

Supplementary Figures

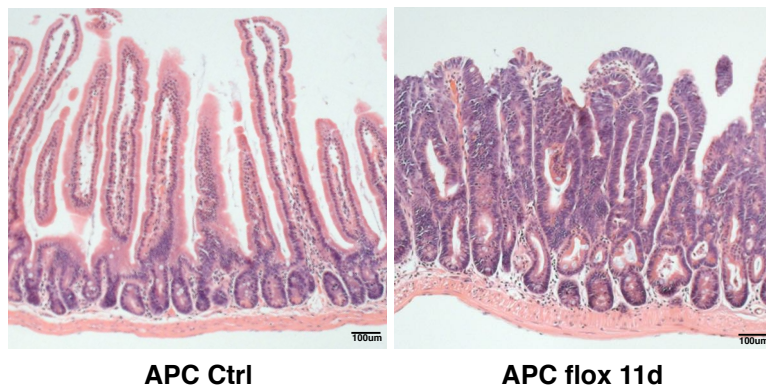


Figure S1. Conditional deletion of *Apc* in *Lrig1*⁺ progenitor cells resulted in expanded crypts in intestinal tissues

H&E stained sections of intestines from *Lrig1*-*Apc* control and mutant mice 11 days post 4-OHT application.

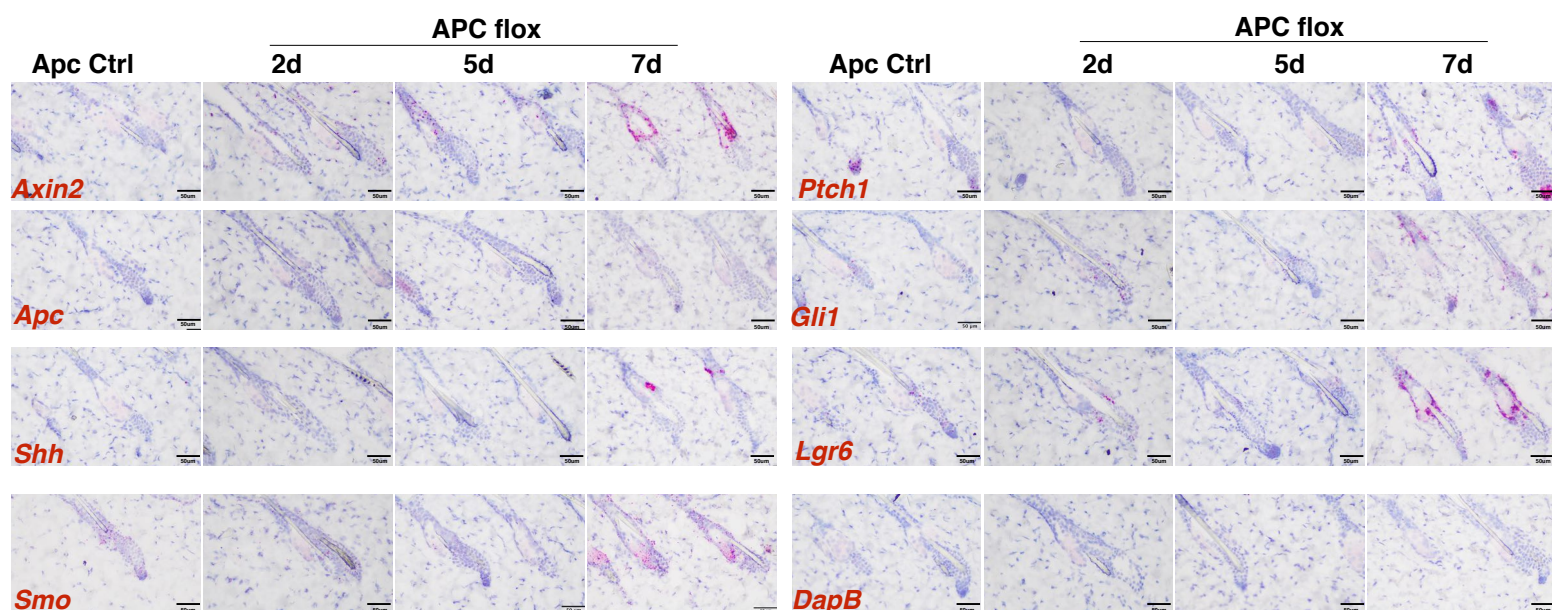


Figure S2. Hedgehog signalling was upregulated upon APC loss/Wnt activated RNA *in situ* hybridization of genes in Hedgehog signaling pathways in *Lrig1-Apc* mutants and controls, at Day 2, 5 and 7 following 4-OHT application. *Shh*, Sonic hedgehog; *Smo*, smoothened. Scale bars, 100 μ m.

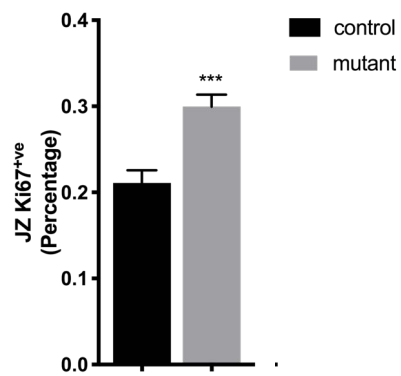


