

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 [Authors & Referees](#) 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 using FACSDiva software, CytoExpert software and Flowjo V.9, 10. Histology images were collected using FLUOVIEW software. ELISA data was collected using Microplate Manager V.6 software.

Data analysis

Graphpad Prism 7, Flowjo V.9, 10, Microplate Manager V.6, PAVIS, trim_galore (version 0.6.4), bowtie (version 1.2.2), macs2 (version 2.1.2), ChIPseeker, deeptools (version 3.3.0), BMap, MapSum, CalcCoverage (MPTC), DiffBind (R package), DESeq2 (R package), enrichR (R package), IMGT/C-QUEST

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. 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

Gene expression data of B220+ AA4.1+, B220+AA4.1-CD23+ CD21Int, B220+ AA4.1- CD23- CD21lo cells analyzed by RNAseq is utilized in Fig.5. Gene expression data of B220+ AA4.1- CD21 Int-lo cells analyzed by RNA-seq is utilized in Fig.7. These data is available on the GEO data base with the following accession number, GSE137914.

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 was determined to ensure reproducibility of experimental results with statistical significance, which is based on our previous studies and by availability of experimental animals as well.
Data exclusions	No data was excluded.
Replication	Biological and technical replicates were performed. Most of experiments were usually reproduced 2 to more than 3 independent times to ensure the reproducibility of findings. The only exceptions were experiments with NGS analysis, each of which had two replicates performed in one experiment. These information is included in figure legends.
Randomization	Randomization was not performed. All experimental groups were based on genotype of mice. Whenever possible, age/sex-matched mice were used.
Blinding	Histochemistry experiments were performed in a blind manner. Other experiments were not performed blinded.

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
☐	☒ Animals and other organisms
☒	☐ Human research participants
☒	☐ Clinical data

Methods

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

Antibodies

Antibodies used	Antibodies specific to B220 (RA3-6B2), IgM (II/41), CD93 (AA4.1), CD21/CD35 (8D9), IgD (11-26), I-A/I-E (M5/114.15.2), CD80 (16-10A1), GL-7, CD8a (53-6.7), CD62L (MEL-14), CD25 (PC61.5), CD4 (RM4-5), CD11b (M1/70), CD11c (N418), Ly6G (Gr-1) (RB6-8C5), NK1.1 (PK136), PD-1 (J43), CD19 (1D3), c-kit (2B8), CD43 (eBioR2/60), CD80 (16-10A1), CD86 (GL-1), CD40 (HM40-3), CD27 (LG.7F9), ICOSL (7E.17G9), IFN-gamma (XMG1.2), IL-4 (11B11), IL-17 (TC11-18H10) and Foxp3 (FJK-16s) are from ebioscience. Antibodies from CD23 (B3B4), CD44 (IM7), CD95 (Jo2), CD138 (281-2), CD4 (GK1.5), CXCR5 (2G8) and Bcl6 (K112-91) are from BD Pharmingen. Anti-C3 (RmC11H9) Ab is from CEDARLANE. Anti-mouse IgG2c pAb (STAR 135F) is from BioRad. Anti-CD20 (5D2) mAb and Anti-CD86 (GL-1) mAb are from Genentech and Bio X Cell, respectively.
Validation	All antibodies used were passed manufacturer's quality controls and validated for indicated applications. Depleting antibodies were further tested at different dilutions for efficient elimination of target cells in our validation studies.

Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)	A20 (ATCC)
Authentication	A20 cells were authentication by flow cytometry analysis with cell surface markers reported in previous publications.
Mycoplasma contamination	These lines were not tested for mycoplasma contamination.

Commonly misidentified lines
(See [ICLAC](#) register)

No misidentified cell lines was used.

Animals and other organisms

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

Laboratory animals

Mus musculus; Tet2 flox, Tet3 flox, CD19-Cre, H2-Ab1 flox, CD45.1, MD4 Tg, ML5 Tg, OT II Tg, TCR7 Tg; Mice used are at the age of 3-to 8- week old. C57BL6 Lpr used at the age around 32-week old.

Wild animals

No wild animals were used.

Field-collected samples

Study did not involve field-collected samples.

