

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 (<i>n</i>) 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
<i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i> |
| ☒ | ☐ 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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted
<i>Give P values as exact values whenever suitable.</i> |
| ☒ | ☐ 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 <i>d</i> , Pearson's <i>r</i>), 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

Leica Application Suite v4.8
AxioVision (Carl Zeiss)
Zen (Carl Zeiss)
BD FACSDiva Software v6.1.3

Data analysis

ImageJ v1.47
GraphPad Prism v6.0
Imaris v9.1.0
Summit v4.3

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/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

All other data that support the findings of this study are available from the corresponding author upon reasonable request.

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](https://www.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 method was used to predetermine sample size. Required experimental sample sizes were estimated based on previous established protocols in the field. The sample sizes were adequate as the differences between experimental groups were reproducible. All n values are clearly indicated within the figure legends.
Data exclusions	No data was excluded from the analysis.
Replication	All experiments were performed at least three times with similar results. The live imaging data showed in Fig. 3d-e and extended data figure 9d-e and h-k were generated from one representative video respectively.
Randomization	Mice were randomly divided into treatment groups.
Blinding	No experiments presented in this study required blinding.

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

Primary antibodies used in IHC:
 goat-anti- α SMA (Abcam, ab5694, 1:50)
 rabbit-anti-TUBB3 (Abcam, ab18207, 1:100)
 rat-anti-THY1(CD90) (Abcam, ab3105, 1:100)
 rat-anti-CD24 (BD biosciences, 553146, 1:50)
 rabbit-anti-DPP4(CD26) (Abcam, ab28340, 1:150)
 rabbit-anti-PECAM1(CD31) (Abcam, ab28364, 1:10)
 rat-anti-CD34 (Abcam, ab8158, 1:100)
 rabbit-anti-COLLAGEN I (Rockland, 600-401-103-0.1, 1:150)
 rabbit-anti-COLLAGEN III (Abcam, ab7778, 1:150)
 rabbit-anti-COLLAGEN VI (Abcam, ab6588, 1:150)
 rabbit-anti-DLK1 (Abcam, ab21682, 1:200)
 rat-anti-ERTR7 (Abcam, ab51824, 1:200)
 rat-anti-F4/80 (Abcam, ab90247, 1:400)
 rabbit-anti-LYVE1 (Abcam, ab14917, 1:100)
 rat-anti-MOMA2 (1:100, ab33451, Abcam)
 goat-anti-PDGFR α (R&D systems, AF1062, 1:50)
 rat-anti-LY6A (Biolegend, 122502, 1:150)
 rat-anti-CD44 (Abcam, ab119348, 1:100)
 rabbit-anti-NOV/CCN3 (Elabscience, E-AB-15124, 1:20)
 sheep-anti-FAP (R&D systems, AF3715, 1:100)

Secondary antibodies:

PacificBlue-, AlexaFluor488-, AlexaFluor568, or AlexaFluor647-conjugated secondary antibodies against suitable species (Life technologies, 1:500)

Antibodies used for flow cytometry:
 anti-DLK1 (Abcam, ab21682, 1:200)
 FITC-anti-CD9 (eBioscience, 11-0091-81, 1:200)
 anti-CD271(LNGFR) (Miltenyi, 130-110, 1:100)
 APC-anti-F4/80 (eBioscience, 17-4801-82, 1:200)
 AlexaFluor790-anti-NG2 (Santa Cruz, sc-166251 AF790, 1:100)
 FITC-anti-DPP4(CD26) (BioLegend, 137806, 1:200)
 PerCP-eFluor710-anti-ITGB1(CD29) (eBioscience, 46-0291-80, 1:200)
 FITC anti-CD34 (eBioscience, 11-0341-82, 1:200)
 PerCP-Cy5.5-anti-CD24 (eBioscience, 45-0242-80, 1:200)
 APC-anti-ITGA7 (Miltenyi Biotec, 130-103-356, 1:100)
 PerCP-Cy5.5-anti-LY6A(Sca1) (eBioscience, 45-5981-80, 1:200)
 PE-Vio770-anti-PDGFRA (Miltenyi, 130-105-117, 1:100)
 PerCP-Vio700-anti-CD146 (Miltenyi, 130-103-865, 1:100)
 APC-anti-PECAM1(CD31) (BioLegend, 102410, 1:200)
 eFluor660-anti-LYVE1 (eBioscience, 50-0443-82, 1:200)
 APC-LY76(TER119) (BioLegend, 116212, 1:200)
 APC-anti-EPCAM(CD326) (BioLegend, 118214, 1:200)
 APC-anti-PTPRC(CD45) (BioLegend, 103112, 1:200)

Validation

See manufacturers' notes. Antibodies were additionally validated using respective isotype antibodies in immunofluorescence assays.

Animals and other organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research

Laboratory animals

Following mouse strains were used, both males and females, adult at 8-12 weeks old or neonatal at postnatal P0-P2:
 C57BL/6J wild type
 En1Cre (En1tm2(cre)Wrt)
 R26mTmG (Gt(ROSA)26Sortm4(ACTB-tdTomato,-EGFP)Luo)
 R26VT2/GK3 aka "Rainbow" (Gt(ROSA)26Sortm1(CAG-EGFP,-mCerulean,-mOrange,-mCherry)llw)
 R26iDTR (Gt(ROSA)26Sortm1(HBEGF)Awai)
 RAG2-/- (Rag2tm1.1Cgn)
 Fox Chase SCID (CB17/lcr-Prkdcscid/lcrIcoCrl)

Wild animals

The study did not involve wild animals.

Field-collected samples

The study did not involve samples collected from field.

Ethics oversight

Government of Upper Bavaria , Germany

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

Human research participants

Policy information about [studies involving human research participants](#)

Population characteristics

healthy donors between 18 - 65 years of age, both genders, underwent surgeries for skin tumors.

Recruitment

Fresh human skin and scar biopsies, from various anatomic locations, were collected through the Department of Dermatology and Allergology, Klinikum rechts der Isar, Technical University Munich. Informed consent was obtained from all subjects prior to skin biopsies.

Ethics oversight

Ethikkommission der Bayerischen Landesärztekammer, reference number 85/18S.

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

Fascia and dermis were physically separated from the back-skin of C57BL6/J or En1Cre;R26mTmG mice under the fluorescence stereomicroscope as before. Harvested tissue was minced with surgical scissors and digested with an enzymatic cocktail containing 1 mg/ml Collagenase IV, 0.5 mg/ml Hyaluronidase, and 25 U/ml DNase I (Sigma-Aldrich) at 37°C for 30 min. The resulted single cell suspension was filtered and incubated with conjugated/unconjugated primary antibodies (dilution 1:200) at 4° C for 30 min, followed by an incubation with a suitable secondary antibody when needed at 4° C for 30 min. Cells were washed and stained with Sytox blue dye (dilution 1:1000. Life technologies, S34857) for dead cell exclusion.

Instrument

Cells were subjected to flow cytometric analysis using a FACSAria III (BD Bioscience)

Software

Data was collected using the BD FACSDIVA software (BD Bioscience) and analyzed using Summit software (Cytomation)

Cell population abundance

The purity of sorted cells were determined by flow cytometric analysis of the sorted cells with the same gating strategy as during sorting.

Gating strategy

The single cells were gated base on FSC/SSC and FSC-Area/FSC-width. The viable cells were gated within SytoxBlue negative gate, and fibroblasts were gated within lineage-negative (APC-negative) gate (antibodies against lineage markers are APC-conjugated anti-CD45, anti-Ter119, anti-EpCAM, anti-CD31, anti-Lyve1, and anti-Tie2).

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