Figure S3. Increased number of proliferative cells in HF junctional zone of *Lrig1-bcat* skin

Double positive cells of *Ki67* and *Lrig1* were counted in immunofluorescent sections from *Lrig1-bcat* mutant and controls. N=47-75 hair follicles from 2 mice in each group, respectively. Data are mean $\pm$ SEM. ***p<0.001.

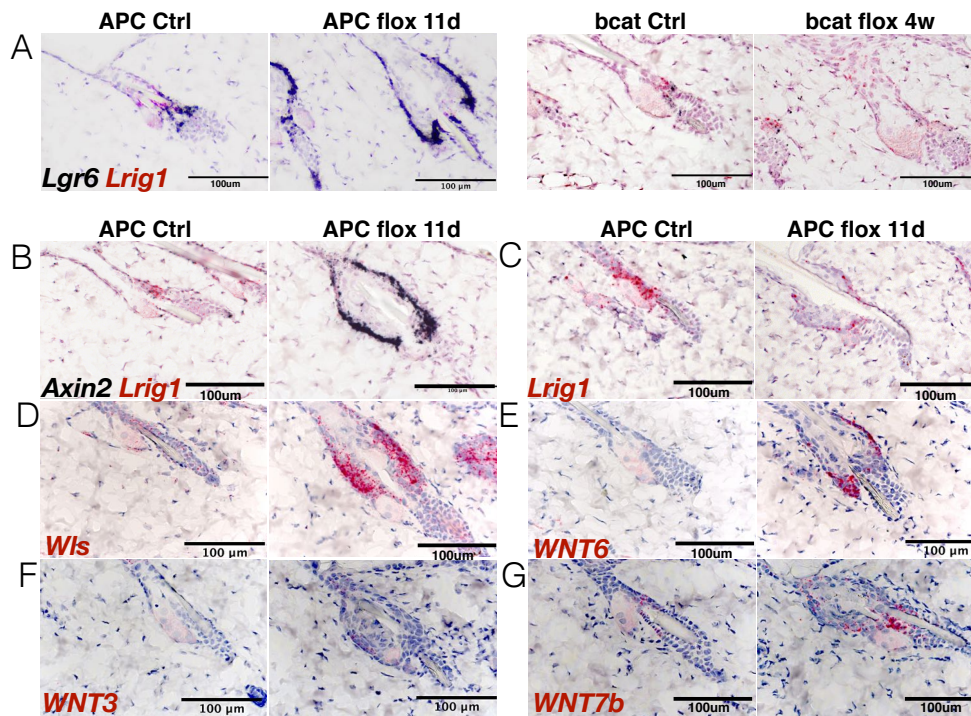


Figure S4. Modulations of Wnt signaling resulted in various gene expression changes in the progenitor cells

(A) Duplex RNA *in situ* hybridization of *Lgr6* (black) and *Lrig1* (red) were performed on sections from *Lrig1-Apc* and *Lrig1-bcat* mutants and their controls.

