

Reporting Summary

Nature Research 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 Research 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

Flow cytometry data was collected on LSR Fortessa (BD Biosciences);
Leica TCS Sp8 STED and Leica LAS X Core (3.7.2.22383) software for confocal fluorescence microscopy data collection;
HITACHI H-7650 or PHILIPS CM-120 and RADIUS, 2.0 (EMSIS GmbH, Muenster, Germany) software for transmission electron microscope data collection;
RNA-seq: platform BGISEQ-500 sequencer;
RSEM v1.2.30 (<https://github.com/deweylab/RSEM/releases>);
GSEA v4.2.3 (<http://www.gsea-msigdb.org/gsea/downloads.jsp>);
Bowtie2 v 2.3.4.2 (<http://bowtie-bio.sourceforge.net/bowtie2/index.shtml>);
IPA (according to IPA Ingenuity Web Site, www.ingenuity.com. Ingenuity Systems Inc., Redwood City, CA)
edgeR (v3.20.9) (Robinson et al., 2010)
Limma v3.42.2
cluster Profiler v3.14.3

Data analysis

Flow cytometry data was analyzed using FlowJo (v10) software.
Statistical analysis and graphs were generated using GraphPad Prism v7.
IF staining images and western blot image quantitation were performed by ImageJ (1.52a).
RNA-seq analysis was followed the software documentations, no special changes.

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 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 RNA-seq data have been deposited at the Gene Expression Omnibus (GEO accession number: GSE143698). The gene signature up-regulated in Tfh cells relative to their expression in non-Tfh cells were from GEO (GEO accession-code: GSE21379).

mouse genome (mm9) (<ftp://hgdownload.cse.ucsc.edu/goldenPath/mm9>).

All the data of this study are available.

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](https://www.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	Sample size (or number of repeats) was chosen based on what is common in the field, and what was practical to do. Sample size was determined to be adequate based on the reproducibility between independent experiments. If differences between groups were closed to statistical significance ($P = 0.1-0.05$), more mice were used for a more rigorous test of statistical analysis.
Data exclusions	No data were excluded from the analyses.
Replication	All experiments were replicated independently and all experiments were reliably reproduced. Number of repeats is provided in the text and figure legends where appropriate.
Randomization	age- and sex-matched animals were used in all experiments.
Blinding	The investigators were blinded during data collection and/or 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
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies
<input checked="" type="checkbox"/>	<input type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology
<input type="checkbox"/>	<input checked="" type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Human research participants
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern

Methods

n/a	Involved in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input type="checkbox"/>	<input checked="" type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

Antibodies

Antibodies used

Application: Flow cytometry (FC) - Quality routinely tested by the manufactory

1. (FITC) anti-B220 (BD Biosciences) Cat: 553088, clone: RA3-6B2, lot: 5064828, Species: Rat, Application: FC (Routinely Tested), dilution: 1:100
2. allophycocyanin (APC) anti-IgM (BD Biosciences) Cat: 550676, Clone: II/41 (RUO), lot: 5159597, Species: Rat, Application: Flow cytometry (Routinely Tested), dilution: 1:100
3. phycoerythrin (PE) anti-CD24, (BD Biosciences) Cat: 553262, clone: M1/69 (RUO), lot:84497, Species: Rat, Application: Flow

