

1 **Figure S1. Phenotypical analyses of mice treated with Que.**

- 2 (A) Left, representative hair coats of mice topically treated with vehicle, 0.1 mM Que, 0.3 mM Que,  
3 3 mM Que, and 30 mM Que on day 29 post-treatment. Right, quantification for appearance of  
4 melanin pigmentation in mouse skin treated with vehicle, 0.1 mM Que, 0.3 mM Que, 3 mM  
5 Que, and 30 mM Que. Vehicle,  $n = 8$ ; 0.1 mM Que,  $n = 8$ ; 0.3 mM Que,  $n = 8$ ; 3 mM Que,  $n =$   
6  $8$ ; 30 mM Que,  $n = 8$ . Two-way ANOVA with Sidak's test was used and data are presented as  
7 the mean  $\pm$  SEMs.
- 8 (B) Left, representative hair coats of oral gavage of vehicle, 0.125 mg/kg Que and 0.625 mg/kg  
9 treated mice on day 54 post-treatment. Right, quantification for appearance of melanin  
10 pigmentation in mouse skin treated with vehicle, 0.125 mg/kg and 0.625 mg/kg Que. Vehicle,  
11  $n = 7$ ; 0.125 mg/kg Que,  $n = 14$ ; 0.625 mg/kg Que,  $n = 7$ . Two-way ANOVA with Sidak's test  
12 was used and data are presented as the mean  $\pm$  SEMs.
- 13 (C) Immunostaining of Ki67 of skin tissue sections on young mice after oral gavage with vehicle  
14 or 0.625 mg/kg Que. Right, the quantitative data of Ki67-positive cells per HF in vehicle- or  
15 Que-treated groups. Vehicle,  $n = 6$ ; Que,  $n = 6$  and 15 HFs were quantified for each individual.  
16 Two-tailed unpaired Student's  $t$ -test was used and data are presented as the mean  $\pm$  SEMs.  
17 Scale bars, 100  $\mu$ m.
- 18 (D) Immunostaining of CD31 of skin tissue sections on young mice after oral gavage with vehicle  
19 or 0.625 mg/kg Que. Right, the quantitative data of CD31-positive area in vehicle- or  
20 Que-treated groups. Vehicle,  $n = 6$ ; Que,  $n = 6$ . Two-tailed unpaired Student's  $t$ -test was used  
21 and data are presented as the mean  $\pm$  SEMs. Scale bars, 100  $\mu$ m.
- 22 (E) Left, H&E staining of skin tissues sections on 22-month mice post-oral gavage with vehicle or  
23 Que. Right, quantitative data of HF length and the percentage of HFs in anagen in vehicle- or  
24 Que-treated groups. Vehicle,  $n = 4$ ; Que,  $n = 4$  and 20 HFs were quantified for each individual.  
25 Two-tailed unpaired Student's  $t$ -test was used and data are presented as the mean  $\pm$  SEMs.  
26 Scale bars, 200  $\mu$ m.
- 27 (F) Immunostaining of CD31 of skin tissues sections on 22 months mice after oral gavage with  
28 vehicle or Que. Right, the quantitative data of CD31-positive area in vehicle- or Que-treated  
29 groups. Vehicle,  $n = 4$ ; Que,  $n = 4$ . Two-tailed unpaired Student's  $t$ -test was used and data are  
30 presented as the mean  $\pm$  SEMs. Scale bars, 100  $\mu$ m.

31 **Figure S2. Single-cell transcriptomic profile analyses of different cell types with Que treatment.**

- 1 (A) The distribution of quality controls, including the median number of genes, sequencing  
2 saturation, and mapping rate in the scRNA-seq data of each sample.
- 3 (B) Scatter plot showing the proportion of mitochondrial genes for each cell.
- 4 (C) Histograms showing the number of genes (left) and unique molecular identifiers (UMIs) (right)  
5 detected in individual cells.
- 6 (D) Boxplot showing the value of ROGUE (a method for accurately quantify the purity of an  
7 identified cell type) of each cell type. Box shows the median and the quartile range (25-75%)  
8 and the length of whiskers represents 1.5× the IQR.
- 9 (E) UMAP plots showing the cell distribution of all samples. Cells are marked by samples (left)  
10 and groups (right).
- 11 (F) UMAPs plots showing the cell distribution of each sample individually.
- 12 (G) Left, heatmap showing row z-score expression of top 50 cell type-specific genes. Right,  
13 enriched GO terms and pathways for marker genes. Abbreviations for each cell type are the  
14 same as those in Figure 2B.
- 15 (H) UMAP plots showing the expression levels of *Lef1* and *Mki67*. The threshold is shown on the  
16 bottom.
- 17 (I) Circular plots showing the number and proportion of TDEGs for different cell types in each  
18 module. Cell type acronyms are the same as in Figure 2B.
- 19 (J) Circular plots showing the TDEGs shared by at least two cell types (Frequency  $\geq 2$ ) in  
20 module 2 and module 3.

