nature portfolio

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Reporting Summary

Nature Portfolio 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 Portfolio 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	Data were collected using standard laboratory instruments and software.
Data analysis	graphpad prism 11；FlowJo 10; IGV 2.19.7; image J; LightCycler 96; NIS-Element viewer

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 Portfolio 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 description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

Provide your data availability statement here.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	n/a
Reporting on race, ethnicity, or other socially relevant groupings	n/a
Population characteristics	n/a
Recruitment	n/a
Ethics oversight	n/a

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

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 not determined using statistical methods. Instead, they were selected according to established practices in the field and based on prior studies involving mouse genetics and stem cell experiments, with sufficient biological replicates included to ensure reproducibility.
Data exclusions	No data were excluded from this study, except for low-quality reads from RNA-seq and MeRIP-seq that were filtered out during standard bioinformatic processing and mice that did not survive due to sickness / fighting wounds were exluded.
Replication	All experiments included at least three biological replicates, and the number of biological replicates for each experiment is detailed in the figure legends and Methods section.
Randomization	Randomization was not applicable, as experimental groups were defined by hair cycle and genotype. To control for potential litter effects, experiments were performed using animals from multiple independent litters.
Blinding	Blinding was not applicable, as experimental groups were defined by hair cycle or genotype.

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
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

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

Antibodies

Antibodies used

For the immunofluorescence or immunochemistry staining:
1. ALKBH5 (abcam, ab195377, 1:200)
2. METTL3 (proteintech, 67733-1-Ig, 1:200)
3. CD34 (eBioscience, 14-0341-82; 1:200)
4. Ki67 (Abcam, ab15580; 1:500)
5. LEF1 (Cell Signaling Technology, 2230; 1:200)
6. GATA3 (Cell Signaling Technology, 5852; 1:400)
7. KRT6 (Covance, PRB-169P; 1:500)
8. SOX9 (Millipore Sigma, AB5535; 1:500)
9. cleaved-caspase-3 (Cell Signaling Technology, 9661; 1:500)
10. MCAM (Cell Signaling Technology, 81701; 1:400)

For the flow cytometry and FACS:
1. CD34-PE (BioLegend, 152204,1:100)
2. CD49f-AF700 (Invitrogen, 56-0495-82)
3. LGR5-FITC (R&D system, FAB8240G)

Validation

All antibodies used in this study were obtained from commercial sources or established repositories. Validation was performed by the manufacturers and is supported by prior publications demonstrating specificity in mouse system.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)

HaCaT cell line

Authentication

The cell line have been authenticated via short tandem repeat (STR) analysis.

Mycoplasma contamination

The cell line tested negative for mycoplasma contamination.

Commonly misidentified lines
(See ICLAC register)

No commonly misidentified cell lines were used in the study.

Animals and other research organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in Research

Laboratory animals

Mettl3fl/fl (strain, Exon 5 be designed as conditional knockout region, Cyagen); Krt5-CreERT2 (strain, 029155, The Jackson Laboratory); Rosa26-tdTomato (strain, 007909, The Jackson Laboratory); Rosa26-mTmG (strain, 007676, The Jackson Laboratory). Alkbh5fl/fl mice were provided by Dr. Xiong Cao from the National Key Laboratory of Neurobiology at Southern Medical University, Guangzhou, China. Lgr5EGFP-Ires-CreERT2 mice were provided by Dr. Weijie Zhou from the State Key Laboratory of Organ Failure Research, Department of General Surgery, Guangdong Provincial Key Laboratory of Precision Medicine for Gastrointestinal Tumor, Nanfang Hospital, Southern Medical University, Guangzhou, Guangdong, China.

Wild animals

The study did not involve wild animals.

Reporting on sex

The mice used in this study were not separated by sex.

Field-collected samples

The study did not involve samples collected from field.

Ethics oversight

All mice were bred and housed under specific pathogen-free conditions and used in experiments following the National Institutes of Health Guide for the Care and Use of Laboratory Animals, with approval from the Scientific Investigation Board of Southern Medical University (D2025171), Guangzhou, China. The animal facility was maintained under strictly controlled environmental conditions at a constant temperature of 25 °C and a relative humidity of 50–60%. All bedding, chow, and drinking water were autoclaved to ensure the integrity of the microbiological barrier system.

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

Plants

Seed stocks: n/a

Novel plant genotypes: n/a

Authentication: 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: For single-cell preparation, dorsal skin tissues were excised from mice, and the subcutaneous fat layer was carefully removed using a surgical blade. The processed skin samples were incubated in pre-warmed trypsin–EDTA solution at 37 °C for 35–45 min. A single-cell suspension was obtained by scraping the epidermal side and filtering, which was subsequently passed through 70 μm and 40 μm cell strainers to achieve a single-cell suspension. The cells were pelleted by centrifugation at 350 × g for 10 min at 4 °C, resuspended in phosphate-buffered saline (PBS) containing 3% fetal bovine serum (FBS), and stained with primary antibodies.

Instrument: Flow cytometry analysis was performed on BD LSRFortessa, the HFSCs sorting were performed on Beckman Coulter MoFlo cell sorter.

Software: The data was analyzed by FlowJo 10.

Cell population abundance: HFSCs typically represented ~6–8% of total epidermal single-cell suspensions in 8-10 weeks adult mice.

Gating strategy: Bulge-HFSCs were gated as integrin α6+CD34+LGR5-, HG-HFSCs were gated as integrin α6+CD34-LGR5+.

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