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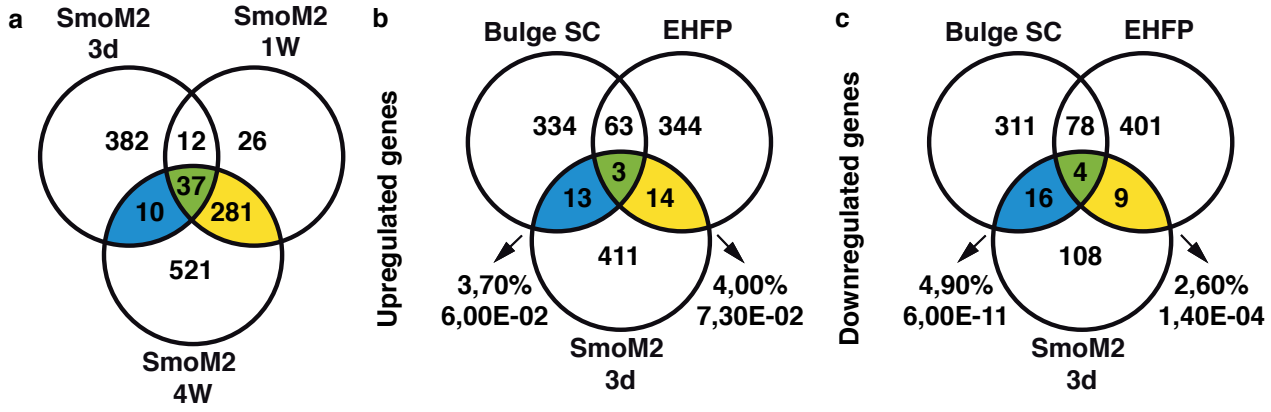

Figure S1 Transcriptional analysis of FACS isolated IFE cells 3 days following SmoM2 expression. (a) Venn diagrams showing the similarities and the differences between the number of upregulated genes differentially regulated by SmoM2 in adult IFE cells 3 days, 1week and 4 Weeks after SmoM2 expression in a6HCD34- cells. (b-c) Venn diagrams showing the similarities and the differences between the genes differentially upregulated genes (b) or downregulated genes (c) 3 days after TAM administration, with the EHFP and adult bulge SC signature. Arrows indicate the percentage and the hypergeometric P-value of the overlap between SmoM2 signature and EHFP or bulge SC signature.