(B-G) RNA *in situ* hybridization of Duplex: *Axin2* (black) and *Lrig1* (red) (B), single plex: *Lrig1* (C), *Wls* (D), *Wnt6* (E), *Wnt3* (F) and *Wnt7b* (G) in *Lrig1-Apc* mutant and control. Scale bars, 100µm.

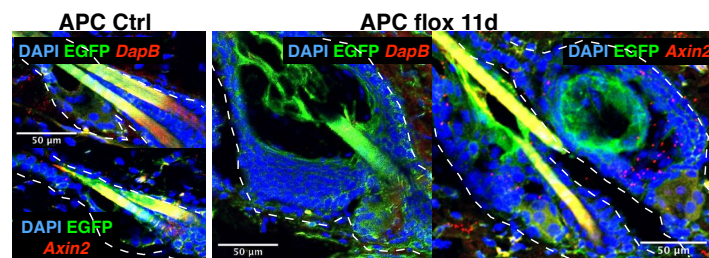


Figure S5. *Axin2* expressions in *Lrig1*-traced cells

Fluorescent *in situ* hybridization of *Axin2* in *Lrig1-Apc-mTmG* mutant and control mice. Red dots indicate *Axin2* transcripts. *Axin2* was highly expressed in eGFP⁺ cells. *DapB*, negative control. Scale bars, 50 μm.

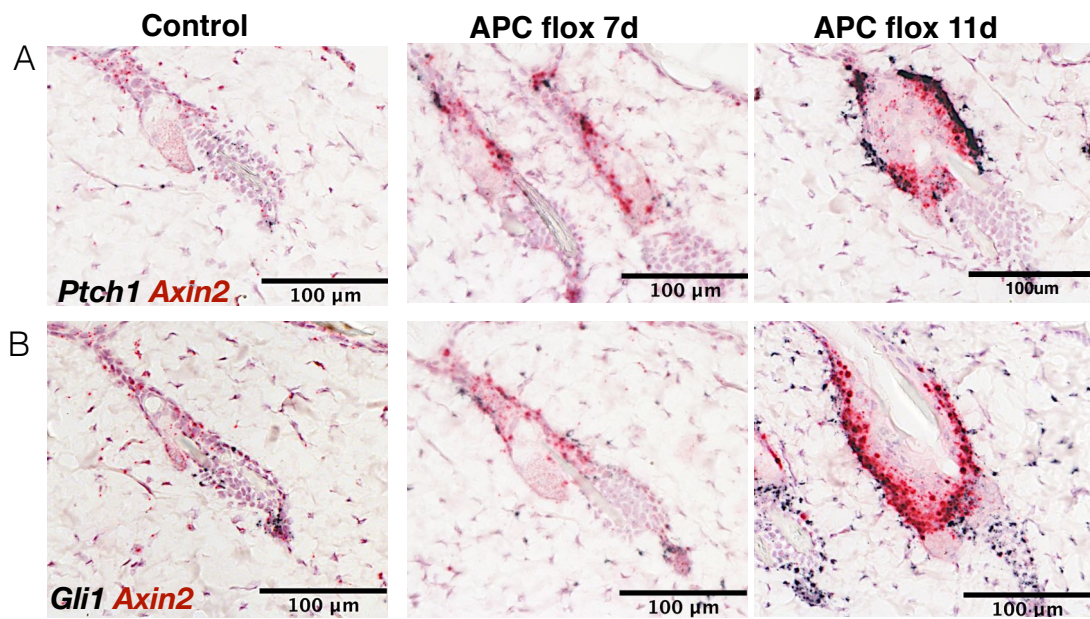


Figure S6. Hedgehog signalling was induced by Wnt in the basal layers of *Lrig1-Apc* JZ cyst

Duplex RNA *in-situ* hybridisation of *Ptch1* and *Axin2* (A) & *Gli1* and *Axin2* (B) in *Lrig1-Apc* mutants from Day 7, Day 11 and controls. Scale bars indicate 100µm.

