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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	FV10-ASW Software (4.02), FV31S-SW Software (2.3.2.169), MxPro Software (3.00), BD FACS Diva Software (version 6.1.3), cellSens Standard (version 3.1), QuantaSoft (version 1.7)
Data analysis	Excel (Microsoft), GraphPad Prism 6, GraphPad Prism 9, ImageJ (1.53K), Flowjo (version 10), GSEA (4.1.0), 10x Genomics Cell Ranger (6.1.1), scanpy (1.8.2), Loupe Browser (6.0.0)

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 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

Microarray data were deposited in the GEO public database (accession code GSE158611 and GSE248613).
Bulk RNA-seq data were deposited in the GEO public database (accession codes GSE248614 and GSE249074).

scRNA-seq data were deposited in the GEO public database (accession code GSE252031). The raw scRNA sequencing data were processed using the 10X Genomics Cell Ranger package and aligned to the mm10 reference genome.
GitHub: https://github.com/seitalab/mohri_et_al_young_epi_vs_old_epi

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	Both sexes were randomly included in this study.
Reporting on race, ethnicity, or other socially relevant groupings	Race, ethnicity, or other socially relevant groupings was not considered in study design.
Population characteristics	Potential research participants agreed to the use of their skin tissue samples, which were collected for the diagnosis or treatment of skin diseases, for research purposes. Patients of various ages with facial melanocytic lesions were randomly chosen for the potential sample lists.
Recruitment	Research participants were recruited from patients with facial melanocytic lesions who consented to the research use of their skin samples, which were originally collected for diagnostic or therapeutic purposes. The methods and procedures for the recruitment of potential participants were approved by the IRB. Written informed consent was obtained from all participants. None of the patients were compensated for their involvement in the study.
Ethics oversight	The histopathological analysis of human samples was approved by the Tokyo Medical and Dental University, presently Institute of Science Tokyo (M2016-046) (M2016-015-04), Yamagata University (2023-281) and the University of Tokyo (2023-25-0720).

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	No statistical methods were used to predetermine the sample size. The sample size was selected based on previous papers (Inomata et al., 2009; Morinaga et al., 2021, etc). In compliance with local animal ethics, experiments were designed to use the minimum number of mice necessary to obtain the required data. All n values are clearly indicated in the figure legends.
Data exclusions	DBP mice that failed to respond to tamoxifen-induced recombination (non-responders) were excluded from the analysis. Their inclusion would have confounded the interpretation of conditional gene deletion effects.
Replication	The number of replicates for each experiment is indicated in the corresponding figure legend. All replication attempts yielded consistent results.
Randomization	All mice in this study were first grouped by genotype, and then, within each genotype group, the mice were randomly allocated to the various experimental conditions (control, IR, DMBA, UVB, etc.).
Blinding	No blinding was performed since the same researchers performed both data acquisition and analysis.

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 immunostaining, the following primary antibodies were used: Rat monoclonal anti-CD117 (BD, 553868, clone ACK45, 1:150), Rabbit polyclonal anti-β-galactosidase (MP Biomedicals, 55976, 1:100), Chicken polyclonal anti-GFP (abcam, ab13970, 1:500), Rabbit polyclonal anti-Keratin5 (Covance, PRB-160P, 1:500), Rabbit polyclonal anti-Keratin5 (abcam, ab53121, 1:200), Chicken polyclonal anti-Keratin15 (Covance, PCK-153P, 1:500), Chicken polyclonal anti-Keratin15 (BioLegend, 833904, 1:300), Rat monoclonal anti-CD49f (ITGA6) (BD, 555734, clone GoH3, 1:200), Rat monoclonal anti-P-Cadherin (Takara, M109, 1:200), Rabbit monoclonal anti-Histone H2A.X (Ser139) (CST, 9718, clone 20E3, 1:100), Rabbit polyclonal anti-KITL (IBL, 18111, 1:50), Rabbit polyclonal anti-S100 (DAKO, Z0311, 1:100), Rabbit polyclonal anti-Neuronal ClassIII β-Tubulin (Covance, PRB-435P, 1:1000) and Rat monoclonal anti-p21 (abcam, ab107099, clone E70,1:100). Secondary antibodies conjugated with Alexa Fluor 488, 594 or 680 (Life Technologies, 1:200) were used. For flow cytometry analysis, the following antibodies were used: Rat monoclonal anti-CD49f-PE (BD, 555736, clone GoH3, 1:25) and Rat monoclonal anti-Scal-APC (Miltenyi Biotec, 130-102-343, clone D7, 1:100).

