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Reporting Summary

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Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. 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
☐	☒	An indication of 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 statistics 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
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	No software were used for data collection in this study.
Data analysis	We used GraphPad Prism 7 for unpaired two-tail Student t-test, one/two-way ANOVA followed by multiple-comparisons test and Kaplan-Meier method. FlowJo 10.0 FACS software were used to analyze data obtained from Flow Cytometer.

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/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

The datasets generated during the current study are available from the corresponding author on reasonable request.

Field-specific reporting

Please select 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/authors/policies/ReportingSummary-flat.pdf

Life sciences study design

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

Sample size	For in vitro and mouse in vivo experiments, sample sizes were chosen according to the basis of previous publications in the immunology field, without prior power analysis. We usually used more than 4 mice per group to ensure the statistically significant difference could be obtained from unpaired two-tailed Student's t-test or ANOVA analysis followed by multiple-comparisons test. On the other hand, we also tried to minimize the animal number to follow the guidelines of the animal experiments in our animal protocol. We described the exact numbers of animals/samples for each experiments in the figure legends.
Data exclusions	There were no excluded data or samples from the analysis in this study.
Replication	Experimental findings were reliable reproduced.
Randomization	During the study, we randomly chose the mice from the same littermates for each experiment group. We also randomly chose the age- and sex- matched littermates for control groups.
Blinding	As the gene-deficient mice (Map3k14-cKO, Tnfrsf1b–/–, Rorc–/–, Nfkb2lym1/+) were preliminary analyzed in other studies, and to definitely identify/distinguish the differences of immune functions among these genes, it was not necessary for us to be blinded to group allocation because this method is usually appropriate for the first investigation of a function-unknown gene.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☒	☐ Unique biological materials
☐	☒ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology
☐	☒ Animals and other organisms
☒	☐ Human research participants

Methods

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

Antibodies

Antibodies used

The following fluorochrome-labeled antibodies specific to mouse (m) proteins and their corresponding isotype controls were purchased from eBioscience: APC- or PE-conjugated anti-mIL-17A (eBio17B7), FITC- or APC-conjugated anti-mIFN-γ (XMG1.2), PE-conjugated anti-mIL-22 (1H8PWSR), PE-Cy7-conjugated anti-mCD3 (17A2), Pacific blue-conjugated anti-mCD4 (GK1.5), PerCp-Cy5.5-conjugated anti-mCD8 (53-6.7), PE-Cy7-conjugated anti-mNK1.1 (PK136), PE-Cy7-conjugated anti-mB220 (RA3-6B2), PE-Cy7-conjugated anti-mCD11b (M1/70), PE-Cy7-conjugated anti-mCD11c (N418), PE-Cy7-conjugated anti-mGr-1 (RB6-8C5), PE-Cy7-conjugated anti-mTer-119 (TER-119), FITC-conjugated anti-mCD45 (30-F11), APC-conjugated anti-mRORγt (B2D), APC- or PE-Cy7-conjugated anti-mMHCII (M5/114.15.2), PE- or FITC-conjugated anti-mCD80 (16-10A1), PE- or FITC-conjugated anti-mCD86 (GL1), PE- or Pacific blue-conjugated anti-mCD127 (A7R34), PE-conjugated anti-mCD103 (2E7), APC-conjugated anti-mCD62L (MEL-14), PE-conjugated anti-mCD44 (IM7), APC-conjugated anti-mEpCAME (G8.8), APC-conjugated anti-mCD317 (BST2), PerCp-Cy5.5-conjugated anti-mCCR7 (4B12) and eFluor 506 conjugated fixable viability dye. Purified anti-mCD16/32 (2.4G2), PE conjugated anti-mCD120b (TR75-89), FITC-conjugated anti-mIgA (c10-3), FITC-conjugated anti-mCD90.2 (30-H12), PE-Cy7 conjugated anti-mCXCR5 (2G8), and APC-conjugated anti-mPD-1 (J43) were purchased from BD Pharmingen. PE-conjugated anti-mAPRIL (A3D8), and Alexa Fluor647-conjugated anti-mTLR5 (ACT5) were purchased from BioLegend. PE-conjugated anti-mBAFF (121808) was purchased from R&D Systems. For in vivo blocking study, anti-mouse IL-17A (17F3), anti-mouse IL-12p40 (C17.8) and their isotype controls (mouse IgG1, rat IgG2a) were purchased from BioXcell. Anti-mouse pIgR was purchased from R&D.

Anti-Actin (C-4,1:10,000) was from Sigma, and anti-p100/p52 (TB4, 1:8,000) was from National Cancer Institute Preclinical

Repository. Antibodies for RelB (C-19, 1:1000), Lamin B (C-20, 1:1000), NIK (H248, 1:1000), TRAF2 (C-20, 1:1000), TRAF3 (H-122, 1:1000), cIAP2 (H85, 1:1000), phospho-p65 (Ser529, 1:1000), and c-Rel (sc71, 1:3000) as well as a control rabbit IgG (sc-2027, 1:1000) were from Santa Cruz Biotechnology. Antibodies for phospho-IκBα (Ser32, 1:1000), p65 (D14E12) and anti-p100/p52 (D7A9K) were purchased from Cell Signaling Technology Inc.

Validation

All the antibodies used for flow cytometry, IB and CHIP assay were validated according to the manufacturers instructions and largely described in the literature.

Animals and other organisms

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

Laboratory animals

Map3k14-flox mice (on C57BL/6 background), provided by Genentech, were generated using loxP system targeting exon 2 of the Map3k14 gene48. The Map3k14-flox mice were crossed with Cd11c-Cre transgenic mice (B6 genetic background, Jackson Laboratories) to create Map3k14 DC-conditional KO or Map3k14-cKO (Map3k14 fl/flCd11c-Cre) and wild-type (Map3k14+/+Cd11c-Cre) mice. Il10–/– mice were purchased from Jackson Lab and crossed with Map3k14-cKO mice to produce Il10–/–Map3k14-cKO and control Il10–/– mice. Rorc–/– and Tnfrsf1b–/– mice were purchased from Jackson Lab. Nfkb2lym1 mice were provided by R. Starr (Walter and Eliza Hall Institute of Medical Research). All KO and conditional KO mice were crossed using heterozygous breeders to generate littermate KO and wild-type control mice for experiments. Mice were maintained in a specific pathogen-free facility, and all animal experiments were in accordance with protocols approved by the Institutional Animal Care and Use Committee of the University of Texas MD Anderson Cancer Center. We usually used sex-matched mice with 8-10 weeks old for this study.

Wild animals

This study did not involve the use of wild animals.

Field-collected samples

This study did not involve the use of field-collected samples.

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

Cells were blocked with Fc blocker(CD16/32), and stained for specific surface markers. For intracellular staining, cells were fixed and permeabilized and stained for intracellular cytokines by fixation/permeabilization kit (BD bioscience).

Instrument

Flow cytometry data were collected by LSRII and FACSFortessa.

Software

Flow cytometry data were analyzed by FlowJo software (TreeStar, Ashland, OR).

Cell population abundance

For IEC sorting, we recovered 1-2 x10^6 cells post sorting.
For intestine DC sorting, we recovered 0.5-1 x 10^6 cells post sorting.

Gating strategy

For immune cells, first we gated the lymphocytes based on the FSC-A and SSC-A. After that, we gated on the single cells, and then gated on CD45+ cells. The specific cell population was gated on the indicated surface markers as described in the manuscript. We added the gating strategy in Supplementary figure 10.

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