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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

For imaging experiments, multiple microscopes were used in experiments with their corresponding proprietary vendor-specific software, including Zeiss LSM 700 with Zeiss Zen (7.0.7.288); Zeiss LSM 880 with Zeiss Zen (14.0.0.201); EVOS (Thermofisher) with EVOS FL Auto 2 Cell Imaging System (DiamondScope v2.0.1732.0); SP8-STED (Leica) with LAS X (3.5.7.23225); TriMScope (LaVision Biotec) with Imspector (v5.0.273.0); FSX100 microscope (Olympus) with FSX-BSW (03.02.12) and Nikon ACT-1 (2.70) and the NanoZoomer-2.0RS (Hamamatsu) with NDP.toolkit (2.8.24). For spectrofluorometry, Fluoroskan Microplate Fluorometer (Thermo Fisher) was used with Ascent (2.6). For scanning electron microscopy, we used Zeiss Auriga Field-Emission Scanning Electron Microscope with Zeiss SmartSEM (6.00). For proteomics, Thermo Scientific Orbitrap Fusion Tribrid mass spectrometer was used with proprietary Orbitrap Tribrid MS series instrument control software Orbitrap Fusion (3.1 4212.25) and Xcalibur (4.2.28.14). For tissue mechanics, custom-built tensile tester as indicated in manuscript was used with IGOR Pro (6.0) (Wavemetrics). For AFM, JPK NanoWizard III instrument was used with JPK SPM Software (6.1.146)

Data analysis	For image quantification, we used Imaris versions 9.5 or 10.0, as well as FIJI ImageJ (2.0.0-rc-68/1.52i). For histology tissue type analysis, QuPath software (0.3.0) was used. Microsoft Excel and custom Python 3 scripts were used in various cases to perform simple transforms and analysis downstream. Additional software used for image processing and analysis of collagen fibres were Ilastik, ZEN (Zeiss), Dragonfly (OCS), Huygens software (SVI), CT-FIRE (2.0). For AFM analysis we used JPK Data Analysis 7.0.165 and Igor Pro 9. For general statistics, we used Prism 6 or 7 (GraphPad, Inc.). For performing Kolmogorov–Smirnov tests for proteomics, we used Python package scipy.stats.ks_2samp. For bulk transcriptomics data analysis, sequencing adaptor contaminations were removed from reads using Cutadapt and the resulting reads were mapped on the transcriptome (GRCm38 Ensembl gene-build 84) and quantified using RSEM. Circadian rhythmicity was tested using CircaN on the normalized RSEM counts.

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

All the transcriptomics data are available in Gene Expression Omnibus (GEO) and proteomics data in Proteomics Identification Database (PRIDE). The individual GEO accession numbers are as follows: bulk RNA-seq from neutrophils in parabiotic tissues (GSE141745); bulk RNA-seq from tissues at varying circadian timepoints (GSE198770); bulk RNA-seq from TGFbRDN neutrophils (GSE198654); bulk RNA-seq from skin fibroblasts (GSE202738); single cell RNA-seq from skin tissue (GSE229493, GSE271969), ATAC-seq from tissue neutrophils (GSE141285). For proteomics data, they have been deposited to the ProteomeXchange Consortium via the PRIDE partner repository with the dataset identifiers as follows: blood and lung cell lysates (PXD031943); neutropenic tissues (PXD031950); and wounded skin tissue (PXD031952). We additionally made use of following datasets for our analysis: collagen-containing extracellular matrix (GO:0062023); extracellular matrix structural constituent (GO:0005201); collagen fibril organization (GO:0030199); collagen metabolic process (GO:0032963); Tabula Muris dataset to identify cell signatures; GRCm38 Ensembl gene-build 84 as the mouse genome reference; GENCODE vM22 to annotate genes.