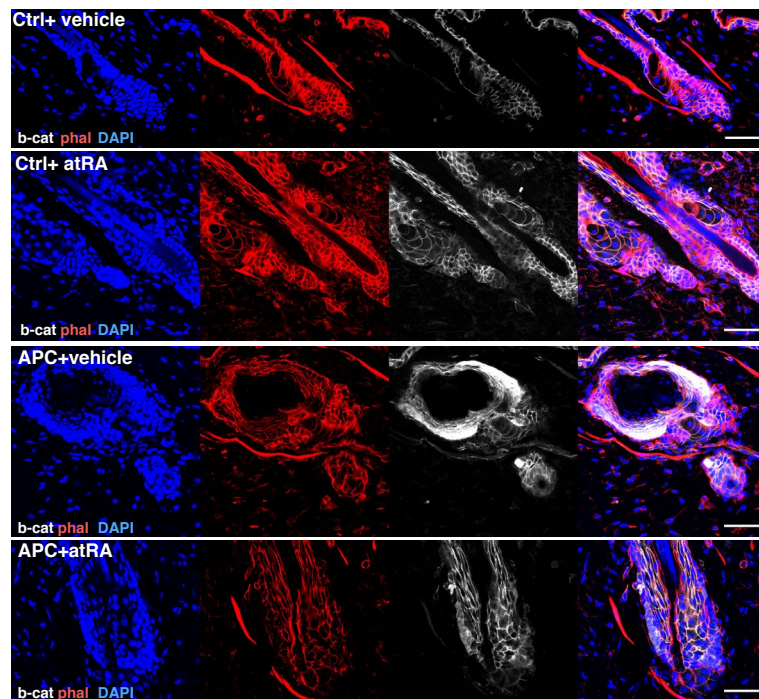


Figure S7. b-catenin nuclear accumulation was reduced by atRA treatment
 Immunofluorescent staining of dorsal skin sections from *Lrig1-Apc* mutant and controls with vehicles or atRA treatments. Immunolabeled with the b-catenin antibody, counterstained with phalloidin to label F-actin (red) and with DAPI to label nuclei (blue). Single color images for b-catenin are shown in gray scale. Scale bars, 50 μ m.