cytometry (Routinely Tested), dilution: 1:100

4. FITC anti-CD41, (BD Biosciences) Cat: 553848, clone: MWReg30, lot:17652, Species: Rat, Application: Flow cytometry (Routinely Tested) , dilution: 1:100
5. Percp-Cy5.5 anti-BCL6, (BD Biosciences) Cat: 562198, clone: K112-91, lot: 6070699, Species: Mouse, Application: Flow cytometry (Routinely Tested) , dilution: 1:100
6. PE-Cy7 anti-CXCR5, (BD Biosciences) Cat: 560617, clone:2G8, lot:5071937, Species: Mouse, Application: Flow cytometry (Routinely Tested), dilution: 1:100
7. APC anti-IL4, (BD Biosciences) Cat: 554436, clone: 11B11, lot:6070957, Species: Rat, Application: Flow cytometry (Routinely Tested) (dilution 1:200)
8. APC-Cy7 anti-IL17a, (BD Biosciences) Cat: 560821, clone:TC11-18H10, lot:5191521, Species: Rat, Application: Flow cytometry (Routinely Tested), dilution: 1:100
9. BV421 anti-IFN- γ , (BD Biosciences) Cat: 563376, clone: XMG1.2, Species: Rat, Application: Flow cytometry (Routinely Tested), dilution: 1:100
10. FITC anti P-selectin, (BD Biosciences) Cat: 553744, clone: RB40.34 lot:7188677, Species: Rat, Application: Flow cytometry (Routinely Tested), dilution: 1:100
11. Pacific Blue anti-CD4, (Biolegend) Cat:100428, clone: GK1.5, lot: B212372, Species: Rat, Application: Flow cytometry (Routinely Tested), dilution: 1:100
12. Percp-Cy5.5 anti-CD19, (Biolegend) Cat: 115534, clone:6D5, lot: B171376, Species: Rat, Application: Flow cytometry (Routinely Tested) dilution: 1:100
13. APC anti-CXCR5, (Biolegend) Cat:145506, clone: L138D7, lot: B215836, Species: Rat, Application: Flow cytometry (Routinely Tested) dilution: 1:100
14. APC anti-CD44, (Biolegend) Cat: 103011, clone: IM7, lot: B207776, Species: Rat, Application: Flow cytometry (Routinely Tested), dilution 1:200
15. APC-Cy7 anti-CD62L, (Biolegend) Cat: 104427, clone: MEL-14, lot: B229840, Species: Rat, Application: Flow cytometry (Routinely Tested) dilution: 1:100
16. PE-Cy7 anti-CD43, (Biolegend) Cat: 121218, clone: 1B11, lot: B164693, Species: Rat, Application: Flow cytometry (Routinely Tested), dilution 1:1000
17. Pacific Blue anti-GL7, (Biolegend) Cat:144613, clone:GL7, lot: B209952, Species: Rat, Application: Flow cytometry (Routinely Tested), dilution 1:200
18. APC anti-Fas/CD95, (eBioscience) Cat: 17-0951-82, clone:15A7, lot: E13624-109, Species: Mouse, Application: Flow cytometry. dilution: 1:100
19. AF700 anti-Foxp3, (eBioscience) Cat: 56-5773-82 , clone: FJK-16s, lot: E09023-1634, Species: Rat, Application: Flow Cytometry, Immunocytochemistry (ICC), Immunofluorescence (IF), Immunohistochemistry (IHC), Immunohistochemistry (Paraffin) (IHC (P)), Immunoprecipitation (IP) dilution: 1:100
20. APC anti-Cd42d (GPV) (eBioscience) Cat: 17-0421-82, clone: 1C2, lot: Species: Armenian Hamster, Application: Flow cytometry. dilution: 1:100
21. anti-CD16/CD32 (Biolegend) Cat:101320, clone:93, lot: B164564, Species: Rat, Application: Flow cytometry (Routinely Tested) dilution: 1:100
22. PE CD62L Monoclonal Antibody (Invitrogen), Clone: MEL-14, Cat: MA5-17803, monoclonal antibody, Lot: E013141632, Species: Rat, Application: Flow cytometry (Routinely Tested) dilution: 1:100
23. APC anti-Mac1(BD Biosciences): clone M1/70, Cat: BD553312, Reactivity: Mouse (QC Testing), Human (Tested in Development), Species: Rat, Application: Flow cytometry (Routinely Tested), dilution 1:200
24. PE anti-CD41(BD Biosciences), Clone: MWReg30, Cat: BD558040, monoclonal antibody, Species: Rat, Application: Flow cytometry (Routinely Tested) dilution: 1:100
25. PE anti-CD138 (BD Biosciences): clone 281-2, Cat: 561070, Lot: 9023581, Species: Rat, Application: Flow cytometry (Routinely Tested) dilution 1:500
26. PerCP/Cy5.5 anti-mouse F4/80 Antibody (Biolegend), Clone BM8, Cat: 123128, monoclonal antibody, Species: Rat, Application: Flow cytometry (Routinely Tested) dilution: 1:100
27. APC/Cy7 anti-mouse CD8a Antibody (Biolegend), Clone: 53-6.7, Cat: 100714, monoclonal antibody, Lot: B162658, Species: Rat, Application: Flow cytometry (Routinely Tested) dilution 1:200
28. APC anti-mouse CD45 Antibody (eBioscience/Invitrogen), Clone: 30-F11, Cat: 17-0451-82, monoclonal antibody, Lot: 4291970, Species: Rat, Application: Flow cytometry (Routinely Tested) dilution 1:200
29. APC CD41 Monoclonal Antibody (Invitrogen), Clone: eBioMWReg30, Cat: 17-0411-82, monoclonal antibody, Species: Rat, Application: Flow cytometry (Routinely Tested) dilution: 1:100
30. PE-Cy7 Rat Anti-Mouse Gr-1 (BD Biosciences), Cat: 552985, monoclonal antibody, Species: Rat, Application: Flow Cytometry. dilution: 1:100
31. Biotin AH anti-mouse CD11c (eBioscience), Clone: N418, Cat: 13-0114-82, Lot: 4292345, Species: AH IgG, Application: Flow cytometry (Routinely Tested). dilution: 1:100
32. PerCP-Cy5.5 Streptavidin (Biolegend), Cat: 405214, Lot: B217949. dilution: 1:200
33. FITC anti-mouse MHC II (I-A/I-E) (eBioscience), Clone: M5/114.15.2, Cat: 11-5321-81, Lot: 4273292, Species: Rat IgG2b, Application: FC (Routinely Tested). dilution: 1:100
34. APC Anti-mouse CD86 (eBioscience), Clone: GL1, Cat: 17-0862-81, Lot: 7082942, Species: Rat IgG2a, kappa, Application: Flow cytometry (Routinely Tested). dilution: 1:100
35. PE anti-mouse CD80 (eBioscience), Clone: 16-10A1, Cat: 12-0801-82, Lot: 4289574, Species: Armenian hamster/IgG, Application: Flow cytometry (Routinely Tested). dilution: 1:100
36. PE-Cy7 anti-mouse CD11b (eBioscience), Clone: M1/70, Cat: 25-0112-81, Lot: 4285186, Species: Rat / IgG2b, kappa, Application: Flow cytometry (Routinely Tested). dilution: 1:100

