nature portfolio

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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	CytExpert (Beckton Coulter), FACS Diva (BD Biosciences), Light Cycler Software v 4.05 (Roche)
Data analysis	FlowJo Software v8, v10 (Treestar), Prism v8, v10.0.3 (GraphPad), Excel v16 (Microsoft), Image J v1.53t

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

Source Data are provided for all figures.

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 methods were performed to pre-determine sample size, but our sample sizes were similar to those in previous publications from our lab (ref. 9)
Data exclusions	CD8 antibody-injected mice whose circulating CD8+ T cells were not depleted were excluded from the experiment.
Replication	Experiments were performed at least twice, and the number of experiments performed are stated in the figure legends.
Randomization	Mice of the same age and sex were randomly assigned to the experimental groups.
Blinding	Plaque assays were analyzed by an investigator blinded to the sample identities. For tissue harvest, investigators were not blinded to the genotype of the mice, but tissue processing order was randomized. Other experiments were not blinded, but samples were processed and analyzed in an identical manner. For flow cytometry of cells isolated from mice tissues and cultures, a master-mix of antibodies was made and added to all samples, and all data were analyzed with the same gating irrespective of the genotype or treatment. Similar master-mixes were made for RT-qPCR assays.

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

Antibodies were used at a 1:100 dilution.
CD3 (145-2C11) Pacific Blue, Biolegend 100334, unavailable
CD3 (17A2) FITC, Biolegend 100204, unavailable
CD3 (17A2) PE, Biolegend 100206, unavailable
CD4 (GK1.5) APC, Biolegend 100412, unavailable
CD8a (53-6.7) FITC, Biolegend 100706, unavailable
CD8a (53-6.7) PerCp-Cyanine5.5, Biolegend 100734, unavailable
CD44 (IM7) Alexa Fluor 700, Biolegend 103026, unavailable
CD103 (2E7) Pacific Blue, Biolegend121418, unavailable
CD103 (2E7) PE/Dazzle 594, Biolegend 121430, unavailable
CD103 (2E7) Pacific Blue, Biolegend 121418, unavailable
CD103 (2E7) PE, Biolegend 121406, unavailable
CCR7 (4B12) PE, Biolegend 120106, unavailable
CD69 (H1.2F3) PE-Cyanine7, Biolegend 104512, unavailable
CD45.1 (A20) Pacific Blue, Biolegend 110722, unavailable
CD45.1 (A20) PE, Biolegend 110708, unavailable
CD45.2 (104) FITC, Biolegend 109806, unavailable
CD45.2 (104) Pacific Blue, Biolegend 109820, unavailable
CD49d (R1-2) APC, Biolegend 103622, unavailable
CD124 (IL4-Ra) (I015F8) PE-Cyanine7, Biolegend 144806, unavailable
TNFa (MP6-XT22) PE-Cyanine7, Biolegend 506324, unavailable
IFN-g (XMG1.2) Brilliant violet 421, Biolegend 505830, unavailable
Human CD2 (RPA-2.10) biotin, Biolegend 300204, unavailable
F4/80 (BM8) Pacific blue, Biolegend 123124, unavailable
B220 (RA3-6B2) Pacific blue, Biolegend 103227, unavailable
CD11b (M1/70) Pacific blue, Biolegend 101224, unavailable
CD11c (N418) Pacific blue, Biolegend 117322, unavailable
CD4 (RM4-5) Pacific blue, Biolegend 100531, unavailable
CD107a (1DB4) APC, Biolegend 121615, unavailable
CD49a (Ha31/8) Alexa Fluor647, BD Biosciences 562113, unavailable
Smad2 (pS465/pS467)/Smad3 (pS423/pS425) PE, BD Biosciences 562586, unavailable
Eomes (Dan11mag) eFluor 450, ThermoFisher Scientific 48-4875-82, unavailable
TGF-BRII (polyclonal) PE, R&D Systems FAB532P, unavailable
CCR7 (4B12) PE, Biolegend 120106, unavailable
TruStain FcX (93), Biolegend 101321, unavailable
Ultra-Leaf CD3 (145-2C11), Biolegend 100339, unavailable
Ultra-Leaf CD28 (37.51), Biolegend 102116, unavailable