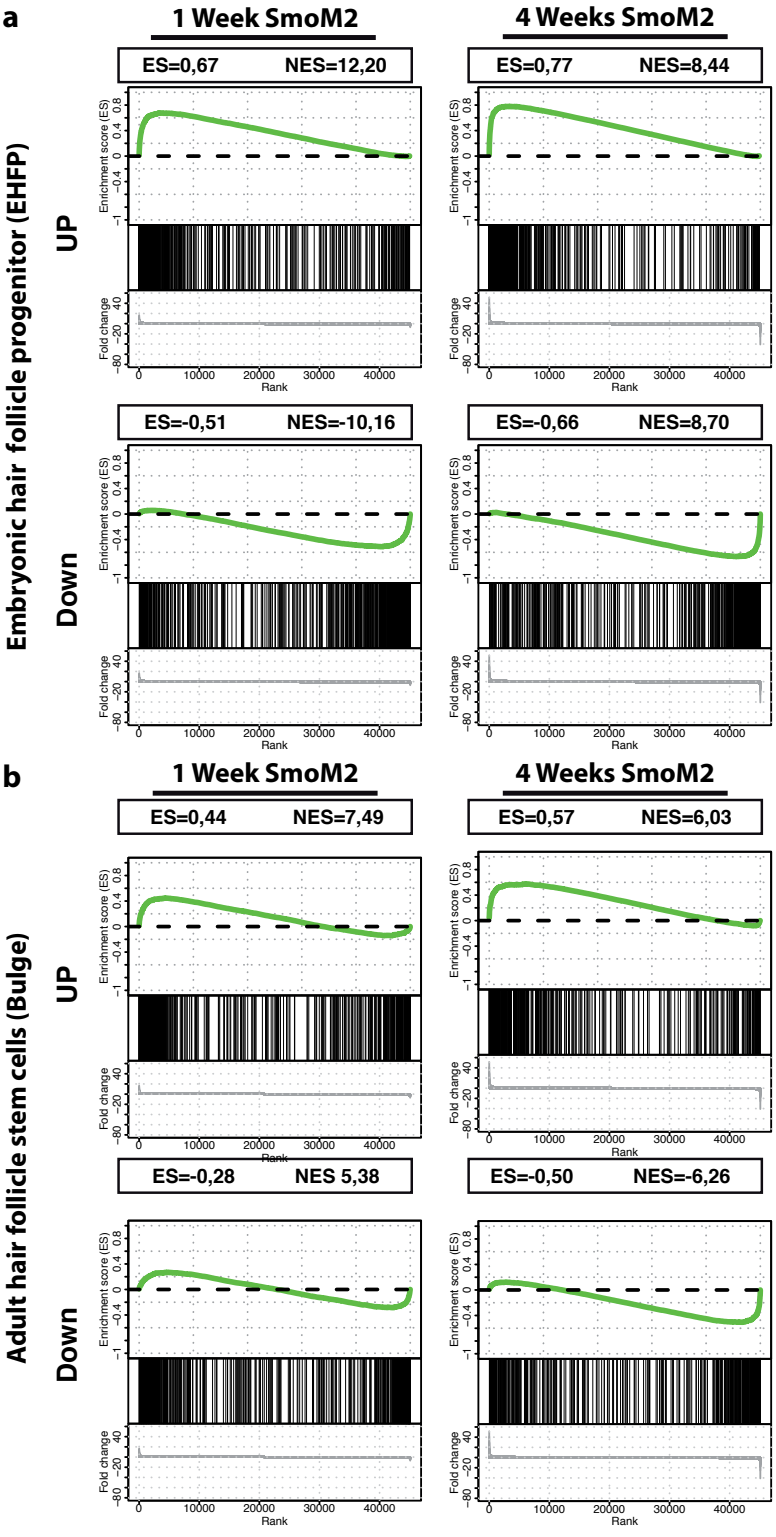

Figure S2 GSEA analysis of the adult hair follicle bulge SC and EHFP gene signatures with the genes regulated by SmoM2. (a) Gene Set enrichment analysis (GSEA) showing the distribution of the EHFP upregulated (upper panel) or downregulated (bottom panel) genes sets within the rank order list of all the microarray gene set of the SmoM2-YFP+ FACS isolated tumor initiating cells (α6HCD34-) 1 week (left) and 4 weeks after SmoM2 expression (right). (b) Gene Set enrichment analysis (GSEA) showing the distribution of the adult α6HCD34H bulge SC upregulated (upper panel) or downregulated (bottom panel) gene sets within the rank order list of all the microarray gene set of the SmoM2-YFP+ FACS isolated tumor initiating cells (α6HCD34-) one week (left) and four weeks after SmoM2 expression (right). Enrichment score (ES) and normalized enrichment Score (NES) are shown for each analysis.

