A   **Seurat clustering**

B   *KRT14 expression*

C   *KRT10 expression*
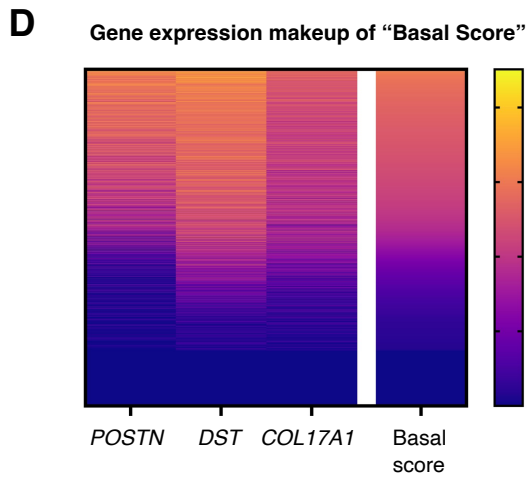
D   **G2M score**

E   **S-Phase score**
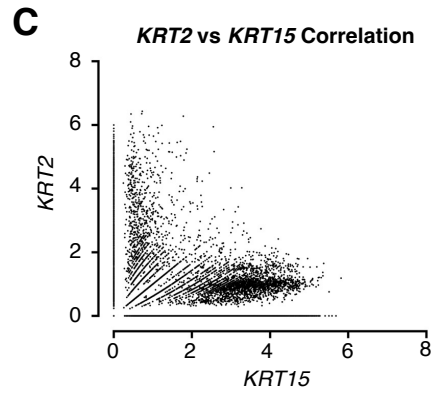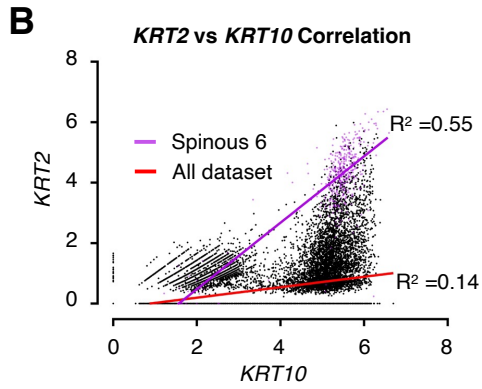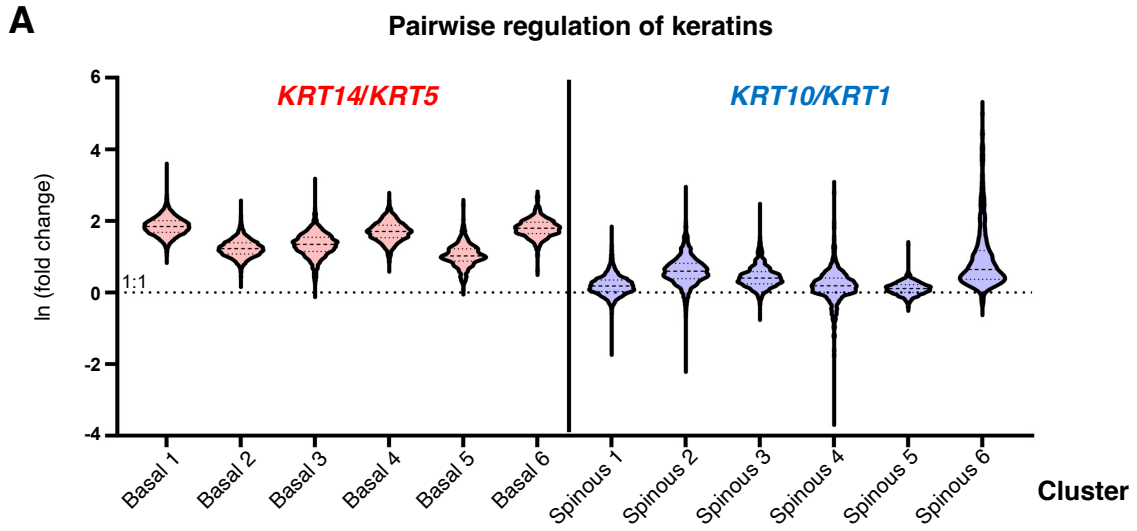
Fig. S1. Single cell RNA-seq analysis of healthy human trunk skin.