Application: WB - Quality tested by the manufactory

37. anti-AKT-Thr308 (Cell Signaling Technology, CST), Cat: 9275L, lot: 3, Species: Rabbit, Application: Immunoprecipitation, Western (dilution 1:1000)

38. anti-AKT-Ser473 (CST), Cat: 4060, lot: 6, Species: Rabbit, Application: Flow Cytometry, Immunofluorescence, Immunohistochemistry, immunoprecipitation, Western (dilution 1:1000)
39. anti-SNAP23-Ser95 (GenScript), Peptide Order No.:C7010CG250, Species: Rabbit, Application: WB Quality tested (dilution 1:1000)
40. anti-Sin1-Thr86 (CST), Cat: 14716s, Species: Rabbit, Application: immune-precipitation, Western (dilution 1:500)
41. anti-SNAP23 (Proteintech), Cat: 10825-1-AP, Species: Rabbit, Applications: WB, IP, IHC, IF, FC, ELISA (dilution 1:500)
42. anti-PTEN (CST), Cat:9559L, lot:7, Species: Rabbit, Application: Immunohistochemistry, Immunoprecipitation, Western (dilution 1:1000)
43. Rabbit anti-GAPDH (CST), Cat:2118s, clone: 14C10, lot: Species: Rabbit, Application: Flow Cytometry, Immunofluorescence, Immunohistochemistry, Western (dilution 1:1000)
44. anti-CD62P (P-selectin) antibody (Abcam), Clone: EPR22850-190, Cat: ab255822, monoclonal antibody, Lot: GR3383644-1, Species: Rabbit, Application: WB, IHC-P. (dilution 1:1000)

