

## 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 analysis

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](#)

## Human research participants

Policy information about [studies involving human research participants and Sex and Gender in Research](#).

Reporting on sex and gender	<input type="text" value="No human research participants were used."/>
Population characteristics	<input type="text" value="See above"/>
Recruitment	<input type="text" value="See above"/>
Ethics oversight	<input type="text" value="See above"/>

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](https://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	<input type="text" value="Sample sizes are similar to those reported in previous publications using a similar approach (Naik and Larsen et al. Nature, 2017, Adam et al. Nature, 2015 )"/>
Data exclusions	<input type="text" value="No data was excluded for the analysis."/>
Replication	<input type="text" value="For our genomic experiments, each sample consisted of 3-4 mice per time point. Replicative analysis showed strong correlations for every one of our data types."/>
Randomization	<input type="text" value="K14rtTA+;TRE-SOX9+ mice were confirmed via early postnatal PCR genotyping. K14rtTA+;TRE-SOX9+ mice were housed with at least 2 K14rtTA + only males. Upon harvest, samples were separated into experimental and control samples and randomly allocated to genomic and immunofluorescence experiments."/>
Blinding	<input type="text" value="Blinding was not possible or relevant in our study. Our mice were phenotypic upon harvesting. Additionally, we conducted a time-course study with D0 as control."/>

## 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
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies
<input type="checkbox"/>	<input checked="" type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology
<input type="checkbox"/>	<input checked="" type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern

### Methods

n/a	Involved in the study
<input type="checkbox"/>	<input checked="" type="checkbox"/> ChIP-seq
<input type="checkbox"/>	<input checked="" type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

## Antibodies

Antibodies used	<input type="text" value="Ly6A/E-APCCy7,BioLegend,cat#108126&lt;br/&gt;CD49f-PECy7,BioLegend,cat#313622&lt;br/&gt;CD34-Alexa660,Invitrogen,cat#50-0341-82"/>
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CD45-biotin, BioLegend, cat#103104  
 CD31-biotin, BioLegend, cat#102404  
 CD140a-biotin, BioLegend, cat#135910  
 CD117-biotin, BioLegend, cat#105804  
 Streptavidin-FITC, BioLegend, cat#405202  
 TruStain FcX, BioLegend, cat#101320  
 SOX9, Millipore, cat#ab5535  
 MYC-tag, Cell Signaling, cat#71D10  
 MLL3/4, Wysocka Lab, cat#N/A  
 totalH3, Active Motif, cat#39763  
 H3K27ac, Active Motif, cat#39133  
 H3K4me1, Cell Signaling, cat#D1A9  
 SOX9, Abcam, cat#ab185966  
 ITGA6, BD, cat#555734  
 KRT14, BioLegend, cat#906004  
 KRT10, Fuchs Lab, cat#N/A  
 EpCAM, Abcam, cat#ab71916  
 KRT6, Fuchs Lab, cat#N/A  
 RUNX1, Abcam, cat#ab229482  
 GATA3, Invitrogen, cat#14-9966-82  
 HA-tag, Cell Signaling, cat#C29F4  
 GFP, Fuchs Lab, cat#N/A  
 RFP, ChromoTek, cat#5F8  
 MYC-tag, Cell Signaling, cat#71D10  
 MYC-tag, Cell Signaling, cat#9B11  
 beta-Actin, Cell Signaling, cat#8H10D10  
 MLL4, Santa Cruz Biotechnology, cat#sc-293217  
 MYC-tag, Cell Signaling, cat#2276S  
 IgG, Cell Signaling, cat#2729S  
 ARID1a, Cell Signaling, cat#12354S  
 ARID1a, Abcam, cat#ab182560  
 JUN, Cell Signaling, cat#3753S  
 BRG1, EpiCypher, cat#13-2002  
 Secondary (all with donkey as host):  
 AF488-Rabbit, Thermo Fisher, A-21206  
 AF488-Chicken, Thermo Fisher, A78948  
 AF546-Rabbit, Thermo Fisher, A10040  
 AF546-Rat, Thermo Fisher, A78947