Uniform Manifold Approximation and Projections (UMAPs) depicting: (A) assigned Seurat clusters; (B) *KRT14* expression levels; (C) *KRT10* expression levels; (D) composite 'G2/M score' and (E) composite 'S Phase score' across all cells in this data set with informative content (n= 27,452 cells, partitioned into 21 clusters). Data set published by Cheng et al. (2018) and reanalyzed using a standard Seurat pipeline (see 'Methods' section). Data set publicly available at EGAS00001002927.

A Pairwise regulation of keratins

KRT14/KRT5   *KRT10/KRT1*

ln (fold change)

1:1

Cluster

Basal 1, Basal 2, Basal 3, Basal 4, Basal 5, Basal 6, Spinous 1, Spinous 2, Spinous 3, Spinous 4, Spinous 5, Spinous 6

B *KRT2* vs *KRT10* Correlation

Spinous 6
All dataset
R² =0.55
R² =0.14

KRT2

KRT10

C *KRT2* vs *KRT15* Correlation

KRT2

KRT15

D Gene expression makeup of "Basal Score"

POSTN   *DST*   *COL17A1*   Basal score

Fig. S2. Additional analyses of scRNAseq data from human trunk skin.

(A) Violin plot of the ratio of !"#$% / !"#'   reads in 'Basal1-6' clusters (left), and the ratio of !"#$&   / !"#$ reads in 'Spinous1-6' clusters (right). A dashed line across the Y-axis depicts a 1:1 balance between the type I and II keratin partners. (B, C) Correlations between specific type I and type II keratin genes across the entire array of epidermal keratinocytes (n= 24,979 cells). (B) !"#(versus !"#$&. Red   lines represent linear correlations, and r^2 values are reported (n=24,979 cells). Magenta line represent linear correlation for keratinocytes in the 'Spinous6' cluster (n= 408 cells). (C) !"#(versus !"#$')*   which provides the equivalent of a negative control in this analysis of pairwais regulation in epidermis. (D) Heatmap relating expression of +,-#., /-#, and 0,1$23$ across the entire array of 24,979 keratinocytes. These three genes were selected to calculate a composite "Basal Score", shown at right. See Suppl. Fig. 1 for source data and main text for additional details. Data set published by Cheng et al. (2018) and reanalyzed using a standard Seurat pipeline (see 'Methods' section). Data set publicly available at EGAS00001002927.
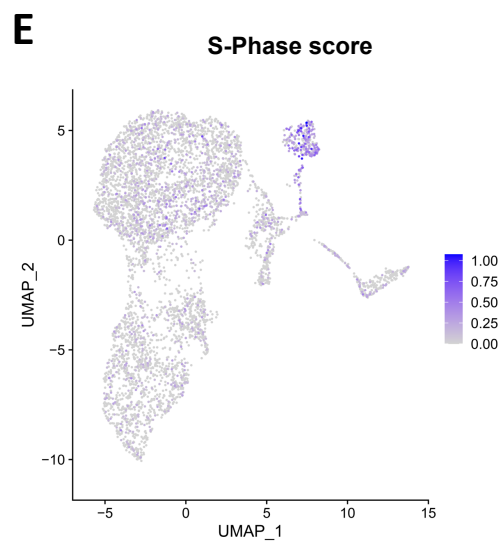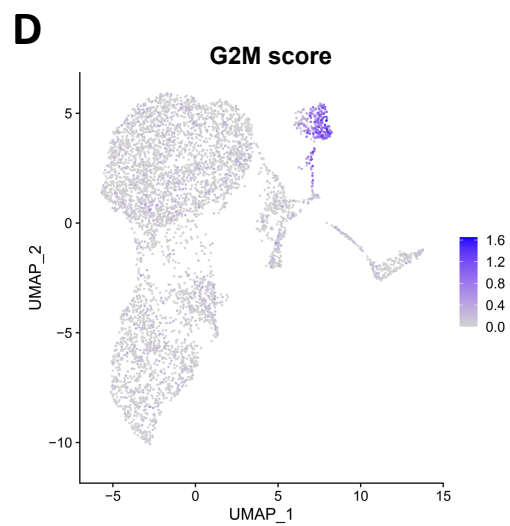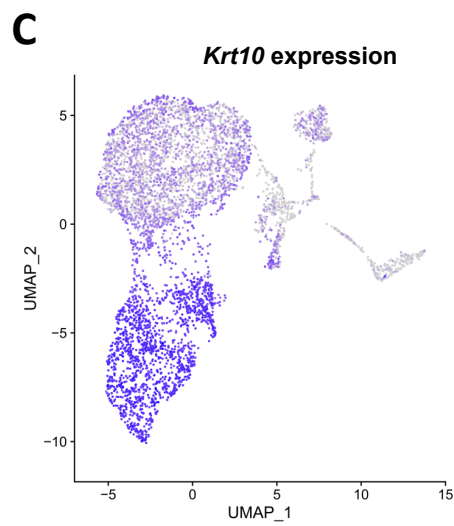
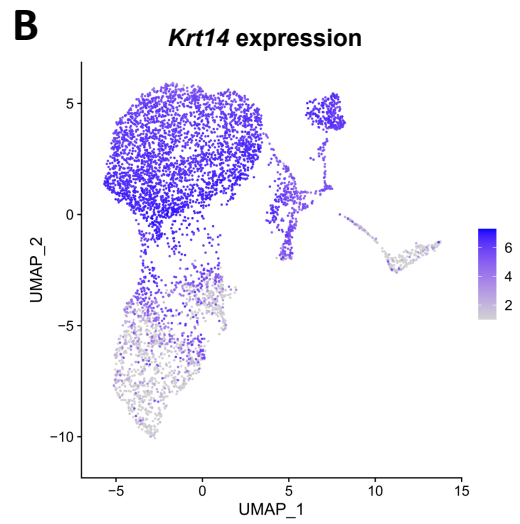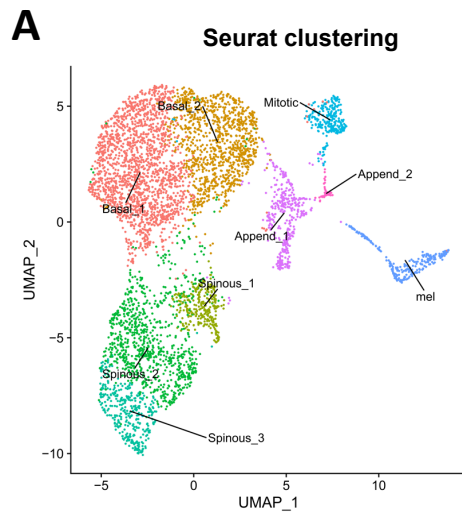**Fig. S3. Single cell RNA-seq analysis of healthy mouse ear skin.**