21 **Figure S3. Transcriptional profiles of HF subclusters upon Que treatment.**

- 22 (A) Dot plot showing the expression levels of representative genes for each HF sub-cell types.
- 23 (B) Violin plots showing the expression levels of HFSC marker genes in different HF subclusters.
- 24 (C) Quiescence scores of HF sub-cell types calculated by expression levels of *Foxc1* target genes.
- 25 (D) Heatmaps showing the expression profiles of transcriptional factors (TFs) along with the  
26 pseudotime, which were divided into three clusters with the expression pattern. Representative  
27 TFs are listed on the right.
- 28 (E) Heatmap showing the gene set scores of signaling pathway related to hair growth in different  
29 HF subclusters with Que treatment.

1 **Figure S4. Single-cell transcriptional analyses of vascularization in response to Que treatment.**

2 (A) UMAP plot showing the distribution of endothelial cells. BE, blood vascular endothelial cell;  
3 LE, lymphatic endothelial cell.

4 (B) UMAP plots showing the expression levels of representative marker genes of BVE and LE.

5 (C) The bar plot showing the differentially expressed signaling pathways identified by the  
6 differences in the information flow of each signaling pathway between the Que and vehicle  
7 group in EC and GL.

8 (D) 3D reconstruction of immunofluorescence staining of VWF in HFJs on day 3 post-treatment  
9 with vehicle or Que. Right, the quantitative data of VWF-positive area in the skin. Vehicle,  $n =$   
10 6; Que,  $n = 6$ . Two-tailed unpaired Student's  $t$ -test is used and data are presented as the mean  $\pm$   
11 SEMs. Scale bar, 50  $\mu$ m.

12 (E) Heatmaps showing the expression profiles of genes involving in angiogenesis (left), migration  
13 (middle), and endothelial cell proliferation (right) pathways.

14 (F) Violin plots showing the transcriptional levels of *Hif-1a* in BVE and LE in vehicle and Que  
15 groups.

16 (G) Western blot analysis of HIF-1 $\alpha$  protein expression levels in skin tissues treated with vehicle or  
17 Que. Vehicle,  $n = 6$ ; Que,  $n = 6$ . Two-tailed unpaired Student's  $t$ -test was used and data are  
18 presented as the mean  $\pm$  SEMs.

19 (H) Western blot analysis of HIF-1 $\alpha$  protein expression levels in skin tissues treated with vehicle  
20 or DMOG. Vehicle,  $n = 6$ ; DMOG,  $n = 6$ . Two-tailed unpaired Student's  $t$ -test was used and  
21 data are presented as the mean  $\pm$  SEMs.

22 **Table legends**

23 Table S1. Marker genes for each cell type in mouse skin.

24 Table S2. Pairwise differentially expressed genes (PDEGs) for each cell type.

25 Table S3. Dynamic differentially expressed genes along the time trajectory (TDEGs) for each cell  
26 type.

27 Table S4. Gene sets used in this study.

28 Table S5. Differentially expressed genes (DEGs) in bulk RNA-seq data.

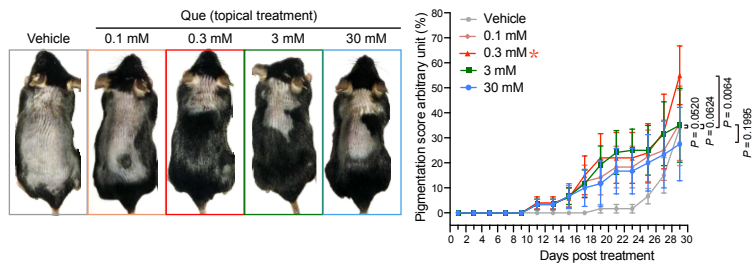
29 Table S6. Antibodies used in this study.