Application: IHC/IF - Quality tested by the manufactory

45. Biotinylated Peanut Agglutinin (PNA, Vector laboratories) Cat: B-1075, lot: X1221, Application: Immunohistochemistry/ Immunocytochemistry, Immunofluorescence, Blotting Applications, Elispot, ELISAs, Glycobiology. dilution 1:200
46. anti-B220 (Biolegend), Cat:103202, Clone: RA3-6B2, lot: B123193, Species: Rat, Application: FC-Quality tested CyTOF®; IHC-F- Verified. dilution 1:100.
47. Alexa Fluor 647 conjugated Goat anti-Rat IgG (Life Technologies) Cat: A21247, Polyclonal, lot: 1654305, Species: Goat, Application: IF, IHC, Flow. dilution 1:500
48. APC Streptavidin (BD Biosciences) Cat: 554067. dilution 1:500
49. Purified anti-mouse CD4 Antibody (Biolegend), Clone: GK1.5, Cat:100401, monoclonal antibody, Species: Rat. dilution 1:200
50. anti-CD31 (BD Biosciences): Clone MEC13.3, Cat: 550274, Species: Rat, Application: Flow cytometry (Routinely Tested), Immunohistochemistry-frozen, dilution 1:100
51. Mouse LYVE-1 Biotinylated Antibody (R&D Systems), Cat: BAF2125, Polyclonal Goat IgG, Species: Goat, Application: WB, IHC. dilution 1:100
52. PE conjugated Goat anti-rat IgG (Rockland) Cat: 612-108-120. Dilution 1:250
53. Goat anti-rabbit IgG (H+L) Highly Cross-Adsorbed Secondary antibody HRP conjugated (Invitrogen) Cat: A16110, Dilution 1:10000
54. AP-conjugated anti-mouse IgG (Jackson ImmunoResearch), Cat: 115-055-146, Dilution 1:500
55. anti-CD3 functional grade antibody (Invitrogen), Catlog: 16-0031-85
56. anti-CD28 functional grade antibody (Invitrogen), Catlog: 16-0281-85
57. anti-β-Actin antibody (Bioworld), Catlog: AP0060 1:10000