(A-D) UMAPs depicting: (A) assigned Seurat clusters; (B) ! 45$% expression levels; (C) !45$& expression levels; (D) composite 'G2/M Score' and (E) composite 'S Phase Score' across all cells in this data set (n=5,446 cells with informative content, partitioned into 9 clusters). Data set published by Lukowski et al. (2018) and reanalyzed using a standard Seurat pipeline (see 'Methods' section). Data set publicly available at E-MTAB-6429.

Suppl. Figure 4
Cohen, Johnson et al.

Mouse ear skin data set

A **Gene expression makeup of "Basal Score"**

B **Distribution of basal score (mouse ear)**
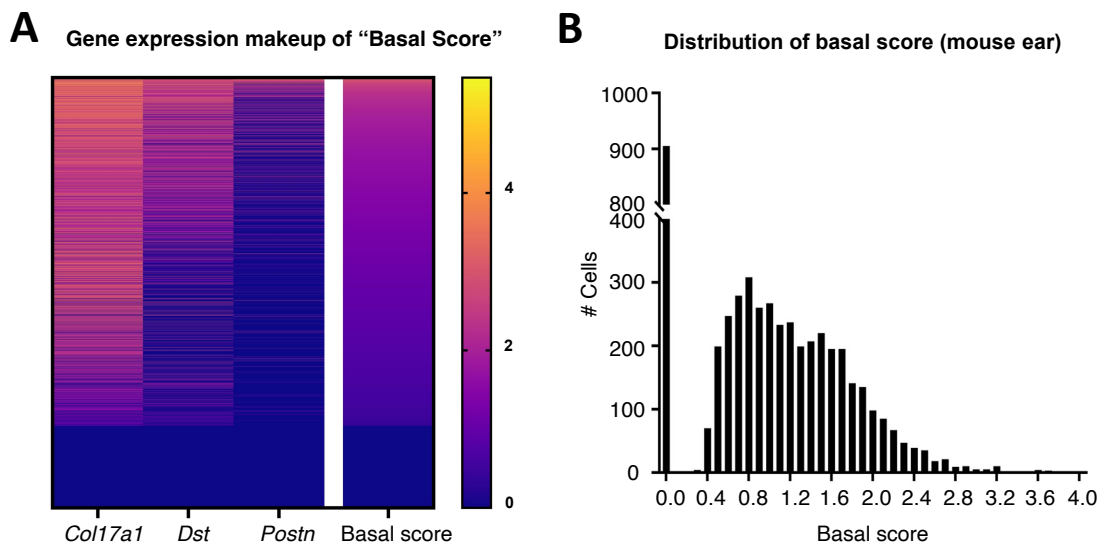
Fig. S4. Additional analyses of scRNAseq data from mouse ear skin.