1 Table S7. Primers used in this study.

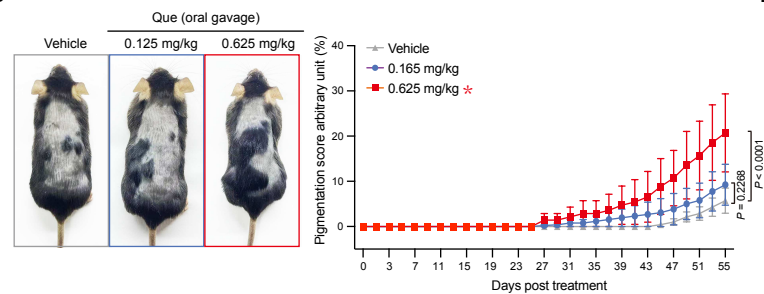
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Figure S1

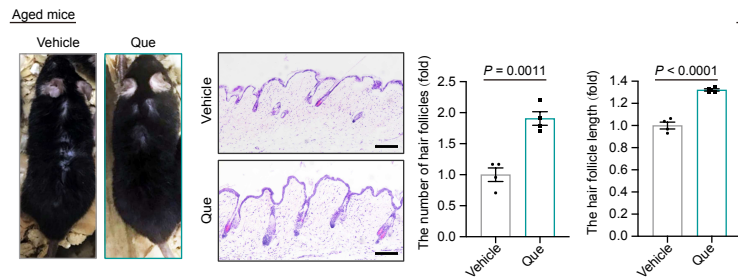
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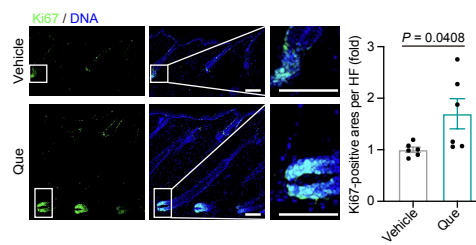
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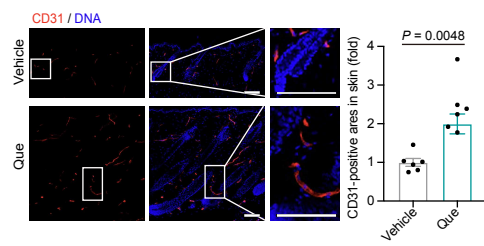
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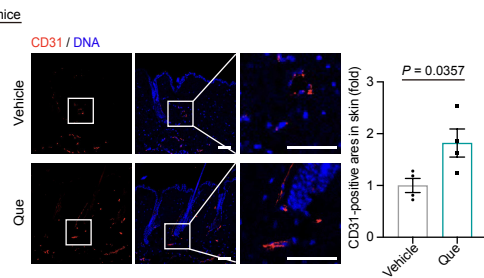