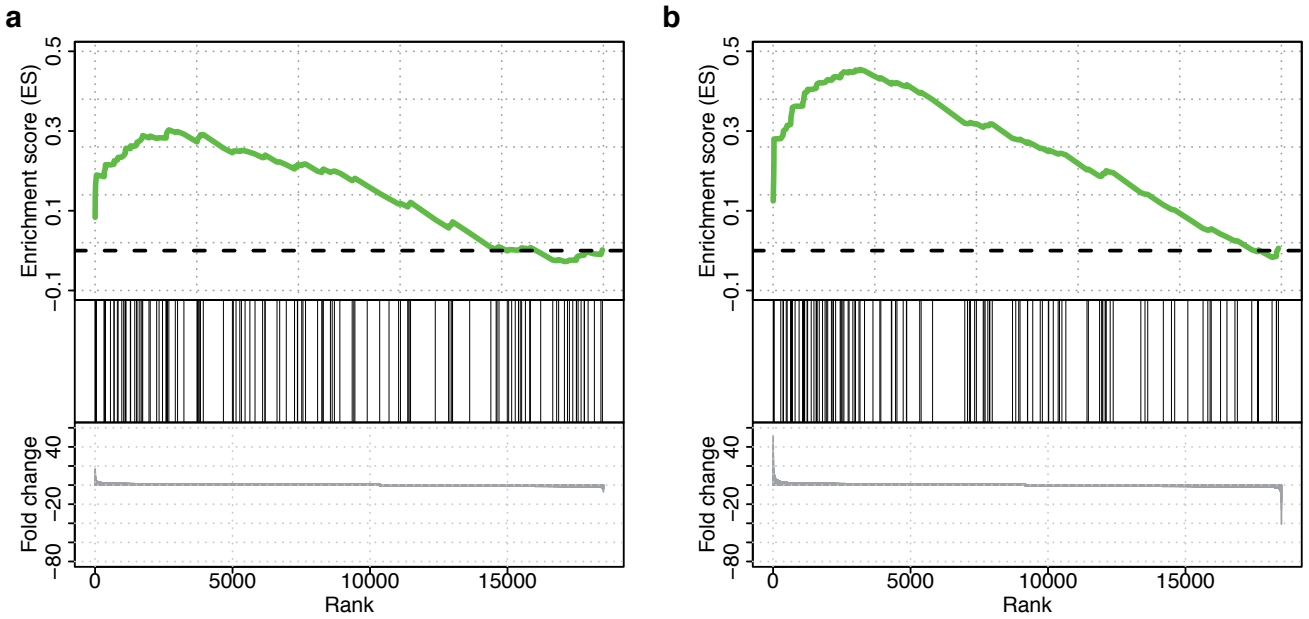

Figure S3 Gene Ontology Enrichment (GO) analysis of SmoM2 signature gene. (a,b) GSEA showing the distribution of HH and canonical-Wnt GO enriched genes 1 week (c) and 4 weeks (d) after SmoM2 expression within the rank order list of microarray gene set.