(A) Heatmap relating expression of +6758, /75, and 069$2:$ across the entire array of 4,761 mouse skin epidermal keratinocytes. These three genes were selected to caculate a 'Basal Score', shown at right. (B) Histogram reporting on the composite 'Basal Score' across the population of mouse skin epidermal keratinocytes. See Suppl. Fig. 3 for source data and main text for additional details. Data set published by Lukowski et al. (2018) and reanalyzed using a standard Seurat pipeline (see 'Methods' section). Data set publicly available at E-MTAB-6429.

**Table S1. Top 10 expressed genes in epidermal keratinocyte clusters.**

Human trunk skin data (complement to Fig. 1B). See Suppl. Fig. 1 for details. Keratin genes are shown in red lettering.

Basal Clusters

Rank	Basal 1	Basal 2	Basal 3	Basal 4	Basal 5	Basal 6
1	*MALAT1*	*MALAT1*	*MALAT1*	*MALAT1*	*KRT14*	*MALAT1*
2	*KRT14*	*KRT14*	*KRT14*	*KRT14*	*MALAT1*	*KRT14*
3	*EEF1A1*	*EEF1A1*	*EEF1A1*	*EEF1A1*	*EEF1A1*	*EEF1A1*
4	*CXCL14*	*KRT5*	*KRT5*	*CXCL14*	*KRT5*	*CXCL14*
5	*KRT5*	*CXCL14*	*CXCL14*	*KRT15*	*PTMA*	*KRT5*
6	*PTMA*	*PTMA*	*PTMA*	*KRT5*	*B2M*	*PTMA*
7	*TMSB4X*	*TPT1*	*B2M*	*PTMA*	*KRT10*	*TMSB4X*
8	*B2M*	*B2M*	*TPT1*	*TMSB4X*	*TPT1*	*B2M*
9	*PERP*	*TMSB4X*	*TMSB4X*	*B2M*	*MT1X*	*NFKBIA*
10	*H3F3B*	*H3F3B*	*JUN*	*H3F3B*	*DMKN*	*PERP*

Mitotic Clusters

Rank	Mitotic 1	Mitotic 2	Mitotic 3
1	*KRT14*	*MALAT1*	*KRT14*
2	*MALAT1*	*KRT14*	*MALAT1*
3	*EEF1A1*	*PTMA*	*KRT5*
4	*KRT5*	*EEF1A1*	*EEF1A1*
5	*KRT10*	*KRT5*	*PTMA*
6	*PTMA*	*B2M*	*MT1X*
7	*B2M*	*KRT10*	*B2M*
8	*PERP*	*H3F3B*	*TPT1*
9	*KRT1*	*TMSB4X*	*PERP*
10	*DMKN*	*TUBA1B*	*DMKN*

Spinous Clusters

Rank	Spinous 1	Spinous 2	Spinous 3	Spinous 4	Spinous 5	Spinous 6
1	*MALAT1*	*MALAT1*	*MALAT1*	*MALAT1*	*MALAT1*	*MALAT1*
2	*KRT10*	*KRT10*	*KRT10*	*KRT10*	*KRT10*	*KRT10*
3	*KRT1*	*EEF1A1*	*EEF1A1*	*KRT1*	*KRT1*	*DMKN*
4	*EEF1A1*	*KRT1*	*KRT1*	*EEF1A1*	*DMKN*	*KRT1*
5	*DMKN*	*KRT14*	*DMKN*	*DMKN*	*EEF1A1*	*CALML5*
6	*B2M*	*DMKN*	*PTMA*	*PERP*	*KRTDAP*	*KRT2*
7	*PERP*	*B2M*	*B2M*	*KRT14*	*PERP*	*KRTDAP*
8	*PTMA*	*PERP*	*TPT1*	*B2M*	*PTMA*	*LOR*
9	*TPT1*	*PTMA*	*PERP*	*PTMA*	*B2M*	*EEF1A1*
10	*DSP*	*H3F3B*	*H3F3B*	*H3F3B*	*TMSB4X*	*PERP*

Table S2. Keratin expression levels across clusters.