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	Sex and gender were not used as a parameter in the selection of samples in this study, and the tissues were collected from both male and female subjects.
Reporting on race, ethnicity, or other socially relevant groupings	No information was collected regarding race, ethnicity, or other socially relevant groups.
Population characteristics	Skin samples collected in Shanghai were non-cancerous, perilesional discarded skin that was excised to access the papillary thyroid carcinoma of the patients. Skin samples collected in New Haven were of non-cancerous, perilesional discarded skin that was excised for the repair of primary defects resulting from Mohs-confirmed surgical excisions of keratinocyte cancers. Lung and spleen samples were collected from perfused organ donors while blood samples were collected from healthy donors.
Recruitment	Skin samples were non-cancerous, perilesional discarded skin that was excised to access the papillary thyroid carcinoma of the patients or non-cancerous, perilesional discarded skin that was excised for the repair of primary defects resulting from Mohs-confirmed surgical excisions of keratinocyte cancers. Lung and spleen samples were collected from perfused organ donors, while blood samples were collected from healthy donors
Ethics oversight	Human skin samples were collected either in Fudan University Shanghai Cancer Center in Shanghai, China, under the Shanghai Cancer Center Institutional Review Board (SCCIRB) protocol 050432-4-2108 or at Yale University under Yale Institutional Review Board (IRB) protocol #2000027571. All protocols were in accordance with the Declaration of Helsinki.

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 sample size. They were determined based on pilot experiments or prior experience
Data exclusions	We used ROUT method with a Q value of 1% to identify and remove outliers. No other data was excluded.
Replication	Experimental findings were confirmed in independent experiments and found to be reliably reproducible. All experiments were successfully repeated at least 2 times.
Randomization	No specific randomization method was followed in this study. Allocation of mice to groups ensured similar distribution of age and gender, when appropriate.
Blinding	• Blinding was not performed in this study as the experiments and animal handling were performed by individual investigators. Whenever possible, automated analyses were performed and quantitative results were provided. Findings were validated with different techniques and at different institutions in the USA, Germany, Spain, and China as a way of minimizing bias.

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

Antibody / Clone / Species / Manufacturer / Cat# / dilution
o Anti-Col3al / Rabbit polyclonal /Abcam/ ab7778 / 1:200
o IgG isotype / Rabbit polyclonal /Abcam/ ab37415 / 1:200
o Anti-Collal / Rabbit polyclonal / Novus biological/ #600-408 / 1:200
o Anti-Fibronectin / Rabbit polyclonal / Bio-Rad/ #4470-4339 / 1:200
o Anti-Laminin / Rabbit polyclonal /Sigma/ #L9393 / 1:200
o Anti- Col4 / CIV22 / Mouse monoclonal/ Invitrogen / MA5-13437 / 1:100
o Anti-Collal / Rabbit polyclonal /Abcam/ ab21286 / 1:200
o Anti-Laminin / Rabbit polyclonal / Novus Biologicals/ NB300-144 / 1:100
o Anti-Elastin / Rabbit polyclonal /Abcam/ ab21610 / 1:100
o Anti-MPO / Goat polyclonal / R&D Systems/ AF3667 / 1:200
o Anti-PDPN/ eBio8.1.1 (8.1.1) / Syrian hamster monoclonal/ Invitrogen / #14-5381-82 / 1:200
o Anti-Smad3 [p Ser423, p Ser425] / Rabbit polyclonal / Novus biological/ NBP1-77836PE / 1:200
o Lycopersicon esculentum Lectin conjugated to Dylight 649 / Vector Laboratories/ DL-1178-1 / 50µg
o Anti-Mrp14 / 2B10 / Rat monoclonal/ Abcam/ ab105472 / 1:100
o Anti-CD31 SuperBright 436 / PECAM-1 / 390/ Rat monoclonal / ThermoFisher / #62-0311-82 / 10µg
o Anti-Staphylococcus aureus / Rabbit polyclonal /Abcam/ ab20920 / 1:200
o Anti-TNF alpha/ MP6-XT22 /Mouse/ eBioscience / # 14-7321-81 1:200
o iNOS/NOS2 / CXNFT /Mouse/ eBioscience / # 14-5920-82 / 1:200
o Anti-Histone H3 / citrulline R2 +RS+ Rl 7 / Rabbit polyclonal /Abcam/ ab5103 / 1:200
o Anti-goat-Cy2 / Donkey polyclonal / Jackson lmmunoResearch / 705-225-147 / 1:400
o Anti-rabbit lgG Alexa fluor 555 / Donkey polyclonal / Life Technologies/ A-31572 / dilution 1:500
o Anti-rabbit lgG Alexa fluor 647 / Goat polyclonal / Thermofisher / A-21245 / 1:500
o A488-conjugated streptavidin / Biolegend / #405235 / 1:500
o Anti-Syrian hamster Alexa fluor 488 / Goat polyclonal / Invitrogen / A21110 / 1:500
o Anti-Mouse lgG Alexa Fluor 555 / Donkey polyclonal / Life Technologies/ A-31570 / 1:500
o Anti-mouse Ly6G FITC / 1A8 / Rat/ eBioscience / # 11-9668-82 / 1:500
o Anti-mouse Ly6G-AlexaFluor 647 / 1A8 /Rat/ Biolegend / 127610 / 1:200
o Anti-mouse CD11b-BV510 / M1/70 /Rat/ Biolegend / 101245 / 1:200
o Anti-mouse Feeder cells antibody - PE /mEF-SK4 /Rat/ Miltenyi / 130-120-166 / 1:100
o Anti-mouse CD140a (PDGF Receptor a) – APC / APA5/ Rat / eBioscience / 17-1401-81 / 1:200