For CD8+ T cell depletion:
CD8a (YTS169.4), BioXCell BP0117, unavailable (0.3 mg/injection/mouse)
For IL-4 neutralization:
IL-4 (11B11), BioXCell BP0045, unavailable (0.5 mg/injection/mouse)
Rat IgG1 isotype control, BioXcell BP0088 (0.5 mg/injection/mouse)

Validation

All of the antibodies used were commercially validated as described by the manufacturer. Validation information can be found on the manufacturers websites:
https://www.biolegend.com, https://www.rndsystems.com, https://www.thermofisher.com, https://bioxcell.com
Doses used for depletion of CD8+ T cells were based on published studies from our lab (ref. 9), and for IL-4 neutralization in dermatitis was from (ref. 52).

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

Mice aged between 6 and 12 weeks were used in these studies.
Mice were on a C57Bl/6 background and include:
CD45.1+ (B6.SJL-Ptprca Pepcb/BoyJ), Jackson Laboratories, Stock #002014
OT-I (C57BL/6-Tg(TcraTcrb)1100MJb/J), Jackson Laboratories, Stock #003831
Stat6-/- (B6.129S2(C)-Stat6tm1Gru/J), Jackson Laboratories, Stock #005977
Il4-/- (B6.129P2-Il4 tm1Cgn/J), Jackson Laboratories, Stock #002253
Il4ra-/-, F. Finkelman
4Get, C. Sokol
KN2, K. Fairfax
Cd8Cre+ (C57Bl/6-Tg(Cd8-cre)Itan/J) , Jackson Laboratories Stock #008766

	Il4rafl/fl S. Islam CD45.1+ OT-I, Stat6-/- OT-I, Il4ra-/- OT-I, IL4ra-/- CD45.1+CD45.2+, Il4rafl/- and Cd8cre+Il4rafl/- mice were generated by crossing the strains listed above.
Wild animals	No wild animals were used.
Reporting on sex	Female mice were used for experiments. Female mice were used to avoid skin damage by fighting males.
Field-collected samples	No field-collected samples.
Ethics oversight	All experimental studies were approved (protocol 2012N000194) and performed in accordance with guidelines and regulations implemented by the MGH Institutional Animal Care and Use Committee (IACUC).

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	Spleen, thymus and LN were mashed, filtered through a 70 µm cell strainer, and red blood cells were lysed with ACK lysis buffer or with Hybri-Max RBC lysis buffer (Sigma). Skin was processed as previously described (ref. 9. A 1 cm2 area of flank skin was cut into small pieces and placed in 5 mL of digestion buffer (DMEM; 2% FBS; 1% HEPES; 100 µg/mL DNase; 100 µg/mL Liberase TM) for 40 minutes at 37°C under agitation, then quenched with 1.5 mM EDTA and blended using a gentleMACS tissue blender (Miltenyi, C tubes, m_impTumor_01 protocol).
Instrument	Stained samples were acquired using LSRII, Fortessa X20 (BD), or Cytoflex (Beckton Coulter) flow cytometers.
Software	Data were analyzed using FlowJo Software (Treestar)
Cell population abundance	Cells were purified using Miltenyi CD4 isolation kit, Miltenyi CD8 isolation kit, or Stemcell technologies naive CD8 T cell isolation kit. Cell purity was routinely >95% pure.
Gating strategy	Doublets were excluded using FSC-A/FSC-H. Lymphocytes were then gated based on size FSC-A/SSC-A. Dead cells were excluded by fixable viability dye (eFluor506, or eFluor780, Thermo Fisher). For adoptive transfer experiments, cells were gated on CD3+ CD8+ T cells, then on CD45.1 vs. CD45.2. Similar results were obtained when cells were first gated on CD45.1 vs. CD45.2. For tetramer staining, a dump gate was included to exclude B220+, CD11b+, CD11c+, F4/80+ and CD4+ cells. Gating strategy to identify tetramer+ cells is included in the extended data figures. Fluorescence minus one staining or isotype control staining was used to determine positive and negative populations.

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