Validation

Application: Flow cytometry (FC) - Quality routinely tested by the supplier

- (FITC) anti-B220 (BD Biosciences) Cat: 553088 <https://www.citeab.com/antibodies/2411763-553088-bd-pharmingen-fitc-rat-anti-mouse-cd45r-b220>
- allophycocyanin (APC) anti-IgM (BD Biosciences) Cat: 550676 <https://www.citeab.com/antibodies/2411763-553088-bd-pharmingen-fitc-rat-anti-mouse-cd45r-b220>
- phycoerythrin (PE) anti-CD24, (BD Biosciences) Cat: 553262 (RUO) <https://www.citeab.com/antibodies/2410070-553262-bd-pharmingen-pe-rat-anti-mouse-cd24?des=32e2e2082028c5e3>
- FITC anti-CD41, (BD Biosciences) Cat: 553848 <https://www.citeab.com/antibodies/2410014-553848-bd-pharmingen-fitc-rat-anti-mouse-cd41?des=98a92d0e27e527f6>
- Percp-Cy5.5 anti-BCL6, (BD Biosciences) Cat: 562198 <https://www.citeab.com/antibodies/2409220-562198-bd-pharmingen-percp-cy-5-5-mouse-anti-bcl-6?des=d666bd21339e5be8>
- PE-Cy7 anti-CXCR5, (BD Biosciences) Cat: 560617 <https://www.citeab.com/antibodies/2411096-560617-bd-pharmingen-pe-cy-7-rat-anti-mouse-cd185?des=6f00068c58a460d0>
- APC anti-IL4, (BD Biosciences) Cat: 554436 <https://www.citeab.com/antibodies/2413710-554436-bd-pharmingen-apc-rat-anti-mouse-il-4?des=ba3c80da83aa6e69>
- APC-Cy7 anti-IL17a, (BD Biosciences) Cat: 560821 <https://www.citeab.com/antibodies/2406876-560821-bd-pharmingen-apc-cy-7-rat-anti-mouse-il-17a?des=68fdc3a0f2760d81>
- BV421 anti-IFN-γ, (BD Biosciences) Cat: 563376 <https://www.citeab.com/antibodies/2409490-563376-bd-horizon-bv421-rat-anti-mouse-ifn?des=4b432b162b8f12d8>
- FITC anti P-selectin, (BD Biosciences) Cat: 553744 <https://www.citeab.com/antibodies/2410220-553744-bd-pharmingen-fitc-rat-anti-mouse-cd62p?des=816645ee5bf47e22>
- Pacific Blue anti-CD4, (Biolegend) Cat:100428 <https://www.citeab.com/antibodies/517127-100428-pacific-blue-anti-mouse-cd4-antibody?des=dc184b2dcf85680d>
- Percp-Cy5.5 anti-CD19, (Biolegend) Cat: 115534 <https://www.citeab.com/antibodies/518004-115534-percp-cyanine5-5-anti-mouse-cd19-antibody?des=818194cd4dafaef7>
- APC anti-CXCR5, (Biolegend) Cat:145506 <https://www.citeab.com/antibodies/1483674-145506-apc-anti-mouse-cd185-cxcr5-antibody?des=dcc5fda300936ded>
- APC anti-CD44, (Biolegend) Cat: 103011 <https://www.citeab.com/antibodies/517918-103011-apc-anti-mouse-human-cd44-antibody?des=14ad2fec96f9180>
- APC-Cy7 anti-CD62L, (Biolegend) Cat: 104427 <https://www.citeab.com/antibodies/518392-104427-apc-cyanine7-anti-mouse-cd62l-antibody?des=8ac53641fa04cee7>
- PE-Cy7 anti-CD43, (Biolegend) Cat: 121218 <https://www.citeab.com/antibodies/518737-121218-pe-cyanine7-anti-mouse-cd43-activation-associa?des=4159c0e440ad4ffa>
- Pacific Blue anti-GL7, (Biolegend) Cat:144613 <https://www.citeab.com/antibodies/2083023-144613-pacific-blue-anti-mouse-human-gl7-antigen-t?des=1ee3defeaea5d901>
- APC anti-Fas/CD95, (eBioscience) Cat: 17-0951-82