## Validation

The fluorophore conjugated antibodies from and BioLegend were validated for flow cytometry:

Ly6A/E-APCCy7, BioLegend, cat#108126  
 CD49f-PECy7, BioLegend, cat#313622  
 CD34-Alexa660, Invitrogen, cat#50-0341-82  
 CD45-biotin, BioLegend, cat#103104  
 CD31-biotin, BioLegend, cat#102404  
 CD140a-biotin, BioLegend, cat#135910  
 CD117-biotin, BioLegend, cat#105804  
 Streptavidin-FITC, BioLegend, cat#405202  
 TruStain FcX, BioLegend, cat#101320

The following antibodies are validated with western blot:

SOX9, Millipore, cat#ab5535  
 MYC-tag, Cell Signaling, cat#71D10  
 MYC-tag, Cell Signaling, cat#9B11  
 beta-Actin, Cell Signaling, cat#8H10D10  
 MLL4, Santa Cruz Biotechnology, cat#sc-293217 (also validated with KO in this study)

The following antibodies are validated with immunofluorescence:

SOX9, Abcam, cat#ab185966  
 ITGA6, BD, cat#555734  
 KRT14, BioLegend, cat#906004  
 KRT10, Fuchs Lab, cat#N/A  
 EpCAM, Abcam, cat#ab71916  
 KRT6, Fuchs Lab, cat#N/A  
 RUNX1, Abcam, cat#ab229482  
 GATA3, Invitrogen, cat#14-9966-82  
 HA-tag, Cell Signaling, cat#C29F4  
 GFP, Fuchs Lab, cat#N/A  
 RFP, ChromoTek, cat#5F8  
 all secondary antibodies

The following antibodies are validated for CHIP:

MLL3/4, Wysocka Lab, cat#N/A  
 totalH3, Active Motif, cat#39763  
 H3K27ac, Active Motif, cat#39133  
 H3K4me1, Cell Signaling, cat#D1A9

ARID1a, Cell Signaling, cat#12354S  
 ARID1a, Abcam, cat#ab182560  
 JUN, Cell Signaling, cat#3753S  
 BRG1, EpiCypher, cat#13-2002

The following antibodies are validated for coIP:  
 MYC-tag, Cell Signaling, cat#2276S  
 IgG, Cell Signaling, cat#2729S

## Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)	Mouse keratinocyte cell lines from K14rtTA+ or K14rtTA+;TRE-SOX9+ mice. The sex is not available from the cell lines.
Authentication	The cell lines used for this study were generated within the Fuchs laboratory and confirmed by PCR genotyping.
Mycoplasma contamination	These specific Cell lines were not tested for mycoplasma but our lab routinely performs mycoplasma contamination checks of randomly selected lines throughout the year.
Commonly misidentified lines (See <a href="#">ICLAC</a> register)	No cell lines in the ICLAC database 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	Mice {Mus musculus} from 2 transgenic mouse lines: TRE-MYC-SOX9;K14rtTA and K14rtTA only. 3-4 male mice at age 3-9 weeks were pooled per time point analyzed. For skin grafts, 6-8 week old female Nude mice were used as recipients for P0 male mouse skin engraftment.
Wild animals	The study did not involve wild animals.
Reporting on sex	In order to maximize cell numbers and minimize variation due to sex, we used male mice for all experiments. Male mice were generally larger enabling more surface area of the skin to harvest EpdSCs.
Field-collected samples	The study did not involve samples collected from the field.
Ethics oversight	All experimental procedures were conducted with accordance and approval of the Institutional Animal Care and Use Committee (IACUC) – approved protocols at the Rockefeller University (20012-H and 20066-H).