Human trunk skin data (complement to Fig. 1B). See Suppl. Fig. 1 for details.

Basal Clusters

Keratin	Basal 1	Basal 2	Basal 3	Basal 4	Basal 5	Basal 6
KRT14	6.2	5.8	5.8	6	5.7	6.1
KRT5	4.3	4.6	4.4	4.3	4.6	4.3
KRT15	2.8	2.7	3	4.3	1	3.1
KRT10	2.3	1.7	2	2.3	3.4	2.3
KRT1	1.7	1.2	1.5	1.7	3.2	1.6
KRT2	0.3	0.1	0.2	0.3	0.2	0.3

Mitotic Clusters

Keratin	Mitotic 1	Mitotic 2	Mitotic 3
KRT14	5.8	5.2	5.7
KRT5	4.4	4.2	4.6
KRT15	0.9	1	0.5
KRT10	3.7	3.4	3.2
KRT1	3.3	2.7	3.2
KRT2	0.3	0.3	0.2

Spinous Clusters

Keratin	Spinous 1	Spinous 2	Spinous 3	Spinous 4	Spinous 5	Spinous 6
KRT14	2	3.9	3	3.3	1.4	1.8
KRT5	1.8	3.2	2.5	2.3	0.6	0.9
KRT15	0.2	0.7	0.3	0.7	0.2	0.3
KRT10	5	5.2	5	5.4	5.2	5.3
KRT1	4.8	4.6	4.5	5.2	5.1	4.4
KRT2	0.3	0.7	0.5	2.1	1.8	4.2

Table S3. Pairwise correlations across clusters.

Human trunk skin data (complement to Fig. 1, C, D and E). See Suppl. Fig. 1 for details.

Basal Clusters

Pairwise R^2	Basal 1	Basal 2	Basal 3	Basal 4	Basal 5	Basal 6
KRT14-KRT5	0.35	0.47	0.4	0.29	0.67	0.36
KRT10-KRT1	0.04	0.02	0.03	0.04	0.52	0.11
KRT15-KRT5	0	0.01	0	0.01	0.05	0.07
KRT15-KRT14	0.03	0.09	0	0.03	0.06	0.2
KRT2-KRT10	0	0	0	0	0.03	0.01

Mitotic Clusters

Pairwise R^2	Mitotic 1	Mitotic 2	Mitotic 3
KRT14-KRT5	0.67	0.37	0.65
KRT10-KRT1	0.59	0.7	0.51
KRT15-KRT5	0.02	0.02	0.03
KRT15-KRT14	0.04	0.12	0.03
KRT2-KRT10	0.02	0.04	0

Spinous Clusters

Pairwise R^2	Spinous 1	Spinous 2	Spinous 3	Spinous 4	Spinous 5	Spinous 6
KRT14-KRT5	0.45	0.44	0.5	0.54	0.32	0.68
KRT10-KRT1	0.46	0.42	0.51	0.82	0.65	0.35
KRT15-KRT5	0.05	0.04	0	0.15	0.13	0.3
KRT15-KRT14	0.15	0.17	0.01	0.31	0.2	0.35
KRT2-KRT10	0.01	0.01	0.07	0.08	0.03	0.56

Entire Dataset

	All cells
KRT14-KRT5	0.8
KRT10-KRT1	0.84
KRT15-KRT5	0.33
KRT15-KRT14	0.48
KRT2-KRT10	0.14

Table S4. Distribution of Custom G2/M Scores across clusters.

Human trunk skin data (complement to Fig. 2B) and mouse ear data (complement to Fig. 3E). See Suppl. Figs. 1 and 3 for details.

Cluster	# Cells	% of G2M scoring cells
basal_1	1	0%
basal_3	1	0%
basal_4	1	0%
mitotic_1	8	1%
mitotic_2	714	97%
mitotic_3	1	0%
spinous_1	1	0%
spinous_2	1	0%
spinous_3	1	0%
spinous_4	3	0%
spinous_5	2	0%
spinous_6	1	0%
Total	**735**	

G2M score cluster distribution (mouse ear skin data)

Cluster	#Cells	% of G2M scoring Cells
basal_1	19	7%
basal_2	20	8%
mitotic	215	81%
spinous_1	4	2%
spinous_2	8	3%
spinous_3	0	0%
Total	**266**	