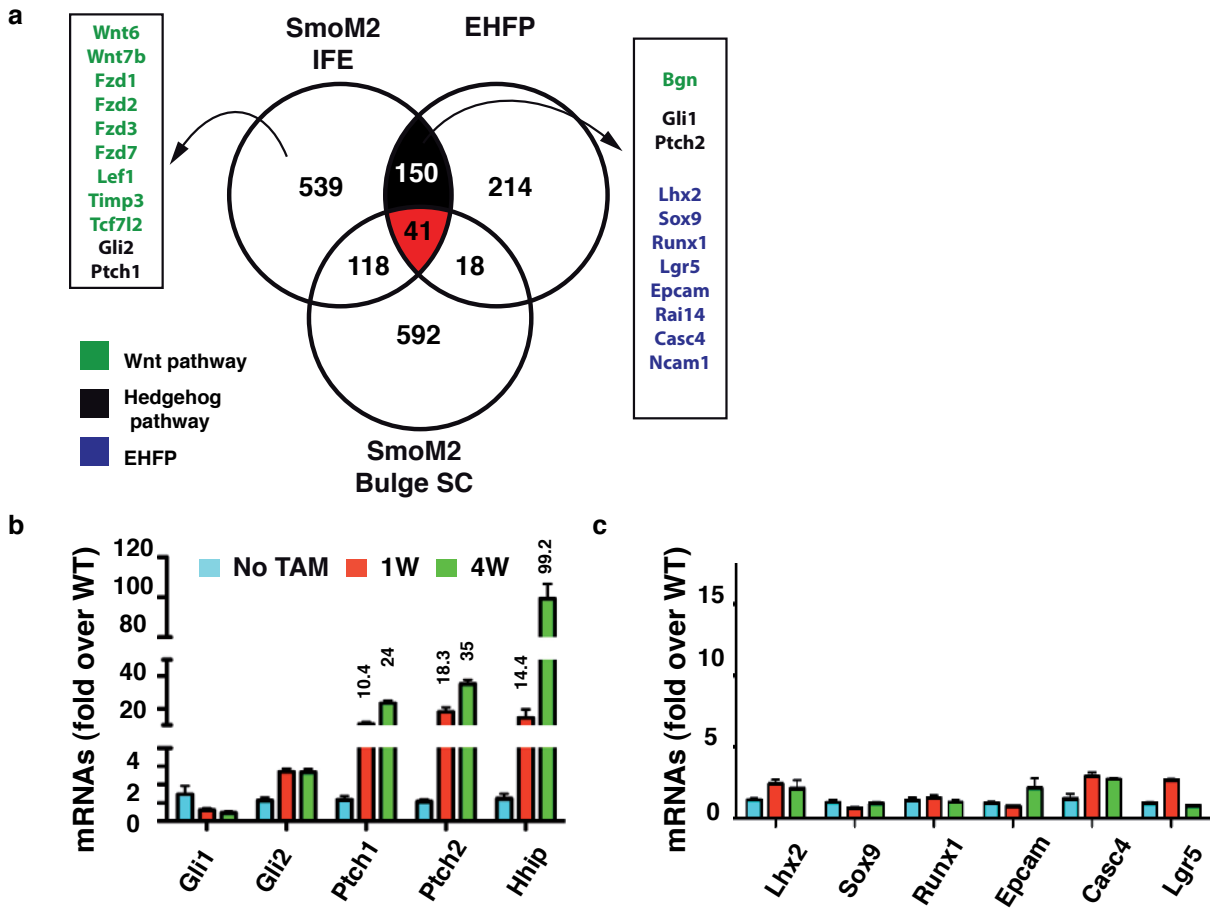

Figure S4 Transcriptional profiling of FACS isolated bulge SC expressing SmoM2. (a) Venn diagram showing the similarities and the differences between the genes upregulated in the EHFP signature [16] and the genes upregulated by SmoM2 in adult IFE cells (a6HCD34-) and bulge SC (a6HCD34+) 4 weeks after SmoM2. The number of common genes between SmoM2 signature in bulge SC and EHFP signature decreases from 192 to 59 genes. The 150 genes highlighted in black represent the genes lost from the common signature in the bulge SC. The 41 genes highlighted in red represent the genes upregulated by SmoM2 by more than 2 fold in both bulge SC and IFE cells. (b,c) Transcriptional analysis of HH target genes (b) and EHFP markers (c) in FACS isolated bulge SC (a6HCD34+) expressing SmoM2 cells one week and 4 weeks after 10 mg TAM administration to K19CREER/Rosa-SmoM2-YFP mice. The errors bars represent s.e.m. of the different replicates (control (No TAM, n=9), 1 week (n=6) and 4weeks (n=4)).

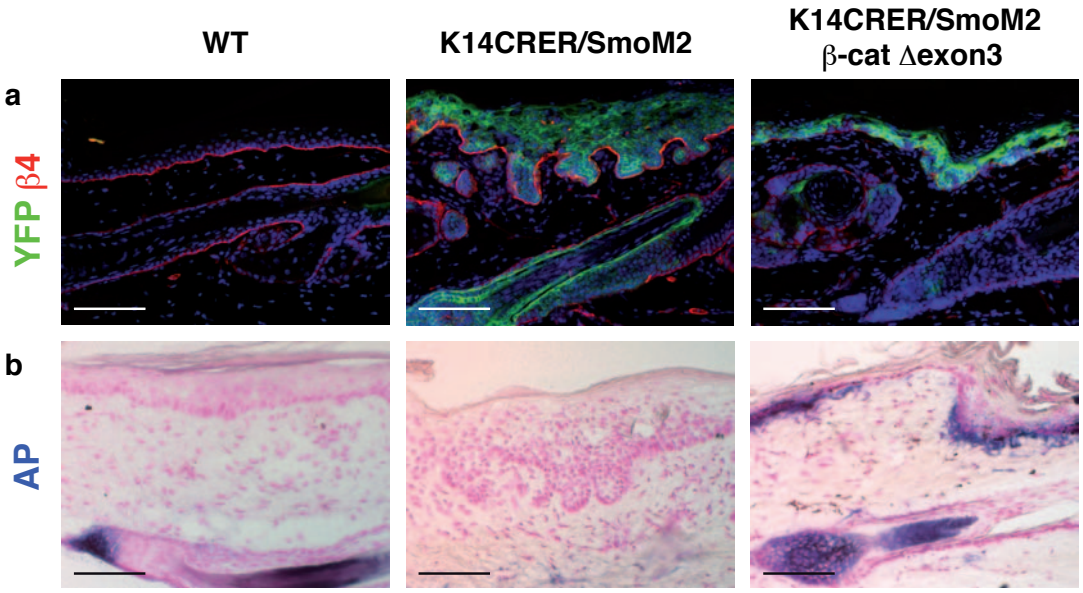

Figure S5 Stabilized β-catenin expression inhibits the progression of SmoM2 induced tumors in the tail epidermis. (a-b) Immunostaining for β4-integrin and SmoM2 (a) and alkaline phosphatase (AP) reaction (b) in wt, K14CREER/SmoM2-YFP and K14CREER/SmoM2-YFP/βcatenin-Δexon3 tail epidermis 4 weeks after 15mg TAM administration showing a delay in tumor progression and the appearance of AP positive cells in the dermis of cells co-expressing SmoM2 and βcatenin-Δexon3. Scale bars, 50μm.