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

## ChIP-seq

### Data deposition

- Confirm that both raw and final processed data have been deposited in a public database such as [GEO](#).
- Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

### Data access links

*May remain private before publication.*

<https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE208072>

### Files in database submission

ATAC:  
 Sample 1-D0\_ATAC\_rep1  
 Sample 2-D0\_ATAC\_rep2  
 Sample 3-W1\_ATAC\_rep1  
 Sample 4-W1\_ATAC\_rep2  
 Sample 5-W2\_ATAC\_rep1  
 Sample 6-W2\_ATAC\_rep2  
 Sample 7-W6\_ATAC\_rep1  
 Sample 8-W6\_ATAC\_rep2  
 Sample 9-W12\_ATAC\_rep1  
 Sample 10-W12\_ATAC\_rep2  
 Sample 11-cultured\_WT\_dox\_rep1  
 Sample 12-cultured\_WT\_nodox\_rep1  
 Sample 13-cultured\_noHMG\_dox\_rep1  
 Sample 14-cultured\_noTA\_dox\_rep1  
 Sample 15-cultured\_WT\_dox\_rep2  
 Sample 16-cultured\_WT\_nodox\_rep2

Sample 17-cultured\_noHMG\_dox\_rep2  
Sample 18-cultured\_noTA\_dox\_rep2  
Sample 19-cultured\_K14AFOS\_dox\_rep1  
Sample 20-cultured\_K14AFOS\_dox\_rep2  
Sample 21-cultured\_K14SOX9AFOS\_dox\_rep1  
Sample 22-cultured\_K14SOX9AFOS\_dox\_rep2  
Sample 23-cultured\_K14SOX9ARID1a\_dox\_rep1  
Sample 24-cultured\_K14SOX9ARID1a\_dox\_rep2  
MINT-ChIP:  
Sample 1-D0\_H3K4me1\_rep1\_rep2  
Sample 2-D0\_H3K27ac\_rep1\_rep2  
Sample 3-D0\_totalH3\_rep1\_rep2  
Sample 4-W1\_H3K4me1\_rep1\_rep2  
Sample 5-W1\_H3K27ac\_rep1\_rep2  
Sample 6-W1\_totalH3\_rep1\_rep2  
Sample 7-W2\_H3K4me1\_rep1\_W12\_H3K4me1\_rep1\_rep2  
Sample 8-W2\_H3K4me1\_rep2  
Sample 9-W2\_H3K27ac\_rep1\_W12\_H3K27ac\_rep1\_rep2  
Sample 10-W2\_H3K27ac\_rep2  
Sample 11-W2\_totalH3\_rep1\_W12\_totalH3\_rep1\_rep2  
