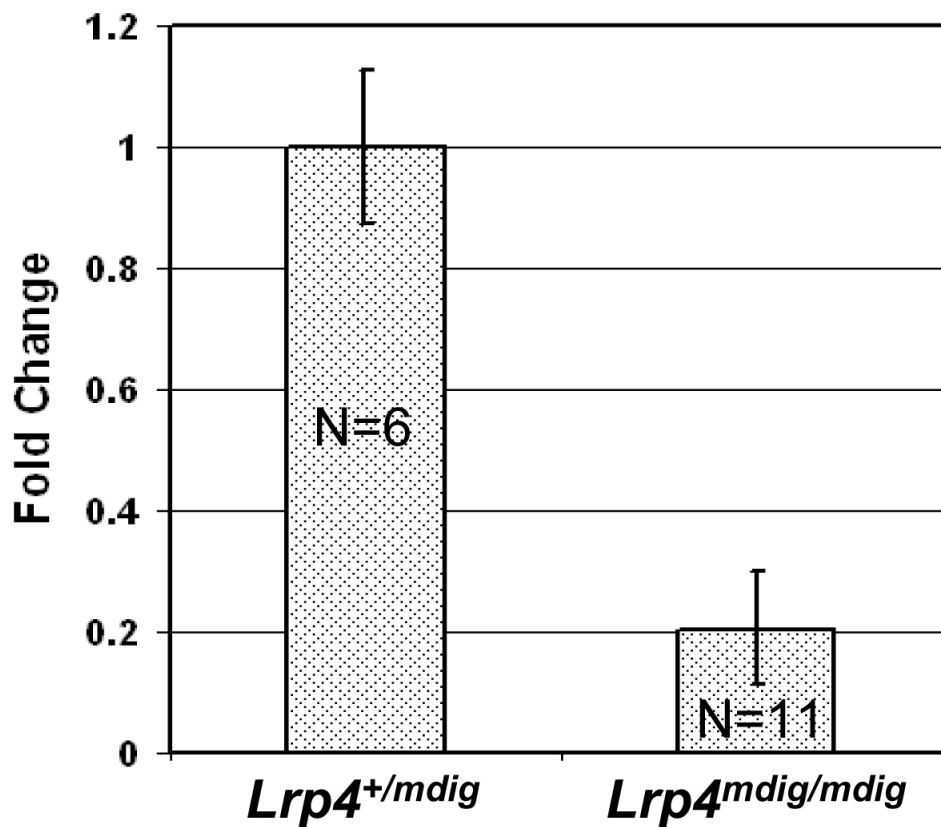
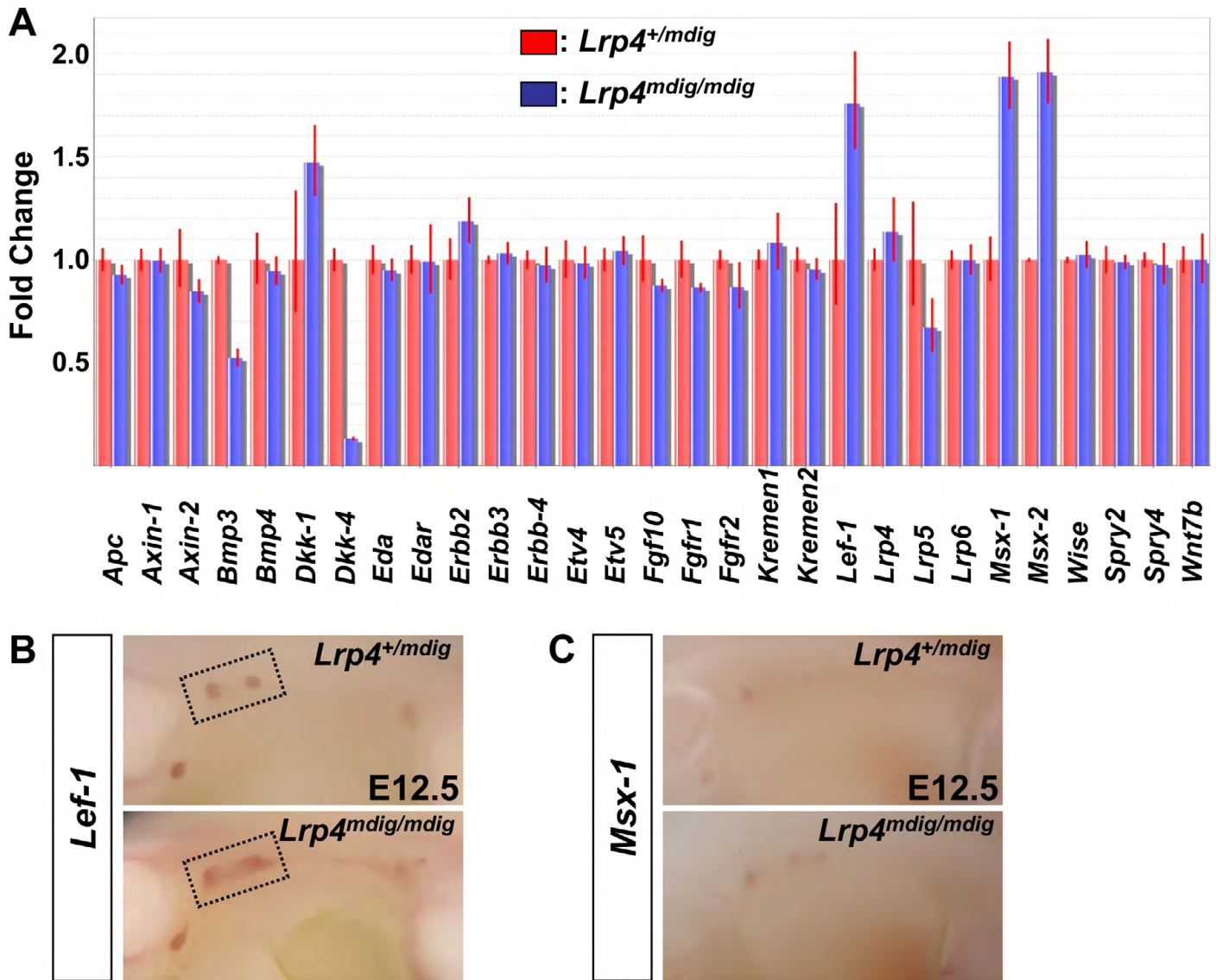


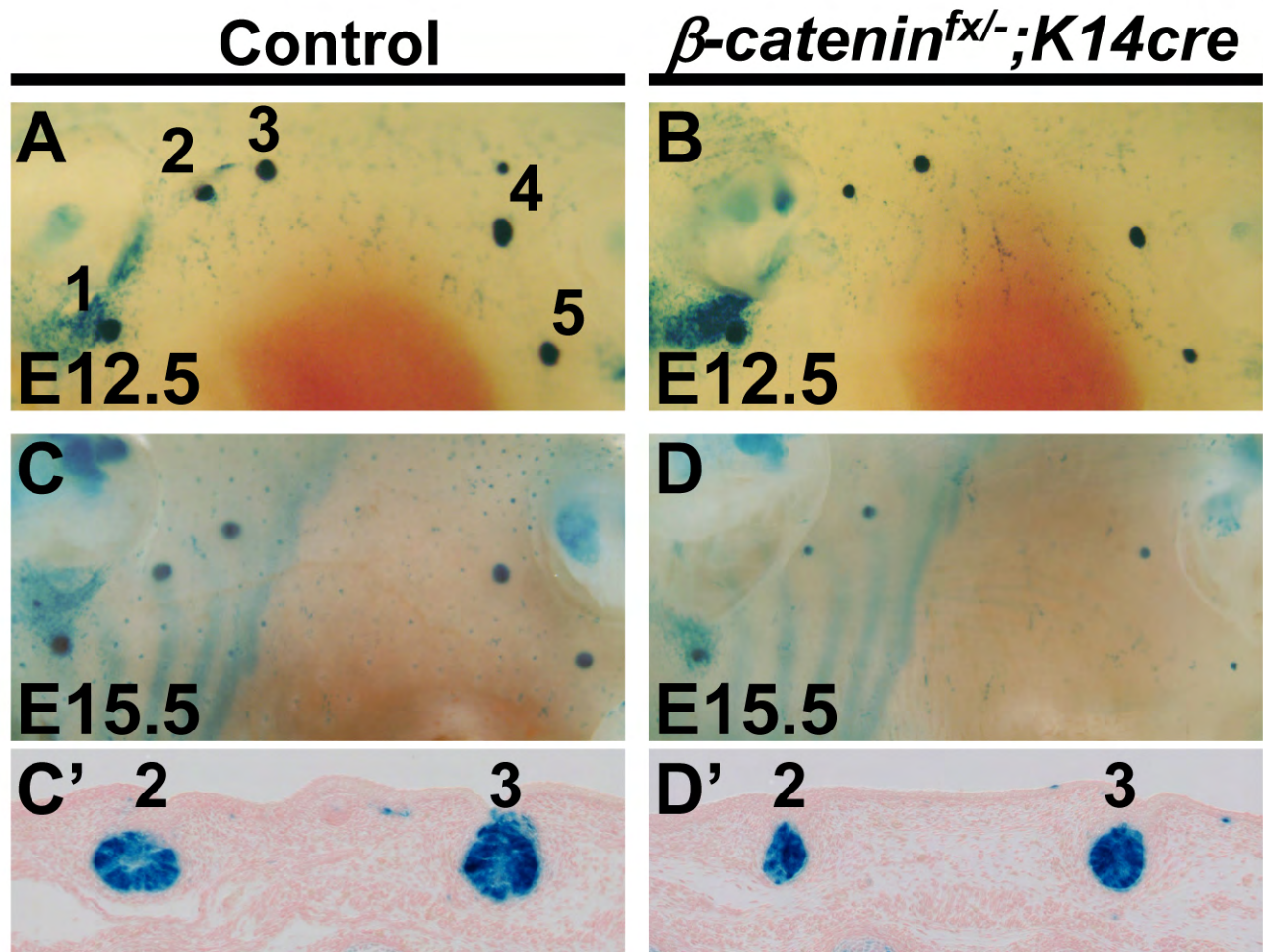
**Fig. S1. Similar mammary defects in different *Lrp4* mutant mice.** (A-D) Allelic combinations of *Lrp4* mutations result in abnormal patterning of mammary placodes as shown by *TopGal* expression. Ectopic *TopGal*-expressing cells are present in the interplacodal regions of mutant mice (arrows).



**Fig. S2. Reduced number of proliferating cells in the interplacodal epithelium of *Lrp4* mutant mice.** Relative number of BrdU-positive epithelial cells between mammary placodes 2 and 3 at E12.5 on stained sections. Average number of labeled cells in control mice is 27.8. Data are mean±s.d.

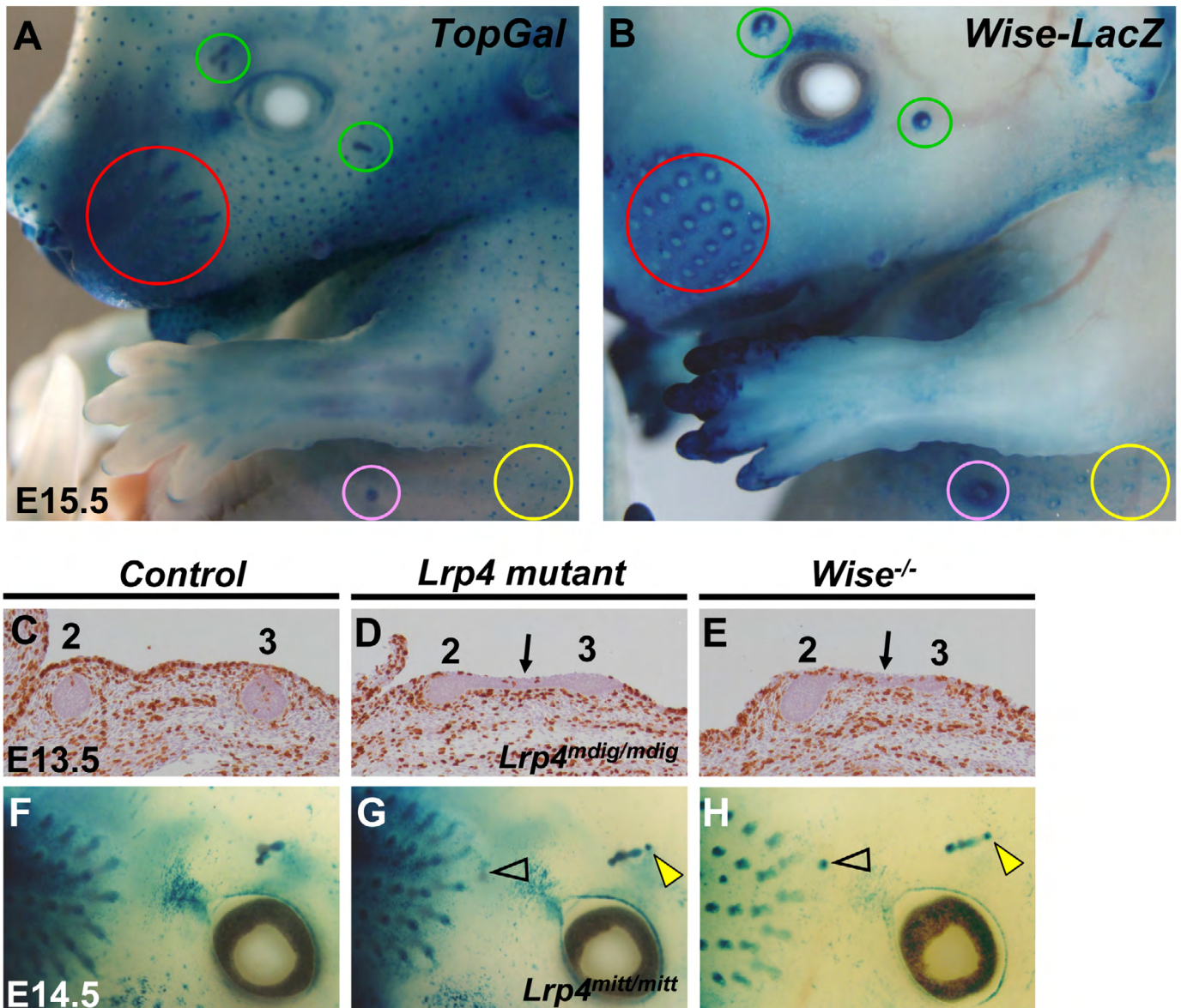


**Fig. S3. Gene expression analyses of *Lrp4* mutant mammary placodes.** (A) Real-time PCR was performed with TaqMan assays (Life Technologies) using cDNA from mammary placodes 2/3 and surrounding epithelial and mesenchymal tissues dissected from E12.5 embryos. Twelve to 14 dissected areas (the area marked with rectangles in B) from control and mutant embryos were pooled for RNA extraction. Error bar was calculated from four replicates for each probe using DataAssist (Life Technologies). (B,C) *In situ* hybridization shows increases in *Lef1* (B) and *Msx1* expression.