Ethics oversight

All mice were maintained in a specific pathogen-free animal facility following institutional guidelines and with protocols approved by the animal care and use committees at Osaka University, Tokyo University of Science and kyushu University.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

ChIP-seq

Data deposition

☒ Confirm that both raw and final processed data have been deposited in a public database such as [GEO](#).

☒ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links

May remain private before publication.

The data of ChIP-seq and bisulfite-seq is available on the GEO data base with the following accession numbers, GSE137666 and GSE137621 , respectively.

Files in database submission

HDAC1 ChIP-seq, HDAC2 ChIP-seq, Bisulfite-seq, Acetylated H3 ChIP-seq

Genome browser session

(e.g. [UCSC](#))

Provide a link to an anonymized genome browser session for "Initial submission" and "Revised version" documents only, to enable peer review. Write "no longer applicable" for "Final submission" documents.

Methodology

Replicates

For ChIP-seq and Bisulfite-seq experiments, at least two independent replicates per experimental group were performed.

Sequencing depth

Around 7-25 million of single end reads were obtained each sample for ChIP-seq. Around of 760-804 million of reads were obtained each sample for Bisulfite-seq.

Antibodies

Anti-HDAC1 (GTX100513;GeneTex), Anti-HDAC2 (GTX109642; GeneTex), Anti-acetylated H3 (06-599, Merck Millipore)

Peak calling parameters

For computational analysis of ChIP-seq, adaptor and quality trimming was performed using trim_galore program (version 0.6.4) then reads were uniquely aligned to mm10 genome using bowtie program (version 1.2.2) with “-n 3 -m 1 -a --best -strata” option. Peaks were identified using macs2 program (version 2.1.2) with setting minimum QVALUE cutoff = 0.01. Each Input samples was used as their control in macs2. Identified peaks were annotated the genomic feature with an R package of ChIPseeker based on TxDb.Mmusculus.USU.mm10.knownGene. After check the replicate quality individually , bigwig files were created from bam and data were visualized with deeptools (version 3.3.0) with “--binSize 100. Peak distribution was also profiled by deeptools in range of 2kbp flanking region from TSS, TES and gene body based on mm10.RefSeq.Curated.gene. For analysis of bisulfite-seq, the reads were mapped to the reference genome composed of mm10 mouse and enterobacteria phage lambda using BMap program. The bisulfite conversion rate was estimated from the reads mapped to the spiked-in unmethylated lambda. The alignments were summarized using an in-house pipeline comprised of programs named MapSum, and CalcCoverage29 (MPTC).

Data quality

Around 91-98% of total reads were aligned to mm10 reference genome and about 61-71% of total reads were mapped on mm10 uniquely for ChIP-seq. Around 83-88% of total number of reads were mapped on mm10 reference for Bisulfite-seq.

Software

trim_galore (version 0.6.4), bowtie (version 1.2.2), macs2 (version 2.1.2), ChIPseeker, deeptools (version 3.3.0), BMap, MapSum, CalcCoverage (MPTC), DiffBind (R package), enrichR (R package)

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

Spleens and skin-draining LNs were minced and single-cell suspension were passed through 70 micrometer strainers and red blood cell (RBC)s were lysed with 1x RBC lysis buffer (eBioscience). For peritoneal cell analysis, 1ml of preparation medium (2% FCS RPMI 1640) was injected into the peritoneal cavity of mice. The mice were gently shaken to dislodge the cells, followed by harvest the peritoneal fluid. For bone marrow (BM) cells, single-cell suspension was obtained by flashing BM cells out with the preparation medium from femur of mice. Then, RBCs were lysed as described.

Instrument

BD FACSCanto II, BD FACSARIA II, Beckman Coulter Cytoflex S

Software

FACSDiva , CytoExpert, Flowjo V.9, 10.

Cell population abundance

The purity of sorted cells was > 95%, checked post sort.

Gating strategy

Before gating on the cells of interest shown in figure legend and method section, cells were gated by FSC-A/SSC-A to exclude debris and then FSC-H/FSC-W to gate on singlet cells, followed by exclusion of dead cells using the viability dye.

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