Sample 12-W2\_totalH3\_rep2  
Sample 13-W6\_H3K4me1\_rep1  
Sample 14-W6\_H3K4me1\_rep2  
Sample 15-W6\_H3K27ac\_rep1  
Sample 16-W6\_H3K27ac\_rep2  
Sample 17-W6\_totalH3\_rep1  
Sample 18-W6\_totalH3\_rep2  
Bulk RNA-Seq:  
Sample 1-RNA\_D0\_rep1  
Sample 2-RNA\_D0\_rep2  
Sample 3-RNA\_W1\_rep1  
Sample 4-RNA\_W1\_rep2  
Sample 5-RNA\_W2\_rep1  
Sample 6-RNA\_W2\_rep2  
Sample 7-RNA\_W6\_rep1  
Sample 8-RNA\_W6\_rep2  
Sample 9-RNA\_W12\_rep1  
Sample 10-RNA\_W12\_rep2  
Sample 11-RNA\_SOX9neg\_rep1  
Sample 12-RNA\_SOX9neg\_rep2  
Sample 13-RNA\_SOX9pos\_rep1  
Sample 14-RNA\_SOX9pos\_rep2  
Cut-and-Run:  
Sample 1-SOX9CNR\_D0\_rep1  
Sample 2-SOX9CNR\_D0\_rep2  
Sample 3-SOX9CNR\_W1\_rep1  
Sample 4-SOX9CNR\_W1\_rep2  
Sample 5-SOX9CNR\_W2\_rep1  
Sample 6-SOX9CNR\_W2\_rep2  
Sample 7-SOX9CNR\_W6\_rep1  
Sample 8-SOX9CNR\_W6\_rep2  
Sample 9-SOX9CNR\_W12\_rep1  
Sample 10-SOX9CNR\_W12\_rep2  
Sample 11-mllCNR\_D0\_rep1  
Sample 12-mllCNR\_D0\_rep2  
Sample 13-mllCNR\_W1\_rep1  
Sample 14-mllCNR\_W1\_rep2  
Sample 15-mllCNR\_W2\_rep1  
Sample 16-mllCNR\_W2\_rep2  
Sample 17-mllCNR\_WTsox9\_nodox\_rep1  
Sample 18-mllCNR\_noHMG\_dox\_rep1  
Sample 19-mllCNR\_noTA\_dox\_rep1  
Sample 20-mycCNR\_WTsox9\_dox\_rep1  
Sample 21-mycCNR\_WTsox9\_nodox\_rep1  
Sample 22-mycCNR\_noHMG\_dox\_rep1  
Sample 23-mycCNR\_noTA\_dox\_rep1  
Sample 24-mllCNR\_WTsox9\_nodox\_rep2  
Sample 25-mllCNR\_noHMG\_dox\_rep2  
Sample 26-mllCNR\_noTA\_dox\_rep2  
Sample 27-mycCNR\_WTsox9\_dox\_rep2  
Sample 28-mycCNR\_WTsox9\_nodox\_rep2  
Sample 29-mycCNR\_noHMG\_dox\_rep2  
Sample 30-mycCNR\_noTA\_dox\_rep2  
Sample 31-mllCNR\_WTsox9\_dox\_rep1  
Sample 32-mllCNR\_WTsox9\_dox\_rep2  
Sample 33-JunCNR\_WTsox9\_nodox\_rep1

