nature research

Corresponding author(s): Ya-Chieh Hsu

Last updated by author(s): Feb 12, 2021

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	BD FACSDiva (v8.0.2), ZEN 2.3 SP1 (black 64 bit)
Data analysis	Trim Galore! (v0.4.1), STAR (v2.5.3), DESeq2 (v1.22.2), GraphPad Prism (v8.4.2), ImageJ (v1.52h), FlowJo (v10.0.7), RStudio (v1.1.453), R (v3.5.1), Salmon (v1.55), Phobius (web-accessible signal peptide prediction tool, Kall research lab), Adobe Photoshop (v.21.2.4), Adobe Illustrator (v.24.3).

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

Sequencing data that support the findings of this study have been deposited in GEO with the accession number GSE135705 (https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE135705).

DAVID web-accessible tool (v6.8) is available at https://david.ncifcrf.gov/.
MetazSecKB web-accessible tool is available at proteomics.ysu.edu/secretomes/animal/.
Source data for all main figures and Extended Data 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	No statistical methods were used to predetermine sample size. Sample sizes were determined based on prior studies and literatures of the field using similar experimental paradigms: Zhang et al. Nature 577:676-681 2020, Shwartz et al. Cell 182:578-593 2020, Wang et al. Cell Stem Cell 24:654-669 2018, Wang et al. Science 351:613-7 2016, Lay et al. PNAS 113:E1506-15 2016, Hsu et al. Cell 157:935-49 2014.
Data exclusions	No data was excluded from the analysis.
Replication	For in vivo experiments using rodents, biological replicates and independent cohorts of mice were used, and all experiments were replicated independently at least twice. For in vitro experiments, both biological and technical replicates were used, and all experiments were replicated independently at least twice to ensure reproducibility. Replication information is included in 'Statistics and Reproducibility' (Methods). All attempts at replication were successful. For RNA sequencing analysis, the data were from biological replicates and a single evaluation was performed per experimental data set.
Randomization	Mice were randomly assigned to control or experimental groups whenever possible, except in experiments that 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 when specific genotypes or surgical models had to be identified 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 and archaeology
☐	☒ Animals and other organisms
☒	☐ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

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

Antibodies

Antibodies used	CD34 (eBioscience, CAT 14-0341-82, Clone RAM34, Lot E019241, Dilution 1:100) CD140a (R&D Systems, CAT AF1062, Clone N/A, Lot HMQ0219071, Dilution 1:100) P-Cadherin (R&D Systems, CAT AF761, Clone N/A, Lot FHQ0319094, Dilution 1:400) GFP (Abcam, CAT ab290, Clone N/A, Lot GR196475-1, Dilution 1:5000) Cleaved Caspase-3 (Cell Signaling Technology, CAT 9661S, Clone D175, Lot 45, Dilution 1:300) Sox9 (Millipore Sigma, CAT AB5535, Clone N/A, Lot 3063352, Dilution 1:500) Phosphorylated histone H3 (Cell Signaling Technology, CAT 3377S, Clone D2C8, Lot 7, Dilution 1:500) Glucocorticoid Receptor (Cell Signaling Technology, CAT 3660S, Clone D8H2, Lot 4, Dilution 1:100) Pdgfra-biotin (eBioscience, CAT 13-1401-82; Clone APA5, Lot 2173826, Dilution 1:250) CD45-eflour450 (eBioscience, CAT 48-0451-82; Clone 30-F11, Lot 2197161, Dilution 1:250) CD31-PE-Cy7 (eBioscience, CAT 25-0311-81; Clone 390, Lot 2158713, Dilution 1:200) Sca-1-PerCP-Cy5.5 (eBiosciences, CAT 45-5981-82, Clone D7, Lot 2074537, Dilution 1:1000) CD24-FITC (eBioscience, CAT 11-0242-82; Clone M1/69, Lot 1993126, Dilution 1:250) Streptavidin-APC (eBioscience, CAT 17-4317-82; Clone N/A, Lot 2133221, Dilution 1:500) CD49f (Integrin alpha 6)-PE (eBioscience, CAT 12-0495-82; Clone GoH3, Lot 1984120, Dilution1:500) CD34-eFlour660 (eBioscience, CAT 50-0341-82; Clone RAM34, Lot 2106860, Dilution 1:100)
Validation	Description of antibody validations are provided by each commercial manufacture on their associated website.