o Anti-mouse CD90.2 -FITC /53-2.1/Rat/ 11-0900-81/ 1:200
o Anti-GFP / chicken polyclonal / Invitrogen / A10262 / 1:200
o Anti-RFP (mCherry) / rabbit polyclonal / Invitrogen / 600-401-379 / 1:200
o Anti-mouse Ly6G-AlexaFluor488 / 1A8 / Rat / Biolegend /127626 / 1:200
o Anti-human CD45 APC-Cy7 / HI30 / mouse / Biolegend / 304014 / 1:200
o Anti-human CD3 PE-Cy7 / HIT3a / mouse / Biolegend / 300316/ 1:200
o Anti-human CD19 PE-CY7 / HIB19 / mouse / Biolegend / 302216/ 1:200
o Anti-human CD56 PE-CY7 / 5.1H11 / mouse / Biolegend / 362510/ 1:200
o anti-human CD66b Alexa Fluor 594 / G10F5 / BD Biosciences / 562940 / 1:200
o anti-rabbit IgG Alexa fluor 647 / Life Technologies / A-21245 / 1:200
o anti-human CD45 APC / clone 2D1/ mouse/ Biolegend/ 368512/ 1:200
o anti-human CD66b-PE Cy7 / G10F5 / mouse / Biolegend 305116 / 1:200
o anti-human CD16 - BV421 / B73.1 / mouse / Biolegend/ 360724 / 1:200
o goat anti-rat Alexa Fluor488 (A11006, Invitrogen) 1:500
o goat anti-rabbit Alexa Fluor 647 (ab150079, Abcam) 1:500

Validation

Antibodies listed above are all used in flow cytometry or histology experiments of mouse or human-derived material, and have been validated by the listed manufacturing companies. The validation materials can be found on the manufacturers' website as the vendor and the catalog number for each primary and secondary antibody is provided. Each antibody was handled according to the manufacturer's instructions and was individually titrated prior to use to identify the optimal concentration in the required application, as reported in the manuscript. The specificity of staining was controlled based on staining of cells from knock out mice or simultaneous analysis of cell population of known phenotype or use of IgG. All FACS experiment included adjustment by single antibody staining.