Figure S2

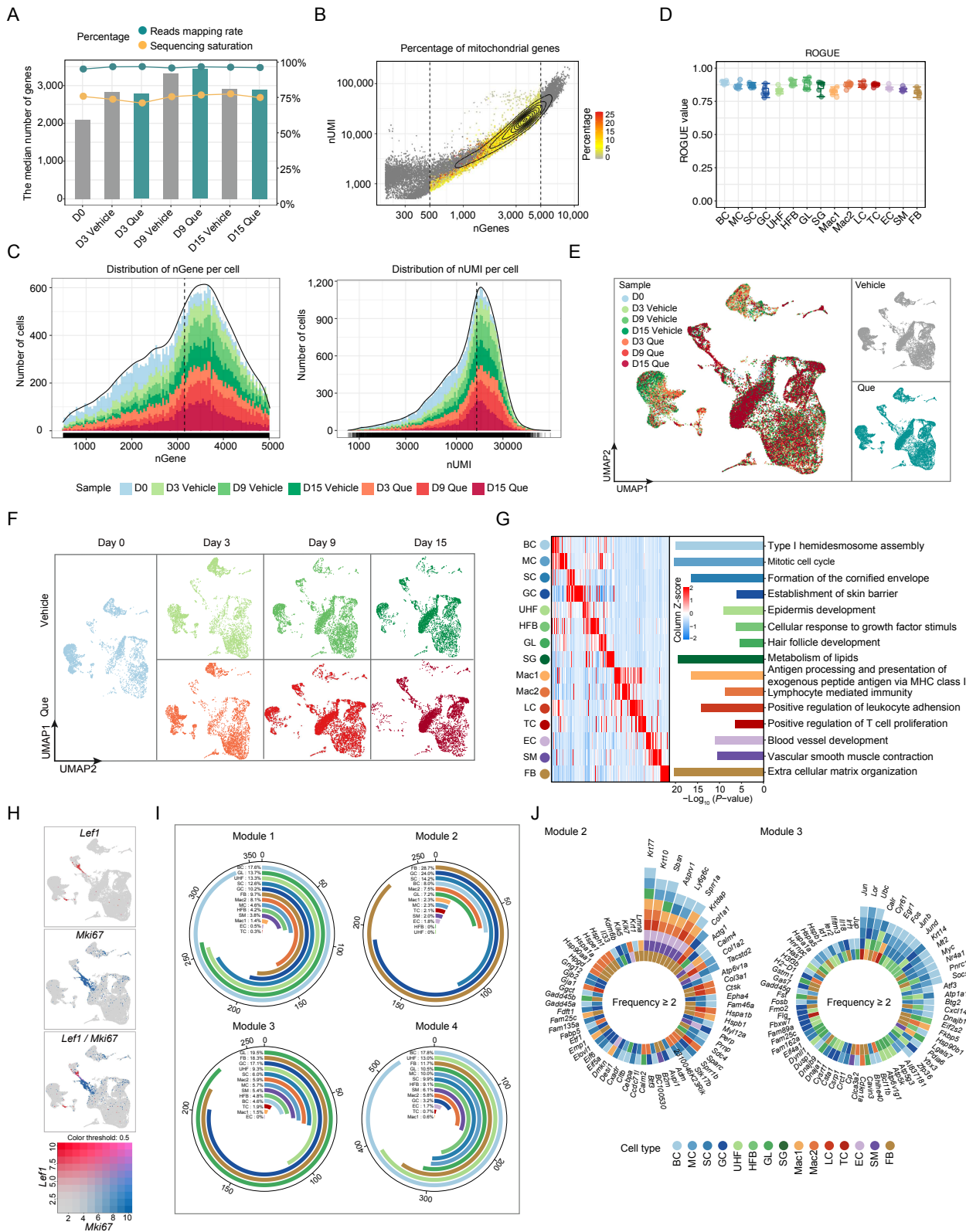
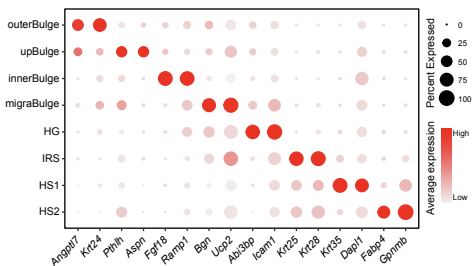
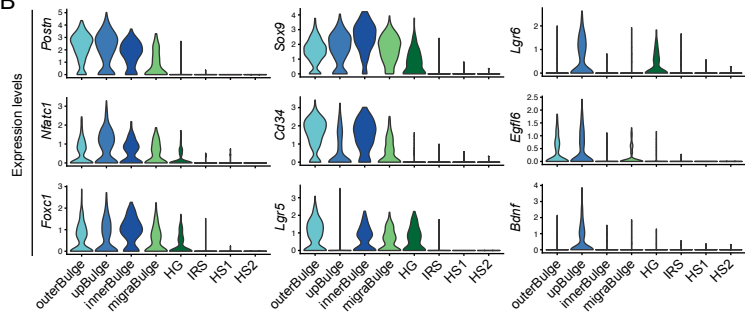


Figure S3

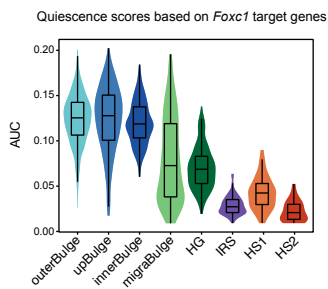
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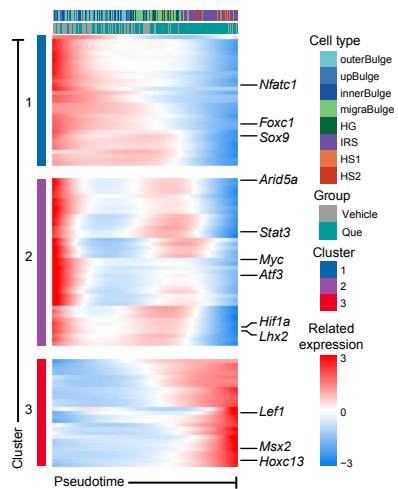
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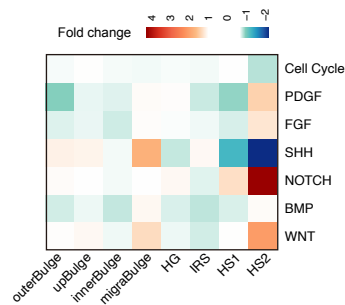


Figure S4

