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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	BD FACSDiva (8.0.2), ZEN 2.3 SP1 (black 64 bit)
Data analysis	ImageJ (1.52h), Imaris (x64 9.3.0), Prism (7.00), Trim Galore! (0.4.1), STAR (2.5.3), DESeq2 (1.22.2), FlowJo (v10.0.7), DAVID (6.8), RStudio (Version 1.1.453), R (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/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

Sequence data that support the findings of this study have been deposited in GEO with the accession codes GSE131566 (https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE131566).
Source data for all figures are provided with the paper.

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	Sample sizes were determined based on prior studies and literatures of the field using similar experimental paradigms.
Data exclusions	No data were excluded from analysis
Replication	For in vivo experiments using rodent, biological replicates and independent cohorts of mice were used; for in vitro experiments, biological replicates as well as technical triplicates were used to ensure reproducibility. All attempts at replication were successful.
Randomization	The mice were randomly assigned into different experimental groups whenever possible, except in experiments required specific genotypes.
Blinding	For LC-MS-MS analysis, RNA-seq library preparation, and sequencing, experimenters were blinded to experimental conditions. Blinding was not possible in mouse studies due to the need to identify specific genotypes or treat mice with different chemicals according to experimental designs.

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

TRP2 (Santa Cruz, CAT 10451, Clone D18, Lot k2114, Dilution 1:400)
Tyrosine hydroxylase (Millipore, CAT AB152, Clone N/A, Lot 3072361, Dilution 1:1000)
Tyrosine hydroxylase (Millipore, CAT AB1542, Clone N/A, Lot 3168710, Dilution 1:150-1:300)
c-Fos (Abcam, CAT 190289, Clone N/A, Lot GR3253255-1, Dilution 1:400)
γ-H2AX (Cell Signaling Technology, CAT 9718, Clone 20E3, Lot 17, Dilution 1:400)
Phospho-Histone H3 (Cell Signaling Technology, CAT 3377S, Clone D2C8, Lot 7, Dilution 1:250)
Cleaved Caspase-3 (Cell Signaling Technology, CAT 9664S, Clone 5A1E, Lot 45, Dilution 1:300)
GFP (Abcam, CAT ab290, Clone N/A, Lot N/A, Dilution 1:800)
CD3 (eBioscience, CAT 14-0032-81, Clone 17A2, Lot 4342633, Dilution 1:800)
CD11b (eBioscience, CAT 14-0112-81, Clone M1/70, Lot E03529-1632, Dilution 1:400)
Phospho-CREB (Cell Signaling Technology, CAT 9198, Clone 87G3, Lot 14, Dilution 1:800)
MITF (Abcam, CAT ab12039, Clone C5, Lot GR3206967-1, Dilution 1:400)
CD140a (Invitrogen, CAT 13-1401-82, Clone APA5, Lot 1993111, Dilution 1:200)
CD45 (Invitrogen, CAT 13-0451-82, Clone 30-F11, Lot 1989134, Dilution 1:400)
Sca1 (Invitrogen, CAT 13-5981-82, Clone D7, Lot 4346548, Dilution 1:1000)
CD34 (Invitrogen, CAT 13-0341-82, Clone RAM34, Lot 1993111, Dilution 1:100)
CD117 (Biolegend, CAT 135136, Clone ACK2, Lot B251908, Dilution 1:400)

Validation

TRP2 (Santa Cruz, CAT 10451): Mouse, Immunohistochemistry, validated on manufactures's website: http://www.emdmillipore.com/US/en/product/Anti-Tyrosine-Hydroxylase-Antibody,MM_NF-AB152#overview

Tyrosine hydroxylase (Millipore, CAT AB152): Mouse, Immunohistochemistry, validated on manufactures's website: http://

www.emdmillipore.com/US/en/product/Anti-Tyrosine-Hydroxylase-Antibody,MM_NF-AB152#overview

Tyrosine hydroxylase (Millipore, CAT AB1542): Mouse, Immunohistochemistry, validated on manufactures's website:http://www.emdmillipore.com/US/en/product/Anti-Tyrosine-Hydroxylase-Antibody,MM_NF-AB1542#overview

c-Fos (Abcam, CAT 190289, Clone N/A): Mouse, Immunohistochemistry, validated on manufactures's website: https://www.abcam.com/c-fos-antibody-ab190289.html#top-500

γ-H2AX (Cell Signaling Technology, CAT 9718): Mouse, Immunohistochemistry, validated on manufactures's website: https://www.cellsignal.com/products/primary-antibodies/phospho-histone-h2a-x-ser139-20e3-rabbit-mab/9718

Phospho-Histone H3 (Cell Signaling Technology, CAT 3377S): Mouse, Immunohistochemistry, validated on manufactures's website: https://www.cellsignal.com/products/primary-antibodies/phospho-histone-h3-ser10-d2c8-xp-rabbit-mab/3377