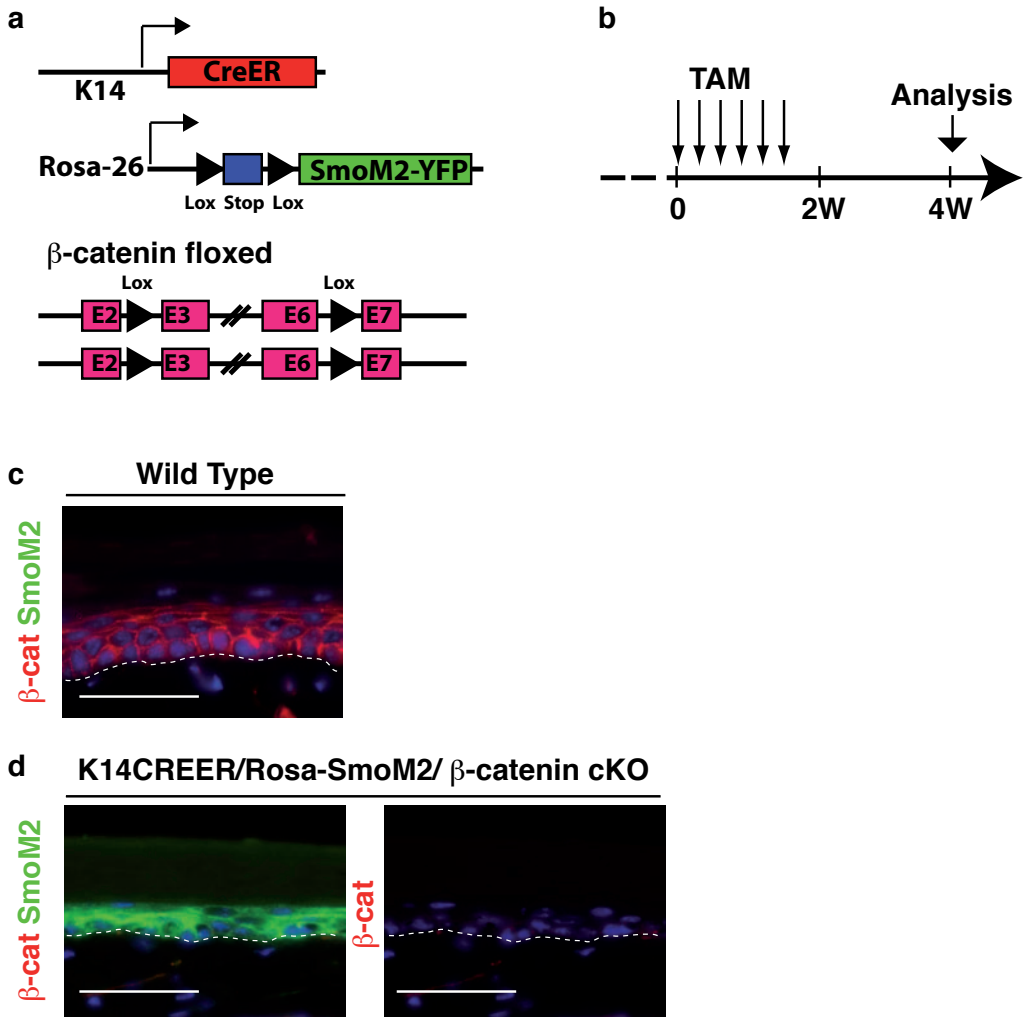

Figure S6 Combined SmoM2 expression and β-catenin deletion in the adult skin epidermis. (a) Scheme representing the genetic strategy used to express SmoM2 in β-catenin deficient epidermal cells. (b) Scheme summarizing the protocol used to induce the SmoM2 expression and the deletion of β-catenin in adult interfollicular tail epidermis. (c, d) immunostaining of β-catenin (red) and SmoM2 (green) in the untreated tail epidermis (c) and 4 weeks after 15mg of TAM administration (d) in K14CREER /Rosa-SmoM2/ β-catenin floxed/floxed mice. Scale bars, 50 μm.