Validation	CD34 (eBioscience, CAT 14-0341-82, Clone RAM34): Mouse, Immunohistochemistry, validated on manufacture's website: https://www.thermofisher.com/antibody/product/CD34-Antibody-clone-RAM34-Monoclonal/14-0341-82 CD140a (R&D Systems, CAT AF1062, Clone N/A): Mouse, Immunohistochemistry, validated on manufacture's website: https://www.rndsystems.com/products/mouse-pdgf-ralpha-antibody_af1062 P-Cadherin (R&D Systems, CAT AF761, Clone N/A): Mouse, Immunohistochemistry, validated on manufacture's website: https://www.rndsystems.com/products/mouse-p-cadherin-antibody_af761 GFP (Abcam, CAT ab290, Clone N/A): Mouse, Immunohistochemistry, validated on manufacture's website: https://www.abcam.com/gfp-antibody-ab290 Cleaved Caspase-3 (Cell Signaling Technology, CAT 9664S): Mouse, Immunohistochemistry, validated on manufacture's website: https://www.cellsignal.com/products/primary-antibodies/cleaved-caspase-3-asp175-5a1e-rabbit-mab/9664 Sox9 (Millipore Sigma, CAT AB5535, Clone N/A): Mouse, Immunohistochemistry, validated on manufacture's website: https://www.sigmaaldrich.com/catalog/product/mm/ab5535 Phospho-Histone H3 (Cell Signaling Technology, CAT 3377S): Mouse, Immunohistochemistry, validated on manufacture's website: https://www.cellsignal.com/products/primary-antibodies/phospho-histone-h3-ser10-d2c8-xp-rabbit-mab/3377 Glucocorticoid Receptor (Cell Signaling Technology, CAT 3660S, Clone D8H2): Mouse, Immunohistochemistry, validated on manufacture's website: https://www.cellsignal.com/products/primary-antibodies/glucocorticoid-receptor-d8h2-xp-rabbit-mab/3660 Pdgfra-biotin (eBioscience, CAT 13-1401-82; Clone APA5): Mouse, FACS, validated on manufacture's website: https://www.thermofisher.com/antibody/product/CD140a-PDGFRA-Antibody-clone-APA5-Monoclonal/13-1401-82 CD45-eflour450 (eBioscience, CAT 48-0451-82; Clone 30-F11): Mouse, FACS, validated on manufacture's website: https://www.thermofisher.com/antibody/product/CD45-Antibody-clone-30-F11-Monoclonal/48-0451-82 CD31-PE-Cy7 (eBioscience, CAT 25-0311-81; Clone 390): Mouse, FACS, validated on manufacture's website: https://www.thermofisher.com/antibody/product/CD31-PECAM-1-Antibody-clone-390-Monoclonal/25-0311-82 Sca-1-PerCP-Cy5.5 (eBiosciences, CAT 45-5981-82, Clone D7): Mouse, FACS, validated on manufacture's website: https://www.thermofisher.com/antibody/product/Ly-6A-E-Sca-1-Antibody-clone-D7-Monoclonal/45-5981-82 CD24-FITC (eBioscience, CAT 11-0242-82; Clone M1/69): Mouse, FACS, validated on manufacture's website: https://www.thermofisher.com/antibody/product/CD24-Antibody-clone-M1-69-Monoclonal/11-0242-82 Streptavidin-APC (eBioscience, CAT 17-4317-82; Clone N/A): Streptavidin-APC conjugates was validated to detect biotin conjugated primary antibody in FACS on manufacture's website: https://www.thermofisher.com/order/catalog/product/17-4317-82 CD49f (Integrin alpha 6)-PE (eBioscience, CAT 12-0495-82; Clone GoH3): Mouse, FACS, validated on manufacture's website: https://www.thermofisher.com/antibody/product/CD49f-Integrin-alpha-6-Antibody-clone-eBioGoH3-GoH3-Monoclonal/12-0495-82 CD34-eFlour660 (eBioscience, CAT 50-0341-82; Clone RAM34): Mouse, FACS, validated on manufacture's website: https://www.thermofisher.com/antibody/product/CD34-Antibody-clone-RAM34-Monoclonal/50-0341-82

Animals and other organisms

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

Laboratory animals	Mice were housed in individually ventilated cages at a maximum density of 5 mice per cage with nestlet bedding and a red hut for enrichment and kept on a 12-h light–dark cycle. Room temperature was maintained at 22°C ± 1°C with 30%–70% humidity. Mice were fed ad libitum with rodent diet (Prolab IsoPro RMH 3000 5P75) and water. The study involved the following laboratory animals: C57BL/6 mice (purchased from Jackson Laboratory). K15-CrePGR, Pdgfra-CreER, Sox2-CreER, GR flox, R26-lsl-YFP (purchased from Jackson Laboratory and bred in the unit). Given the inherent differences in the timing of the hair cycle in male mice and female mice, we used female mice aged 5-8 weeks for most experiments. However, adrenalectomy and corticosterone feeding experiments used both males and females aged 5-8 weeks. Also, 17-month-old female mice were used for adrenalectomy experiments. Also, the ages of mice were clearly indicated in results (figure and figure legends).
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 and the Icahn School of Medicine at Mount Sinai. Procedures were approved by 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	For collecting dermal papilla cells, mouse dorsal skin was collected and the skin was incubated in Hank's Balanced Salt Solution at 37 °C for 20-30 minutes on an orbital shaker. Dermal single-cell suspensions were obtained after 0.25% trypsin treatment for 10–20 min at 37°C by gentle scrapping of the dermal side and filter through 70 µm and 40 µm filters. Single cell suspension was centrifuged for 10 minutes at 4°C, resuspended in 0.25% FBS in PBS and stained with fluorescent dye-conjugated antibodies for 30 minutes. For the isolation of hair follicle stem cells (HFSCs), mouse dorsal skin was dissected, and the fat layer was removed using a surgical scalpel. The skin was incubated in trypsin-EDTA at 37°C for 35–45 min on an orbital shaker. Single-cell suspension was obtained by scraping the epidermal side and filtering. Cells were centrifuged for 8 min at 350 g at 4°C, resuspended in 5% fetal bovine serum, and stained for 30–40 min.
Instrument	FACS: BD FACSAria III
Software	BD FACS Diva (8.0.2), FlowJo (v10.0.7)
Cell population abundance	For sorting for RNA-seq, at least 10,000 cells were collected.
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.