Sample 34-JunCNR\_WTSOX9\_dox\_rep1  
 Sample 35-JunCNR\_noHMG\_dox\_rep1  
 Sample 36-Arid1aCNR\_WTSOX9\_nodox\_rep1  
 Sample 37-Arid1aCNR\_WTSOX9\_dox\_rep1  
 Sample 38-Arid1aCNR\_noHMG\_dox\_rep1  
 Sample 39-BRG1CNR\_WTSOX9\_nodox\_rep1  
 Sample 40-BRG1CNR\_WTSOX9\_dox\_rep1  
 Sample 41-BRG1CNR\_noHMG\_dox\_rep1

Genome browser session  
 (e.g. [UCSC](#))

Available upon reasonable request. All processed bigwig files are provided in GEO for visualization.

## Methodology

### Replicates

Each data set was replicated twice at independent times with different cohorts of mice. Experimental replicates were highly concordant and displayed within the extended data.

### Sequencing depth

Sample, Aligned Reads, Paired/Single End reads  
 D0\_Rep1\_ATAC, 43858222, 50bp Paired-end  
 D0\_Rep2\_ATAC, 39846438, 50bp Paired-end  
 W1\_Rep1\_ATAC, 34846318, 50bp Paired-end  
 W1\_Rep2\_ATAC, 37261602, 50bp Paired-end  
 W2\_Rep1\_ATAC, 18838504, 50bp Paired-end  
 W2\_Rep2\_ATAC, 13723684, 50bp Paired-end  
 W6\_Rep1\_ATAC, 30156910, 50bp Paired-end  
 W6\_Rep2\_ATAC, 19672580, 50bp Paired-end  
 W12\_Rep1\_ATAC, 72898350, 50bp Paired-end  
 W12\_Rep2\_ATAC, 19433948, 50bp Paired-end  
 D0\_Rep1\_H3K27ac, 3841033, 50bp Paired-end  
 D0\_Rep2\_H3K27ac, 3121333, 50bp Paired-end  
 W1\_Rep1\_H3K27ac, 711249, 50bp Paired-end  
 W1\_Rep2\_H3K27ac, 3074037, 50bp Paired-end  
 W2\_Rep1\_H3K27ac, 1030516, 50bp Paired-end  
 W2\_Rep2\_H3K27ac, 3928882, 50bp Paired-end  
 W6\_Rep1\_H3K27ac, 7956088, 50bp Paired-end  
 W6\_Rep2\_H3K27ac, 1455927, 50bp Paired-end  
 W12\_Rep1\_H3K27ac, 1258550, 50bp Paired-end  
 W12\_Rep2\_H3K27ac, 1403434, 50bp Paired-end  
 D0\_Rep1\_H3K4me1, 24592016, 50bp Paired-end  
 D0\_Rep2\_H3K4me1, 22063883, 50bp Paired-end  
 W1\_Rep1\_H3K4me1, 6587117, 50bp Paired-end  
 W1\_Rep2\_H3K4me1, 9550526, 50bp Paired-end  
 W2\_Rep1\_H3K4me1, 6041330, 50bp Paired-end  
 W2\_Rep2\_H3K4me1, 10653668, 50bp Paired-end  
 W6\_Rep1\_H3K4me1, 27215545, 50bp Paired-end  
 W6\_Rep2\_H3K4me1, 8697635, 50bp Paired-end  
 W12\_Rep1\_H3K4me1, 6916330, 50bp Paired-end  
 W12\_Rep2\_H3K4me1, 8388474, 50bp Paired-end  
 D0\_Rep1\_Total H3, 37680307, 50bp Paired-end  
 D0\_Rep2\_Total H3, 32670127, 50bp Paired-end  
 W1\_Rep1\_Total H3, 12964069, 50bp Paired-end  
 W1\_Rep2\_Total H3, 13337757, 50bp Paired-end  
 W2\_Rep1\_Total H3, 9340777, 50bp Paired-end  
 W2\_Rep2\_Total H3, 58641446, 50bp Paired-end  
 W6\_Rep1\_Total H3, 40744095, 50bp Paired-end  
 W6\_Rep2\_Total H3, 26969269, 50bp Paired-end  
 W12\_Rep1\_Total H3, 8736431, 50bp Paired-end  
 W12\_Rep2\_Total H3, 11271301, 50bp Paired-end  
 D0\_Rep1\_SOX9\_CNR, 20174088, 50bp Paired-end  
 D0\_Rep2\_SOX9\_CNR, 19645106, 50bp Paired-end  
 W1\_Rep1\_SOX9\_CNR, 23997258, 50bp Paired-end  
 W1\_Rep2\_SOX9\_CNR, 370168, 50bp Paired-end  
 W2\_Rep1\_SOX9\_CNR, 9768786, 50bp Paired-end  
 W2\_Rep2\_SOX9\_CNR, 7253702, 50bp Paired-end  
 W6\_Rep1\_SOX9\_CNR, 30653330, 50bp Paired-end  
 W6\_Rep2\_SOX9\_CNR, 2028772, 50bp Paired-end  
 W12\_Rep1\_SOX9\_CNR, 5090868, 50bp Paired-end  
 W12\_Rep2\_SOX9\_CNR, 20178366, 50bp Paired-end  
 D0\_Rep1\_MII\_CNR, 7024229, 50bp Paired-end  
 D0\_Rep2\_MII\_CNR, 3703596, 50bp Paired-end  
 W1\_Rep1\_MII\_CNR, 10820527, 50bp Paired-end  
 W1\_Rep2\_MII\_CNR, 6310082, 50bp Paired-end  
 W2\_Rep1\_MII\_CNR, 5048765, 50bp Paired-end  
 W2\_Rep2\_MII\_CNR, 5542309, 50bp Paired-end