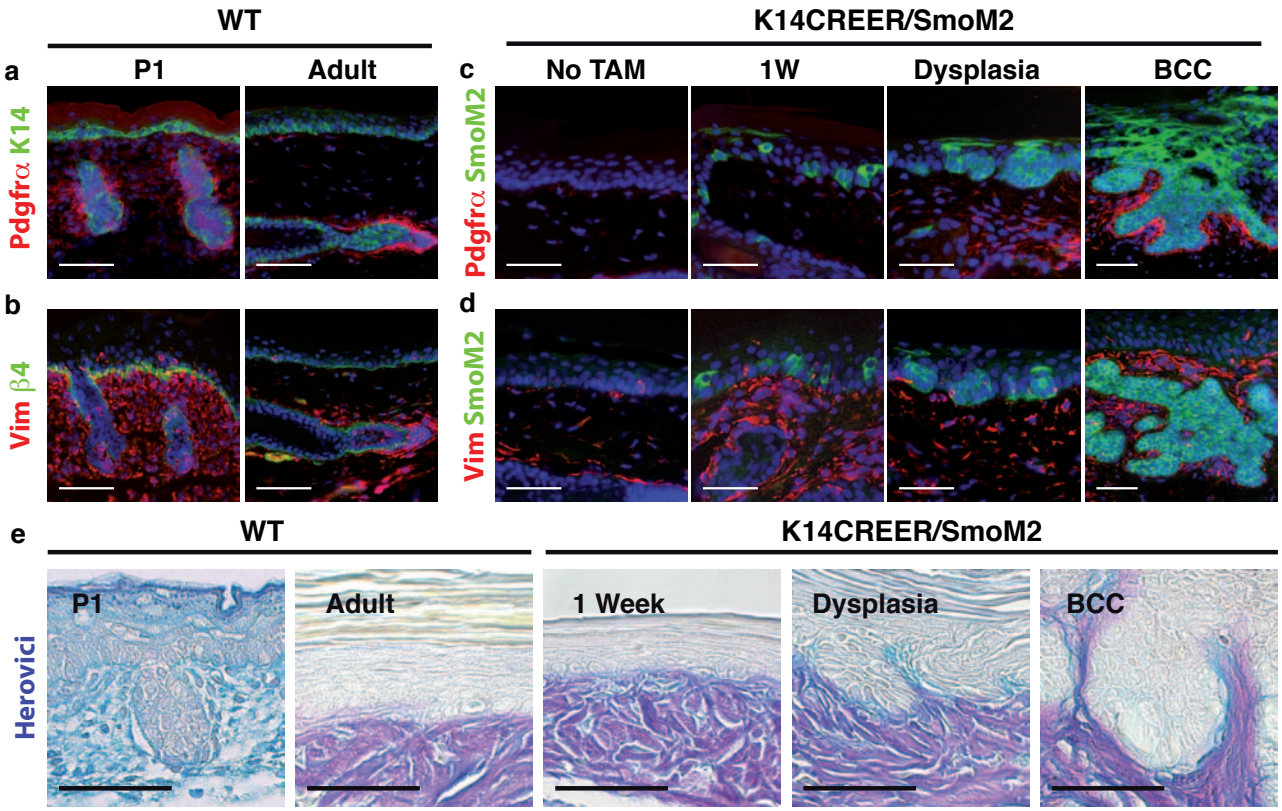

Figure S7 Reprogramming of the dermis into an embryonic/neonatal stage following SmoM2 expression in the epidermis. (a-c) Immunostaining for Pdgfrα and K14 (a) and Vimentin and β4-integrin (b) in neonatal and adult epidermis showing the enrichment of Pdgfrα and Vimentin in the neonatal dermis and their more restricted expression to the dermal papilla and mesenchymal cells surrounding the lower part of the hair follicle in the adult tail skin. (c, d) Immunostaining of Pdgfrα and K14 (c) and Vimentin and β4 (d) before, 1w, 4 weeks and 10 Weeks after TAM administration to K14CRER/SmoM2 mice. Note the strong increase of both Pdgfrα and Vimentin in the dermis cells following SmoM2 expression. (e) Herovici staining in neonatal and adult skin following SmoM2 expression. Note the appearance of light bleu staining representing immature collagen fibers in the dermis underneath SmoM2 expressing epidermis. Scale bars, 50 μm.