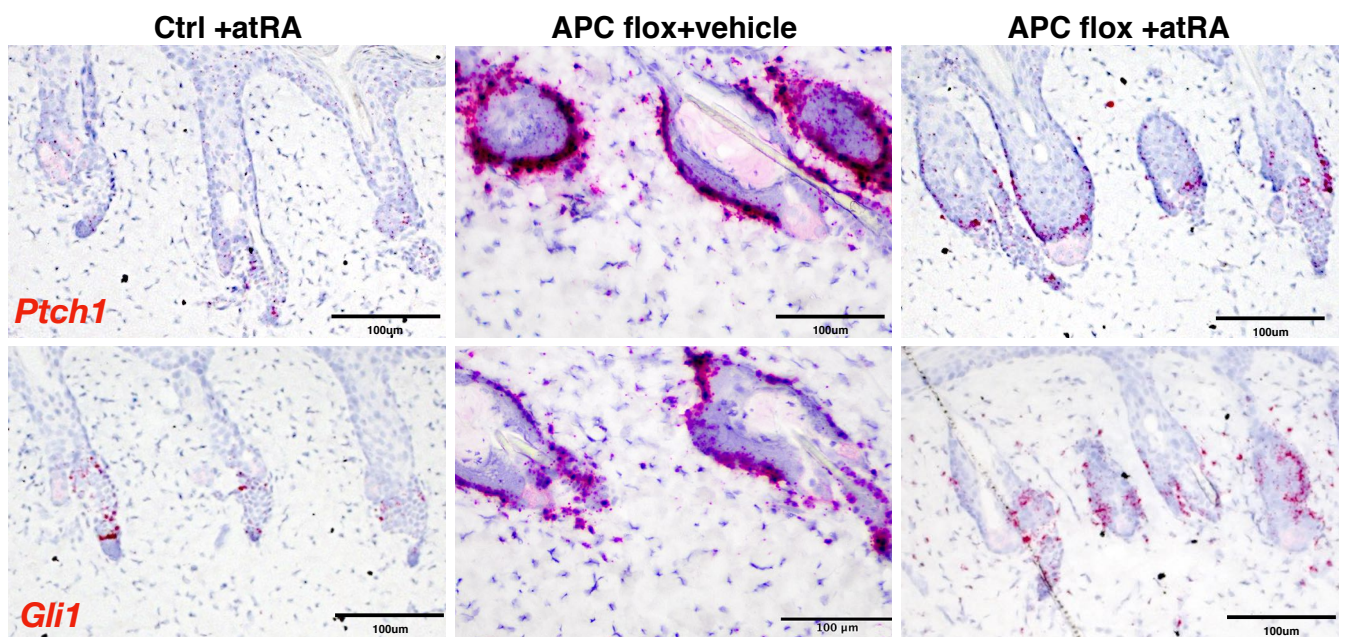


Figure S8 All-trans Retinoic acid reduced Hedgehog activity in *Lrig1-Apc* mice
 RNA *in situ* hybridization of Hedgehog signaling target genes *Ptch1* and *Gli1* in *Lrig1-Apc* mutant and control, treated with vehicle or atRA. Scale bars, 100µm.

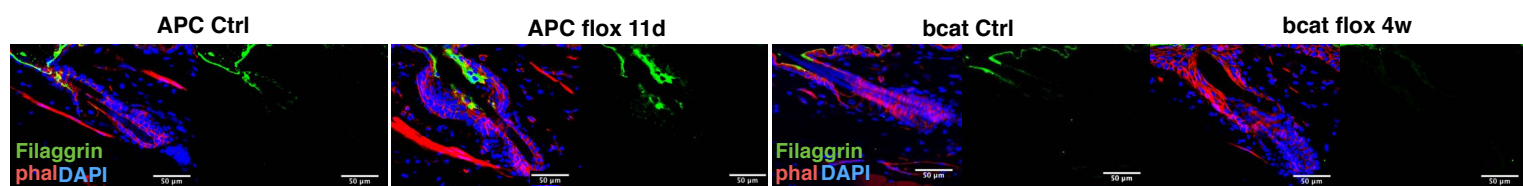


Figure S9 Filaggrin is highly expressed in *Lrig1-Apc* cyst

Immunolabeled with Filaggrin antibody, counterstained with phalloidin to label F-actin (red) and with DAPI to label nuclei (blue). Scale bars, 50 µm.

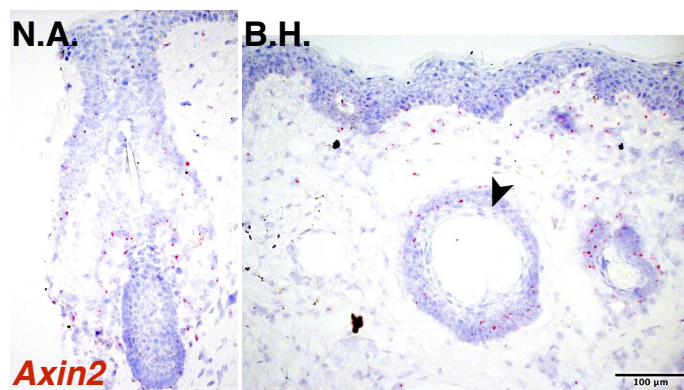


Figure S10 Human acne comedo is Wnt active

RNA *in situ* hybridization of *Axin2* in non-affected (N.A.) hair follicle, sebaceous glands and blackhead (B.H.) comedo from human skin biopsy. Scale bars, 100μm.