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

All mouse lines used were on the C57B1/6J background and housed under specific pathogen-free conditions at the CNIC, SigN or Yale University. All mouse husbandry and experimentation was conducted using protocols approved by local animal ethics committees and authorities . Mice (mus musculus) were mantained in racks with individual ventilation cages according to current Spanish, Singapore and US legislation (RD 53/2013 and EU Directive 63/2010, respectively). Rodents have a dust/pathogen-free bedding, sufficient nesting and environmental enrichment material for the development of species-specific behavior. All the animals have food and water "ad libitum" in environmental conditions of 45-65% of relative humidity, temperature of 21-242C and a light/ dark cycle of 12:12 hours. In addition and in order to preserve animal welfare, an animal health surveillance program is applied for health monitoring, which follows FELASA recommendations for Specific Pathogen Free facilities. Experiments were performed in 6 to 24 week-old male mice unless otherwise noted. All mice strains used are listed below and in the Mice section of the Methods.
Mutant mice Col3 and CNA35-LSL-mCherry mice were generated by Cyagen as described here; Lyz2tml.1Graf were generated by Faust et al., 2000; Ly6gtm26 21(cre,-tdTomato) were generated by Hasenberg et al., 2015; the Tgfbr2-floxed, Mrp8CRE and Rosa26iDTR mice were generated or described by Passegue et al. 2003, Tauriello et al. 2018 and Ballesteros et al. 2020, respectively. All other lines used in the screening experiments were in the C5 7BL/ 6J background and are described in the Methods section.

Wild animals

No wild animals were used in this study.

Reporting on sex

Sex was not used as a variable in this study, although male and female B6 mice were used and controlled for accordingly.

Field-collected samples

No sample were collected in the field in this study.

Ethics oversight

Experimental procedures were reviewed and approved by the institutional animal care and use committees at CNIC, SigN and Yale University.

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

Mice were euthanized and perfused with 10 ml of PBS for blood removal. Skin (ears), colon, bone marrow and spleen were

Sample preparation	harvested as required. For BM cells, femurs were flushed using a 23–gauge needle in PBS containing 2mM EDTA and 2% fetal bovine serum (FBS). Spleens were harvested and homogenized into single-cell suspensions using 70 um nylon mesh sieves and syringe plungers. Ear skins (dorsal and ventral side separately) were harvested and cut dry into small pieces before digested in liberase TM (Roche) and DNase1 (Sigma) for 90 min at 37°C. Skins were then homogenized into single-cell suspensions using 70um nylon mesh sieves and syringe plungers. Colons were harvested and cleaned of fecal matter before cutting longitudinally. Colons were washed in cold PBS and shaken once in 20ml of cold PBS in a falcon tube. Colons were then incubated in 100mM EDTA for 30 min at 37°C in shaking incubator (250rpm). Tubes were shaken once to remove epithelial cells. Colons were cut into pieces and digested in 6-well plates containing liberase TM and DNase1 for 30min at 37° C, and homogenized into single-cell suspensions using 70 um nylon mesh sieves and syringe plungers. Single-cell suspensions were stained with DAPI (1:10000) and the corresponding antibodies. Sorting separation was performed using a FACS Aria cell sorter (BD Biosciences) at the cytometry unit at CNIC or Yale University.
Instrument	We used the following analyzers and sorters: BD LSR II, BD FACSymphony A5, BD FACSCanto, BD FACSAria II, BD FACSAria Fusion
Software	We used BD FACS Diva software to acquire samples and FlowJo v10_9 (Tree Star) for data analysis and visualization.
Cell population abundance	The frequency of neutrophils across tissues ranged from 0.2-60% across tissues, corresponding to approximately 2x10E4 per gram in the intestine to 4x10E6 per femur.
Gating strategy	Neutrophils were considered DAPI-neg CD45+ CD11b+ Ly6Ghi or as indicated in the gating strategies shown in the Suppl. Materials.

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