Cleaved Caspase-3 (Cell Signaling Technology, CAT 9664S): Mouse, Immunohistochemistry, validated on manufactures's website: https://www.cellsignal.com/products/primary-antibodies/cleaved-caspase-3-asp175-5a1e-rabbit-mab/9664

GFP (Abcam, CAT ab290, Clone N/A): Mouse, Immunohistochemistry, validated on manufactures's website: https://www.abcam.com/gfp-antibody-chip-grade-ab290.html?productWallTab=ShowAll

CD3 (eBioscience, CAT 14-0032-81, Clone 17A2): Mouse, Immunohistochemistry, validated on manufactures's website: https://www.thermofisher.com/antibody/product/CD3-Antibody-clone-17A2-Monoclonal/14-0032-82

CD11b (eBioscience, CAT 14-0112-81, Clone M1/70): Mouse, Immunohistochemistry, validated on manufactures's website: https://www.thermofisher.com/antibody/product/CD11b-Antibody-clone-M1-70-Monoclonal/14-0112-82

Phospho-CREB (Cell Signaling Technology, CAT 9198): Mouse, Immunohistochemistry, validated on manufactures's website: https://www.cellsignal.com/products/primary-antibodies/phospho-creb-ser133-87g3-rabbit-mab/9198

MITF (Abcam, CAT ab12039, Clone C5): Mouse, Immunohistochemistry, validated on manufactures's website: https://www.abcam.com/mitf-antibody-c5-chip-grade-ab12039.html

CD140a (Invitrogen, CAT 13-1401-82, Clone APA5): Mouse, FACS, validated on manufactures's website: https://www.thermofisher.com/antibody/product/CD140a-PDGFRA-Antibody-clone-APA5-Monoclonal/13-1401-82

CD45 (Invitrogen, CAT 13-0451-82, Clone 30-F11): Mouse, FACS, validated on manufactures's website: https://www.thermofisher.com/antibody/product/CD45-Antibody-clone-30-F11-Monoclonal/13-0451-82

Sca1 (Invitrogen, CAT 13-5981-82, Clone D7): Mouse, FACS, validated on manufactures's website: https://www.thermofisher.com/antibody/product/Ly-6A-E-Sca-1-Antibody-clone-D7-Monoclonal/13-5981-82

CD34 (Invitrogen, CAT 13-0341-82, Clone RAM34): Mouse, FACS, validated on manufactures's website: https://www.thermofisher.com/antibody/product/CD34-Antibody-clone-RAM34-Monoclonal/13-0341-82

CD117 (Biolegend, CAT 135136, Clone ACK2): Mouse, FACS, validated on manufactures's website: https://www.biolegend.com/en-us/products/apccyanine7-anti-mouse-cd117-c-kit-antibody-13795

Animals and other organisms

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

Laboratory animals	C57BL/6J, Tyr-CreER, K15-CrePGR, Rag1 KO, CD11b-DTR, GR flox, Dreadd flox, Rosa-H2BGFP/mCherry, Rosa26-rtTA, Rosa-mTmG, RIPK3 knockout, Adrb2 flox, TH-CreER, pTRE-P27. All experiments used balanced groups of male and female mice. All experiments are conducted and compared using mice of the same hair cycle stage in comparable age range (P20-P25 for 1st telogen, P31-P36 for full anagen, and P50-P60 for 2nd telogen, or long-term monitoring as specified).
Wild animals	This study did not involve wild animals.
Field-collected samples	This study did not involve field-collected samples.
Ethics oversight	All animals were maintained in an Association for Assessment and Accreditation of Laboratory Animal Care-approved animal facility at Harvard University, Harvard Medical School, and Ribeirao Preto Medical School. Procedures were approved by the Institutional Animal Care and Use Committee of all institutions and were in compliance with all relevant ethical regulations.

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	Mouse dorsal skin was collected, and the fat layer was removed by gentle scrapping from the dermal side. The skin was incubated in 0.25% collagenase in HBSS at 37 °C for 35-45 minutes on an orbital shaker. Single cell suspension was collected by gentle scraping of the dermal side and filtering through 70 µm and 40 µm filters. The epidermal layer was incubated in trypsin-EDTA at 37 °C for 35-45 minutes on an orbital shaker. Single cell suspension was collected by gentle scraping of the epidermal side and filtering through 70 µm and 40 µm filters. The single cell suspension was centrifuged for 5 minutes at 4°C, resuspended in 0.25% FBS in PBS, and stained with fluorescent dye-conjugated antibodies for 30 minutes. For late anagen skin samples, the bottom parts of the hair follicles containing mature melanocytes were removed by gentle scrapping under dissection microscope. The MeSCs located close to the bulge remained and were verified by immunostaining.
Instrument	FACS: BD FACSAria III
Software	BD FACSDiva (8.0.2), FlowJo (v10.0.7)
Cell population abundance	For sorting for RNA-seq, at least 10,000 MeSCs were collected. The purity was verified by expression of GFP driven by lineage specific CreER.
Gating strategy	Positive and negative gates were set using fluorescence minus one (FMO) background intensity controls. Fluorophores were chosen to minimize spectral overlap.

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