- <https://www.citeab.com/antibodies/2039453-17-0951-82-cd95-apo-1-fas-monoclonal-antibody-15a?des=5a4f184b36c6f2fe>
19. AF700 anti-Foxp3, (eBioscience) Cat: 56-5773-82
- <https://www.citeab.com/antibodies/2041735-56-5773-82-foxp3-monoclonal-antibody-fjk-16s-alex?des=f0719ecd65a98ed8>
16. APC anti-Cd42d (GPV) (eBioscience) Cat: 17-0421-82
- <https://www.citeab.com/antibodies/2038769-17-0421-82-cd42d-monoclonal-antibody-1c2-apc-ebi?des=ac72ec51accdc58d>
21. anti-CD16/CD32 (Biolegend) Cat:101320
- <https://www.citeab.com/antibodies/517402-101320-trustain-fcx-anti-mouse-cd16-32-antibody?des=7c26517276959644>
22. PE CD62L Monoclonal Antibody (Invitrogen), Cat: MA5-17803
- <https://www.citeab.com/antibodies/1914201-ma5-17803-cd62l-monoclonal-antibody-mel-14-pe?des=4bd5c36ea9430e6e>
23. APC anti-Mac1(BD Biosciences): clone M1/70, Cat: 553312
- <https://www.citeab.com/antibodies/2408215-553312-bd-pharmingen-apc-rat-anti-cd11b?des=93cc718e1438f50b>
23. PE anti-CD41(BD Biosciences), Cat: 558040
- <https://www.citeab.com/antibodies/2410962-558040-bd-pharmingen-pe-rat-anti-mouse-cd41?des=baa4c50b130eaab4>
25. PE anti-CD138 (BD Biosciences): Cat: 561070
- <https://www.citeab.com/antibodies/2408745-561070-bd-pharmingen-pe-rat-anti-mouse-cd138?des=239232987dbbd816>
26. PerCP/Cy5.5 anti-mouse F4/80 Antibody (Biolegend), Cat: 123128
- <https://www.citeab.com/antibodies/519062-123128-percp-cyanine5-5-anti-mouse-f4-80-antibody?des=853130bbb8558a20>
27. APC/Cy7 anti-mouse CD8a Antibody (Biolegend), Cat: 100714
- <https://www.citeab.com/antibodies/517216-100714-apc-cyanine7-anti-mouse-cd8a-antibody?des=99660e2bfbfa2054>
28. APC anti-mouse CD45 Antibody (Invitrogen), Cat: 17-0451-82
- <https://www.citeab.com/antibodies/2038853-17-0451-82-cd45-monoclonal-antibody-30-f11-apc-e?des=fb9796b2f857d4c5>
29. APC CD41 Monoclonal Antibody (Invitrogen), Cat: 17-0411-82
- <https://www.citeab.com/antibodies/2038692-17-0411-82-cd41a-monoclonal-antibody-ebiomwreg30-m?des=c52e2c775c38043d>
30. PE-Cy7 Rat Anti-Mouse Gr-1 (BD Biosciences) Cat: 552985
- <https://www.citeab.com/antibodies/2411828-552985-bd-pharmingen-pe-cy-7-rat-anti-mouse-ly-6g-a?des=4f43c29b02a5081a>
31. Biotin AH anti-mouse CD11c (eBioscience), Cat: 13-0114-82
- <https://www.citeab.com/antibodies/2038168-13-0114-82-cd11c-monoclonal-antibody-n418-biotin?des=4e7df1637e759939>
32. PerCP-Cy5.5 Streptavidin (Biolegend), Cat: 405214
- <https://www.biolegend.com/en-us/products/percp-cyanine5-5-streptavidin-4212>
33. FITC anti-mouse MHC II (I-A/I-E) (eBioscience), Cat: 11-5321-81
- <https://www.thermofisher.com/antibody/product/MHC-Class-II-I-A-I-E-Antibody-clone-M5-114-15-2-Monoclonal/11-5321-81>
34. APC Anti-mouse CD86 (eBioscience), Clone: GL1, Cat: 17-0862-81, Lot: 7082942, Species: Rat IgG2a, kappa, Application: Flow cytometry (Routinely Tested).
- <https://www.citeab.com/antibodies/2039360-17-0862-82-cd86-b7-2-monoclonal-antibody-gl1-ap?des=e46ae5b220a535ac>
35. PE anti-mouse CD80 (eBioscience), Cat: 12-0801-82
- <https://www.citeab.com/antibodies/2039297-12-0801-82-cd80-b7-1-monoclonal-antibody-16-10a1?des=652ad622c034e309>
36. PE-Cy7 anti-mouse CD11b (eBioscience), Cat: 25-0112-81
- <https://www.citeab.com/antibodies/2038111-25-0112-82-cd11b-monoclonal-antibody-m1-70-pe-cya?des=bcbec43bad1548a7>