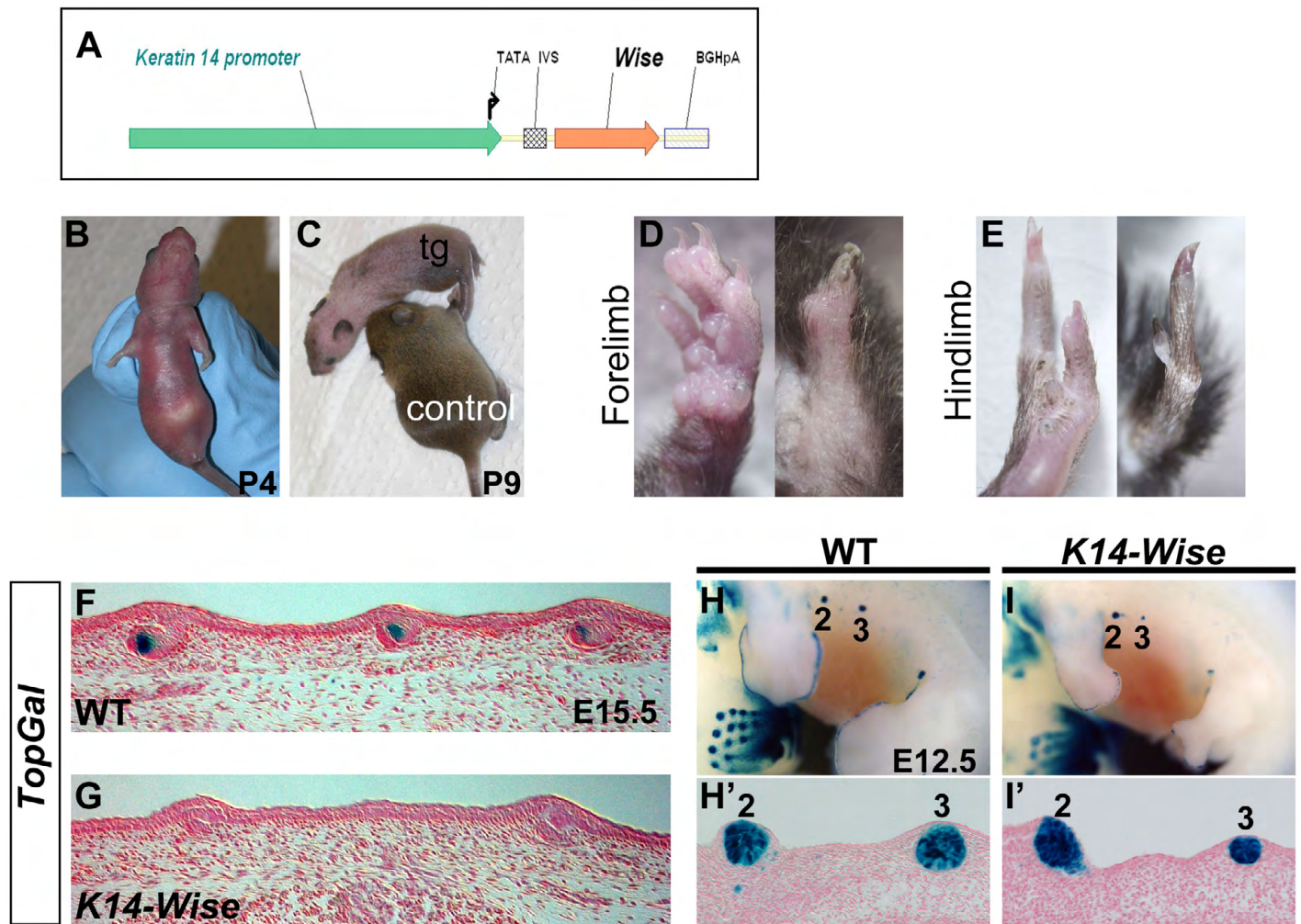


**Fig. S4.  $\beta$ -Catenin is required for growth of mammary buds.** (A-D') Ectodermal inactivation of the gene encoding  $\beta$ -catenin leads to hypoplastic mammary buds.





**Fig. S5. *Lrp4* and *Wise* are required for skin appendage development.** (A,B) Complementary expression pattern of *TopGal* and *Wise-lacZ* in the mystacial (red circles), supra- and sub-orbital (green circles) vibrissal follicles, mammary buds (pink circles) and hair follicles (yellow circles). The *Wise-lacZ* construct was generated by inserting a *lacZ-SV40pA* in-frame into the first coding exon of *Wise* in the 24 kb *EcoRI-SalI* genomic fragment from a mouse BAC clone, RP23-98E22. (C-E) BrdU staining is reduced in the epithelium between mammary buds 2 and 3 (arrows) in *Lrp4* and *Wise* mutants at E13.5. (F-H) *TopGal* expression reveals supernumerary mystacial (open arrowheads) and supra-orbital (yellow arrowheads) vibrissal follicles in *Lrp4* and *Wise* mutants at E14.5.



**Fig. S6. Overexpression of *Wise* disrupts development of limbs and skin appendages.** (A) The *K14-Wise* construct. (B-E) *K14-Wise* mice display hair loss and limb abnormalities. (F,G) Histological sections show disruption in the formation of primary hair follicles in *K14-Wise* mice. (H-I') Abnormal development of mammary placodes and limb buds in *K14-Wise* mice.