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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	BD FACSDiva(V.8.0) was used to collect flow cytometric data.
Data analysis	GraphPad Prism 8 and R4.1.0 were used for statistical test and generate graphs. STAR aligner (version 2.7.9a), featureCounts (version 2.0.1), DESeq2 (version 1.34.0), R software (version 4.1.0), Python (version 3.8.13), Cell Ranger software (version 6.0.1), Seurat R package (version 4.0.6), Scrublet Python package (version 0.2.3), Bowtie2 aligner (version 2.2.5), samtools (version 1.3.1), Picard (version 2.27.1-0), MACS3 (version 3.0.0a7), deepTools (version 3.5.1)

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

All data generated during this study are available within the paper. The accession numbers for the raw data of scRNA-seq and strand-specific total RNA-seq are GSA:CRA007488 and CRA007498. ChIP-seq data are publicly available(GEO accession number: GSE156198)

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	*Use the terms sex (biological attribute) and gender (shaped by social and cultural circumstances) carefully in order to avoid confusing both terms. Indicate if findings apply to only one sex or gender; describe whether sex and gender were considered in study design whether sex and/or gender was determined based on self-reporting or assigned and methods used. Provide in the source data disaggregated sex and gender data where this information has been collected, and consent has been obtained for sharing of individual-level data; provide overall numbers in this Reporting Summary. Please state if this information has not been collected. Report sex- and gender-based analyses where performed, justify reasons for lack of sex- and gender-based analysis.*
Population characteristics	*Describe the covariate-relevant population characteristics of the human research participants (e.g. age, genotypic information, past and current diagnosis and treatment categories). If you filled out the behavioural & social sciences study design questions and have nothing to add here, write "See above."*
Recruitment	*Describe how participants were recruited. Outline any potential self-selection bias or other biases that may be present and how these are likely to impact results.*
Ethics oversight	*Identify the organization(s) that approved the study protocol.*

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 method was used to predetermine sample size. For flow cytometric,3-7 mice per group were used. Based on our previous studies and/or pilot experiments, these sample sizes allow for statistically valid comparisons. For single-cell RNA-seq experiments, more than 2000 cells were collected from each sample and 3 mice for each group. For strand-specific total RNA-seq experiments, 3 mice were used for each group.
Data exclusions	None
Replication	Replicates were used in all experiments as indicated in text, figure legends and methods. All experiments have been repeated as indicated in the figure legends.
Randomization	Six-to ten-week-old mice were used for the experiments. Ctrl and KO mice were genetic background-matched littermates.
Blinding	Experiments were not performed in a blinded manner, as knowledge of the grouping information was essential for the staff to conduct the studies. We chose objective readouts as measurements of our experiments. Therefore, the data were not prone to subjective evaluation.

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

Methods

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

Antibodies

Antibodies used

For flow cytometry experiments, the following antibodies were used:anti-CD4-Alexa Fluor 700(Catalog#56-0042-82, lot#2218011, Clone#RM4-5, eBioscience, Dilution 1:200),anti-CD4-APC-Cyanine7(Catalog#100414, lot#B191178, Clone#GK1.5, Biolegend, Dilution 1:200),anti-CD8-PerCP-Cyanine5.5(Catalog#551162, lot#0163107, Clone#53-6.7, BD, Dilution 1:200), anti-CD8-FITC(Catalog#553031, lot#43137, Clone#53-6.7, BD, Dilution 1:100),anti-CD3-Pacific Blue (Catalog#100214, lot#B363201, Clone#17A2, Biolegend, Dilution 1:200), anti-CD44-APC(Catalog# 559250, lot#96149, Clone#IM7, BD, Dilution 1:100),anti-CD62L-BV421(Catalog#104436, lot#B270184, Clone#MEL-14, Biolegend, Dilution 1:100), anti-B220-APC(Catalog#103212, lot#E024037, Clone#RA3-6B2, Biolegend, Dilution 1:100),anti-NK1.1-APC-Cyanine7(Catalog#560618, lot#2104625, Clone#PK136, BD, Dilution 1:100),anti-CD122-BV786(Catalog#740869, lot#2052618, Clone#TM-β1, BD, Dilution 1:50),anti-CD69-PE(Catalog#, lot#E01331-1631, Clone#H1.2F3, eBioscience, Dilution 1:100),anti-TCRβ-APC (Catalog#553174, lot#49172, Clone#H57-597, BD, Dilution 1:100)anti-CD24-FITC(Catalog#11-0242-82, lot#14961, Clone#M1/69, eBioscience, Dilution 1:100) anti-IFNγ-PE (Catalog#12731182, lot#2450699, Clone#XMG1.2, eBioscience, Dilution 1:100)anti-H3K4me1 (Catalog#5326S, lot#5, Clone#D1A9, CST, Dilution 1:100)anti-H3K4me2 (Catalog#ab32356, lot#GR3264818-5, Clone#Y47, abcam, Dilution 1:100)Goat Anti-Rabbit IgG H&L (PE) (Catalog#ab72465, lot#GR3373112-7, abcam, Dilution 1:500)

Validation

All antibodies used in this study are commercially available. All antibodies have been validated by previous studies from other groups and our laboratory.

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	Lsd1(fl/fl) mice, Lck-Cre mice and YFP-transgenic mice were kind gifts from Dana-Farber Cancer Center, Boston, MA. 6-10 week old male or female C57BL/6 mice were used for experiments.
Wild animals	We did not use any wild animals.
Reporting on sex	This information has not been collected.
Field-collected samples	No field-collected samples were used in this study.
Ethics oversight	All animal experiments were approved by the Capital Medical University Animal Care and Use Committee.

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

Single-cell suspension was prepared from the mouse thymus, spleen, and lymph nodes.

Instrument	BD Aria II was used for cell sorting, BD symphony was used for cell analysis.
Software	BD DIVA software (version 8.0) used for data collection, FlowJo software (version 10.6.2) used for analysis.
Cell population abundance	single-cell suspensions isolated from the thymus were sorted for scRNA-seq. The abundance of the live thymocytes post-sorted was 99%.
Gating strategy	All gates were set based on wild-type mice thymus or spleen after appropriate compensation using single-stained compensation controls. Gating strategy was described in the figure legends and supplementary figures.

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