Application: WB - Quality tested by the supplier

37. anti-AKT-Thr308 (Cell Signaling Technology, CST), Cat: 9275L
<https://www.citeab.com/antibodies/125976-9275-phospho-akt-thr308-antibody?des=436867e9cb87bdab>
38. anti-AKT-Ser473 (CST), Cat: 4060
<https://www.citeab.com/antibodies/123848-4060-phospho-akt-ser473-d9e-xp-rabbit-mab?des=3cb714006e1b6cb0>
39. anti-SNAP23-Ser95 (GenScript), Peptide Order No.:C7010CG250
antibody@genscript.com.cn
40. anti-Sin1-Thr86 (CST), Cat: 14716s
<https://www.citeab.com/antibodies/2444925-14716-phospho-sin1-thr86-d4u9l-rabbit-mab?des=85451e6bdc5ba061>
41. anti-SNAP23 (proteintech), Cat: 10825-1-AP
<https://www.citeab.com/antibodies/976162-10825-1-ap-snap23-antibody?des=1409da2a5c02682d>
42. anti-PTEN (CST), Cat:9559L
<https://www.citeab.com/antibodies/126240-9559-pten-138g6-rabbit-mab?des=629c7fc7d811db12>
43. Rabbit anti-GAPDH (CST), Cat:2118s
<https://www.citeab.com/antibodies/122875-2118-gapdh-14c10-rabbit-mab?des=9f20dfa5bc894376>
44. anti-CD62P (P-selectin) antibody (Abcam), Cat: ab255822
<https://www.citeab.com/antibodies/7431098-ab255822-anti-cd62p-antibody-epr22850-190?des=ea3a7e80582b0d94>

Application: IHC/IF - Quality tested by the manufactory

45. biotinylated Peanut Agglutinin (PNA, Vector laboratories) Cat: B-1075
<https://vectorlabs.com/products/glycobiology/biotinylated-peanut-agglutinin-pna>
46. anti-B220 (Biolegend), Cat:103202
<https://www.citeab.com/antibodies/518048-103202-purified-anti-mouse-human-cd45r-b220-antibody?des=0fe160d0ea483d60>
47. Alexa Fluor 647 conjugated Goat anti-Rat IgG (Life Technologies) Cat: A-21247,
<https://www.citeab.com/antibodies/2401279-a-21247-goat-anti-rat-igg-h-l-cross-adsorbed-secon?des=6a2ffd6dccf71d1b>
48. APC Streptavidin (BD Biosciences) Cat: 554067.
<https://www.bdbiosciences.com/en-au/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/apc-streptavidin.554067>

49. Purified anti-mouse CD4 Antibody (Biolegend), Cat:100401
<https://www.citeab.com/antibodies/517103-100401-purified-anti-mouse-cd4-antibody?des=ce1c672fc0db9961>
50. anti-CD31 (BD Biosciences), Cat: 550274
<https://www.citeab.com/antibodies/3288830-550274-bd-pharmingen-purified-rat-anti-mouse-cd31?des=8c949d1dc6222b5f>
51. Mouse LYVE-1 Biotinylated Antibody (R&D Systems), Cat: BAF2125
<https://www.citeab.com/antibodies/691816-baf2125-mouse-lyve-1-biotinylated-antibody?des=20e529a4d3ea864a>
52. PE conjugated Goat anti-rat IgG (Rockland) Cat: 612-108-120. Dilution 1:250
<https://www.clinisciences.com/en/other-products-186/anti-rat-igg-h-l-goat-antibody-528009664.html>
53. Goat anti-rabbit IgG (H+L) Highly Cross-Adsorbed Secondary antibody HRP conjugated (Invitrogen) Cat: A16110, Dilution 1:10000
<https://www.thermofisher.com/antibody/product/Goat-anti-Rabbit-IgG-H-L-Highly-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A16110>
54. AP-conjugated anti-mouse IgG (Jackson ImmunoResearch), Cat: 115-055-146
<https://shop.lucerna-chem.ch/563445/alkaline-phosphatase-affinipure-goat-anti-mouse-igg-h-l-min-x-hu-bov-hrs-rb-sw-sr-prot>
55. anti-CD3 antibody (Invitrogen), Catalog: 16-0031-85
<https://www.thermofisher.com/antibody/product/CD28-Antibody-clone-37-51-Monoclonal/16-0281-85>
56. anti-CD28 antibody (Invitrogen), Catalog: 16-0281-85
<https://www.thermofisher.com/antibody/product/CD28-Antibody-clone-37-51-Monoclonal/16-0281-85>
57. anti-β-Actin antibody (Bioworld), Catalog: AP0060 1:10000
<https://www.citeab.com/antibodies/2206801-ap0060-actin-i102-polyclonal-antibody>

