2 vs. B220 gating to distinguish myeloid vs. lymphoid populations. 7.1). For myeloid gating: Ly6G vs. CD11b for neutrophils -> SiglecF vs. CD11c for AMs -> SiglecF vs. CD11b for eosinophils -> Ly6C vs. CD11b for monocytes -> MHC-II vs. CD11c for DCs -> XCR1 vs. CD172a for cDC1s and cDC2s. 7.2). For lymphoid gating: CD8 vs. CD4 for CD8, CD4, and double negative T cells -> for double negative T cells, TCRd vs. FSC-A to distinguish gdT cells -> from TCRd- population, CD127 vs. FSC-A to distinguish ILCs. All the target and/or functional populations were further determined by specific markers in Fig. 3, Extended Data Fig. 6h, Extended Data Fig. 9p.

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