Validation

Validation was performed to optimize conditions for specifically staining the target protein with negligible background. All antibodies were well characterized and were also applied according to previously published papers (Inomata et al., 2009; Ueno et al., 2014; Morinaga et al., 2021; Kato et al., 2021).

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)

Normal human embryonic melanocytes (NHEMs) were obtained from ThermoFisher Scientific or Kurabo.

Authentication

Vendor-authenticated NHEMs were utilized for this study. Authentication was confirmed through morphological assessment and growth curve analysis, supported by a Certificate of Analysis from the supplier.

Mycoplasma contamination

The NHEMs were tested negative for mycoplasma contamination.

Commonly misidentified lines
(See ICLAC register)

No commonly misidentified lines were used.

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

The mice were housed individually in cages, with a maximum density of five mice per cage. They were maintained on a 12-hour light/dark cycle, and the ambient temperature was kept at 20–24°C with 50–60% humidity. Mice of both sexes, ranging in age from seven weeks to 29 months, were analyzed.

C57BL/6J and C57BL/6N mice were purchased from Sankyo Labo Service Corporation, Inc., Japan SLC, Inc., and CLEA Japan, Inc. The following mice were used: Kitl-EGFP knock-in mice, Kitl flox mice, K15-EGFP transgenic mice, K15CrePR transgenic mice, Tyr-CreER transgenic mice, Tyr-Cre transgenic mice, K14-Kitl transgenic mice, Rosa26-tdTomato knock-in mice, R26R-H2B-GFP knock-in mice, Dct-LacZ mice, Tyr-Nras transgenic mice, Braf V600E mice, Pten flox mice, I-PpoI knock-in mice, p53 flox mice and TBK1 flox mice. Dct-H2B-GFP knock-in mice and Dct-CreERT2 knock-in mice were generated in our laboratory.

Wild animals

This study did not include wild animals.

Reporting on sex

Both male and female mice were used in this study.

Field-collected samples

This study did not use samples collected from the field.

Ethics oversight

All animal experiments were performed following the Guidelines for the Care and Use of Laboratory Animals, and were approved by the Institutional Committee of Laboratory Animal Experimentation (A2021-186A) (PA21-41).

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

Plants

Seed stocks	*Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.*
Novel plant genotypes	*Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.*
Authentication	*Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.*

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	The dorsal skin was placed dermis down in 0.25% trypsin for 10-13 h at 4°C followed by incubation at 37°C for 20 min or in 0.25 mg/ml thermolysin for 1 h at 37°C to separate the epidermis from the dermis. Single epidermal cell suspensions were obtained by gently scraping the epidermis and then filtering the cells through a 40μM cell strainer. The dermis, after separation from the epidermis by 0.25% trypsin, was digested with 0.2% collagenase for 2-3 h at 37°C to obtain dermal cell suspensions.
Instrument	BD FACSAria II, BD FACSAria IIIu
Software	BD FACS Diva Software (version 6.1.3), Flowjo (Version 10)
Cell population abundance	HFSCs/Hair germ or McSCs were sorted from mouse skin using a BD FACSAria II or BD FACSAria IIIu. The purity of the sorted cells was determined by reanalyzing them using flow cytometry. The purity of the sorted cell fractions was confirmed to be >95%.
Gating strategy	Initial gating was performed on forward scatter area (FSC-A) versus side scatter area (SSC-A) to exclude debris. Then, doublets were excluded using FSC-H versus FSC-W and SSC-H versus SSC-W. Viable cells were identified by excluding 7-AAD-positive events. The subsequent gating strategy is shown in the Extended Data. To distinguish the negative and positive cell populations, unstained samples were used as negative controls.

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