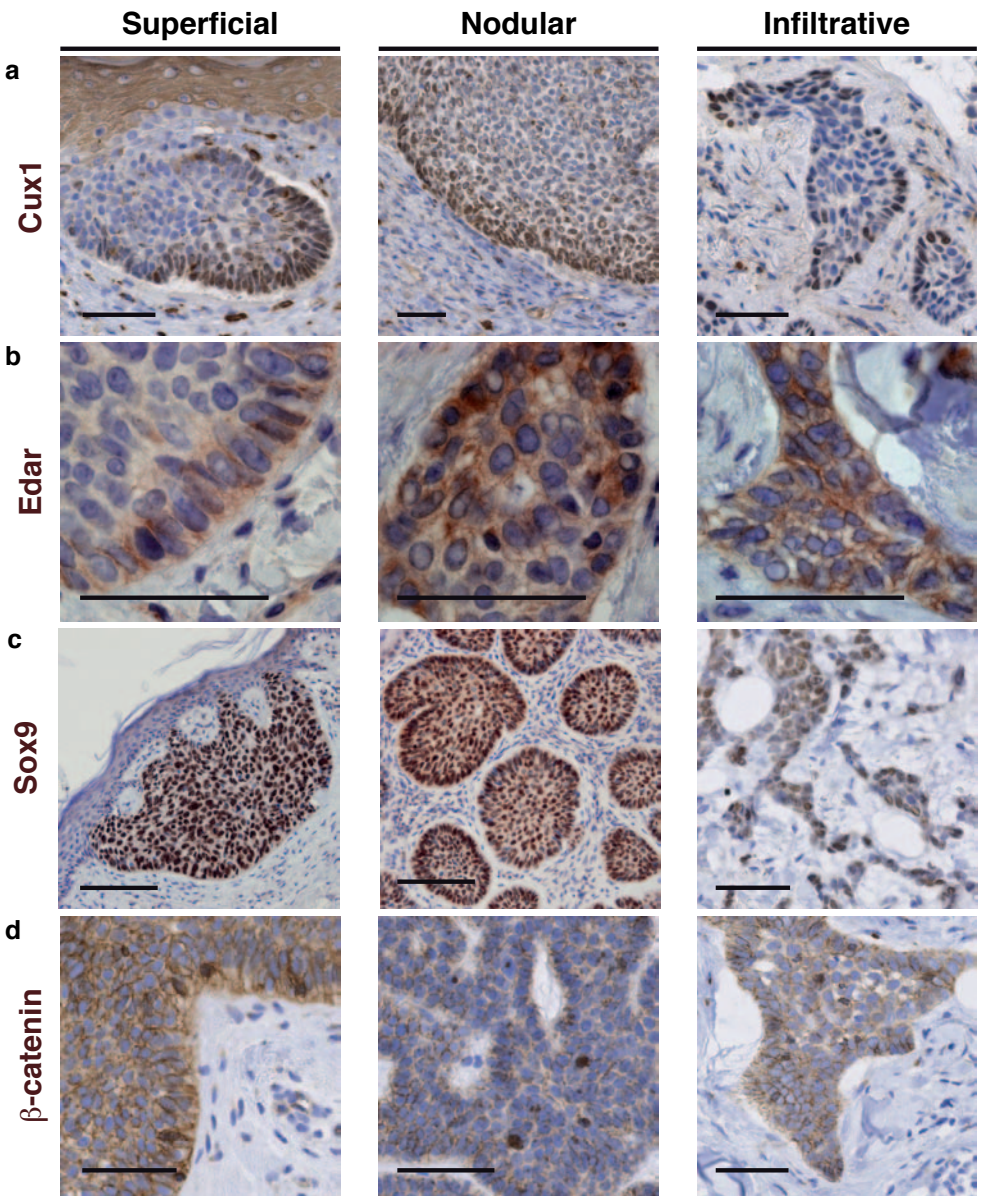

Figure S8 Immunostaining of embryonic hair follicle progenitors and Wnt/β-catenin signaling markers in human basal cell carcinoma. (a-e) Immunostaining of embryonic hair follicle markers Cux1 (a), Edar (b), Sox9 (c) and β-catenin (d). Note the nuclear accumulation of β-catenin in all three BCC subtypes. Scale bars, 50 μm