**Figure S1** (related to Figure 1).

(A) A schematic diagram showing CEC differentiation in 3F or 4F for 4 days, followed by further differentiation in E6 with daily refreshment of the medium.
(B) CEC generation from two hESC lines in E6, 3F or 4F, characterized via flow cytometry for the ratios of cells positive for PAX6 and TP63 (day 10) and KRT15 (day 30).

**Figure S2** (related to Figure 1). CEC generation from H9 hESC in 3F and 4F, characterized via immunostaining and followed by antibody verification.

(A) As differentiated in E6 (Fig. 1D), H9 hESC differentiated in 3F and 4F were also positive for KRT19 and KRT15 at day 45 and KRT3 and KRT12 at day 75. Scale bar, 50 μm for all.
HaCat, a human keratinocyte cell line, was used as a control for immunostaining and verified positive for the epithelial progenitor markers KRT15, and negative for the mature CEC markers KRT3 and KRT12. Scale bar, 50 µm for all.

Figure S3 (related to Figure 1). CEC generation from multiple hESC lines H1 (A), CT3 (B), and Envy (C), detected via immunostaining. The FITC channel was included for detection of GFP in Envy hESC-derived CEC. Scale bar, 50 µm for all.
Figure S4 (related to Figure 2). Genome-wide microarray analysis of target genes for signaling pathways during CEC differentiation. The bottom right figure represents a schematic of the dynamically changing levels of all the analyzed signaling pathways during the differentiation. Statistical analysis was conducted using a paired t test with two tailed. * \( P < 0.05 \), ** \( P < 0.01 \), *** \( P < 0.001 \).

Figure S5 (related to Figure 4). Immunostaining for KRT14 in CEC-recellularized DC. Scale bars: 50 µm.
Figure S6 (related to Figure 5). Further characterization of $B2M^*/H1$ hESC.

(A, B) Immunostaining on WT (A) and $B2M^{-/-}$ (B) hESC for pluripotency markers OCT4, NANOG, and SSEA4. Scale bars: 100 µm.

(C) Differentiation of $B2M^*/$ hESC via embryoid bodies (EB) followed by qPCR analysis of markers for the three germ layers $PAX6$ (ectoderm), $HAND1$ (mesoderm), and $SOX17$ (endoderm). Gene expression was normalized by the expression level of $GAPDH$.

(D) FACS analysis of KRT15 expression in $B2M^*/$ CEC at day 30 of the differentiation in E6. NC, negative control.