	<p>WTSOX9_Nodox_Rep1_Mll_CNR,10946976,50bp Paired-end  noHMG_Dox_Rep1_Mll_CNR,6801070,50bp Paired-end  noTA_Dox_Rep1_Mll_CNR,7902664,50bp Paired-end  WTSOX9_Nodox_Rep1_Myc_CNR,3199032,50bp Paired-end  noHMG_Dox_Rep1_Myc_CNR,2733154,50bp Paired-end  WTSOX9_Dox_Rep1_Myc_CNR,3983006,50bp Paired-end  noTA_Dox_Rep1_Myc_CNR,3532914,50bp Paired-end</p>
Antibodies	<p>SOX9, Millipore, cat#ab5535  MLL3/4, Wysocka Lab, cat#N/A  totalH3, Active Motif, cat#39763  H3K27ac, Active Motif, cat#39133  H3K4me1, Cell Signaling, cat#D1A9  MYC-tag, Cell Signaling, cat#2276S  IlgG, Cell Signaling, cat#2729S  ARID1a, Cell Signaling, cat#12354S  JUN, Cell Signaling, cat#3753S  BRG1, EpiCypher, cat#13-2002</p>
Peak calling parameters	<p>ATAC-Seq: Replicate BAM files were merged, and peak calling was performed using Model-based Analysis of ChIP-Seq 2 (MACS2) with the option of "--keep-dup all" to keep duplicates generated during the combining of experimental replicates.</p> <p>H3K27ac: Replicate BAM files were merged with keep-duplicate option and MACS2 called with standard parameters and total H3 as input.</p> <p>H3K4me1: Replicate BAM files were merged and converted to BEDPE. --treatment was sample and -c was Total H3.</p> <p>Cut-and-Run: D0 to W12 SOX9 peaks were called using SEACR37 from bedGraph files generated from RPKM normalized Bigwig files (bigWigToBedGraph, UCSC Tools) using stringent setting and a numeric threshold of 0.01. Peaks were further filtered to have peak scores &gt; 1800 for a set of high confident peaks.</p>
Data quality	<p>Data was checked for high correlations between replicate samples and enrichment for known regulatory regions such as TSS for ATAC, and H3K27ac. SOX9 CNR was assayed by unbiased motif enrichment at called peaks. MLL3/4 CNR was assayed by enrichment at enhancer elements relative to promoter regions.</p>
Software	<p>Skewer (v0.2.2), R (v 3.6.1), MACS2 (v2.2.7.1), Bowtie2 (v2.2.9), Picard (v2.3.0), Samtools (v1.3.1), Deeptools (v3.1.2), Integrative Genomics Viewer, SEACR, epic2 (v0.0.52), GSEA, profileplyr(v1.4.3) HOMER (v4.10), JASPAR (2018), HINT-ATAC, ChromVar(v1.18.0)</p>

## 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	<p>Backskin of K14rtTA+;TRE-SOX9; and K14rtTA+ only mice were harvested and subjected to 0.25% trypsin/EDTA dissociation for 1 hour at 37C. After neutralization with FACS buffer cell suspension was strained, centrifuged and resuspended prior to antibody staining. A cocktail of antibodies for surface markers was prepared at predetermined concentrations in FACS buffer followed by washing and resuspension in secondary antibody. The cells were washed and resuspended again in FACS buffer containing 100 ng/mL of DAPI and filtered again through 70 uM filter caps before FACS.</p>
Instrument	<p>BD Biosciences FACSria equipped with FACSDiva software for sorting, BD Biosciences FACS Fortessa with FACSDiva software for analysis.</p>
Software	<p>FACSDiva 8.0 for operating the sorter or analyzer.</p>
Cell population abundance	<p>Post sorting of the samples was routinely performed and consistently showed greater than 90% purity of the isolated populations.</p>
Gating strategy	<p>Single cell suspensions of harvested skin cells were first gated on ITGA6+ and Lineage negative (CD140a-, CD45-, CD117-, CD31-) followed by enrichment for EpdSC by gating on cells which were Ly6a+, CD34-, while HFSC were Ly6a-, CD34+. Please see extended data figure 2.</p>

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