Animals and other organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research

Laboratory animals

All mice were crossed on C57BL/6 background.
 Pf4 transgenic mice and mice with loxP-flanked Pten alleles (Pten^{fl/fl}) have been previously described. Rosa26^{mT/mG} (Jax007676) mice were from Nanjing Biomedical Research Institute of Nanjing University. The Rosa26^{mT/mG} reporter mice we used contain a loxP-flanked ('floxed') tandem dimer Tomato gene (mT) and STOP cassette followed by the gene encoding GFP (mG) at the ubiquitously membrane-targeted Rosa26 locus. In this lineage tracing by Cre-Loxp system, PF4-Cre mediated excision of the floxed STOP cassette results in descendible and constitutive expression of GFP. According to different experimental purposes, these mice were crossed to generate Pten^{fl/fl}Pf4-Cre, Rosa26^{mT/mG}Pf4-Cre, Rosa26^{mT/mG}Pten^{fl/fl}Pf4-Cre, respectively. The development of these lymphoproliferative and autoimmune diseases was monitored by frequent visual examination, flow cytometry and histopathological analyses.
 All mice were bred and maintained under a 12-h reverse light/dark cycle and specific pathogen free (SPF) conditions. The animal facility was maintained at a temperature of 22 ± 2 °C with 40-70 % humidity. Age- and sex-matched male and female adult mice were used in each independent experiment. The ages of mice were depended on different experimental design and were clearly described in the manuscript or figure legend.

Wild animals

No wild animals were used in this study.

Field-collected samples

No field-collected samples were used in this study.

Ethics oversight

All mice were housed in specific pathogen-free (SPF) facilities and all animal experiments were performed in strict accordance with protocols approved by Institutional Animal care and Use Committee (IACUC) of Shanghai Jiao Tong University School of Medicine

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

Bone marrow cells were flushed from tibia and femurs with sterile FACS buffer (PBS supplemented with 2% FBS and 2mM EDTA). Lymph nodes and spleens were gently grind against the cell strainer by the plunger from a syringe and single-cell suspensions were filtered through fine mesh. Red blood cells were lysed with ACK lysis buffer. Cells were counted and stained with surface antibodies in FACS buffer, followed by incubation for 30 min on ice. For intracellular staining, cells were fixed and permeabilized using the Foxp3 Fix/Perm kit.

Instrument

Samples were collected on LSR Fortessa cytometer (BD Biosciences).

Software	Flow cytometry data was acquired using BD Diva software. Data analysis was performed using FlowJo (Treestar) software (v10).
Cell population abundance	A minimum of 20000 CD4+ T cells or other indicated cells collected per sample. The purity of the samples within post-sort fractions was above 99% and determined by a LSR Fortessa cytometer (BD Biosciences).
Gating strategy	For flow cytometric analysis all cell populations were gated on live singlets. Lymphocytes were identified by size and granularity in the FSC/SSC scatter. Dead cells and non-singlet events were excluded by 7-amino-actinomycin D staining and the forward scatter area (FSC-A) versus height (FSC-H) characteristics. Further gating depended on experimental design and were clearly described in the manuscript.

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