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Corresponding author(s): Noriaki Ono

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.

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	ZEN 2 (blue edition, ZEISS), FACSDiva v8.0.1 (BD)
Data analysis	Image J (NIH), FlowJo 9.3.3 (TreeStar), GraphPad Prism 5.0

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 figure source data were provided in the supplementary information file. The datasets generated during and/or analyzed during the current study are available in Dryad Digital Repository (https://datadryad.org) with the identifier doi:10.5061/dryad.3qq5bm7.

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	No statistical method was used to predetermine sample size. We chose the numbers of mice to study based on our prior experience that give good standard errors of the mean and good statistics to make it unlikely that we miss a biologically important difference between groups.
Data exclusions	Some of the data were excluded from the study because of the pre-established criteria such as problems or failures in identifying correct genotypes or birth dates, and issues unrelated to the intervention of the study such as spontaneous malnutrition. In any case, we consistently used littermate controls with corresponding genotypes in analysis.
Replication	For all data presented in the manuscript, we examined at least three independent biological samples (three different mice) to ensure the reproducibility. For each series of the experiments, all attempts at replication were successful.
Randomization	The experiments were not randomized. We used all the available mice of the desired genotypes. Mice were allocated to particular groups based on results of PCR-genotying typically performed around one week after birth. Covariates were controlled by considering multiple factors, such as genotypes and general phenotypical data (i.e. body weight). On principle, we did not observe any particular difference among groups.
Blinding	The investigators were not blinded to allocation during experiments and outcome assessment because it was impossible due to following reasons: samples were allocated to particular groups before experiments were initiated based on genotyping results, and given unique identifiers highlighting groups throughout experiments i.e. housing in cages, tissue collections, sample preparation and data acquisition. However, we did not pay particular attention to groups when we were measuring and counting.

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

Unique biological materials

Policy information about availability of materials

Obtaining unique materials	There is no restriction on availability of unique materials (genetically engineered mice) used for this study. These mice will be deposited at a repository upon publication.

Antibodies

Antibodies used	ThermoFisher/eBioscience eFlour450-conjugated CD31 (390, Cat# 48-0311-82, Lot# 4301770) eFlour450-conjugated CD45 (30F-11, Cat# 48-0451-82, Lot # 4295770) eFlour450-conjugated Ter119 (TER-119, Cat# 48-5921-82, Lot# 4295840) Fluorescein isothiocyanate (FITC)-conjugated CD90.2 (30-H12, Cat# 11-0903-81, Lot# E00428-1634) Phycoerythrin (PE)-conjugated CD51 (RMV-7, Cat# 12-0512-81, Lot# E01293-1633) Allophycocyanin (APC)-conjugated CD105 (MJ7/18, Cat# 17-1051-80, Lot# 24407-101) Peridinin chlorophyll protein complex (PerCP)-eFlour710-conjugated CD200 (OX90, Cat# 46-5200-80, Lot# 4298110).

ThermoFisher/Invitrogen
Alexa Fluor 488 goat anti-rabbit IgG (H+L) (Cat# A11034, Lot760000)
Alexa Fluor 647 donkey anti-rabbit IgG (H+L) (Cat# A31573, Lot1322326)
Alexa Fluor 647 donkey anti-goat IgG (H+L) (Cat# A21447, Lot1301819)

EMD-Millipore
Rabbit anti-Sox9 polyclonal antibody (Cat# AB5535, Lot# 2847051, 2922429)

R&D systems
Goat anti-osteopontin (OPN) polyclonal antibody (Cat# AF808, Lot# 0615081, 0617041)

Validation

More detailed information about these antibodies ais available on these manufacturers' websites.

Animals and other organisms

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

Laboratory animals

We used genetically modified mice (mus musculus) for this study. Most of the mouse lines have been backcrossed to a C57/BL6 background. We used female breeder mice in a FVB/N background. Mice with both sexes were used throughout their lifespan (up to 2 years of age). Mouse strains used in the study were as following: PTHrP-creERT2-WPRE, PTHrP-mCherry/null, Cxcl12-GFP/null, Col1a1(2.3kb)-GFP (JAX013134), Dlx5-creERT2 (JAX010705), Col2a1-creERT2 (JAX006774), Rosa26-CAG-loxP-stop-loxP-tdTomato (Ai14: R26R-tdTomato, JAX007914), Rosa26-CAG-loxP-stop-loxP-ZsGreen (Ai6: R26R-ZsGreen, JAX007906), Rosa26-SA-loxP-stop-loxP-DTA (ROSA-DTA, JAX009669) and Rosa26-CAG-loxP-stop-loxP-Confetti (R26R-Confetti, JAX013731), NOD scid gamma (NSG) (JAX005557).

Wild animals

N/A

Field-collected samples

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

Distal epiphyses of femurs were manually dislodged, and attached soft tissues and woven bones were carefully removed using forceps. Dissected epiphyses were incubated with 2 Wunsch units of Liberase TM (Roche) in 3ml Ca2+, Mg2+-free Hank's Balanced Salt Solution (HBSS, Sigma H6648) at 37oC for 60 min on a shaking incubator (ThermomixerR, Eppendorf). After this initial digestion, remaining surrounding soft tissues, including perichondrium and hypertrophic layers, were removed by rolling epiphyses over sterile paper towels (Scott C-fold towels, Kimberly-Clark) for several times. Articular cartilage and secondary ossification centers were subsequently removed. Dissected growth plates were minced using a disposable scalpel (No.15, Graham-Field), and further incubated with Liberase TM at 37oC for 60 min on a shaking incubator. Cells were mechanically triturated using an 18-gauge needle and a 1ml Luer-Lok syringe (BD), and filtered through a 70µm cell strainer (BD) into a 50ml tube on ice to single cell suspension. After washing, tissue remnants were incubated with Liberase TM at 37oC for 30 min on a shaking incubator, and cells were filtered into the same tube. Cells were pelleted and resuspended in appropriate medium for flow cytometry.

Instrument

BD LSR Fortessa (BDBiosciences)

Software

FACSDiva v8.0.1 (BD) & FlowJo 9.3.3 (TreeStar) software

Cell population abundance

N/A

Gating strategy

Single cells were first gated using FSC and SSC denominators. Only CD45 negative fraction was gated and analyzed. Negative 'unstained' control samples were always used as a reference to determine the demarcation between the positive and negative populations.

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