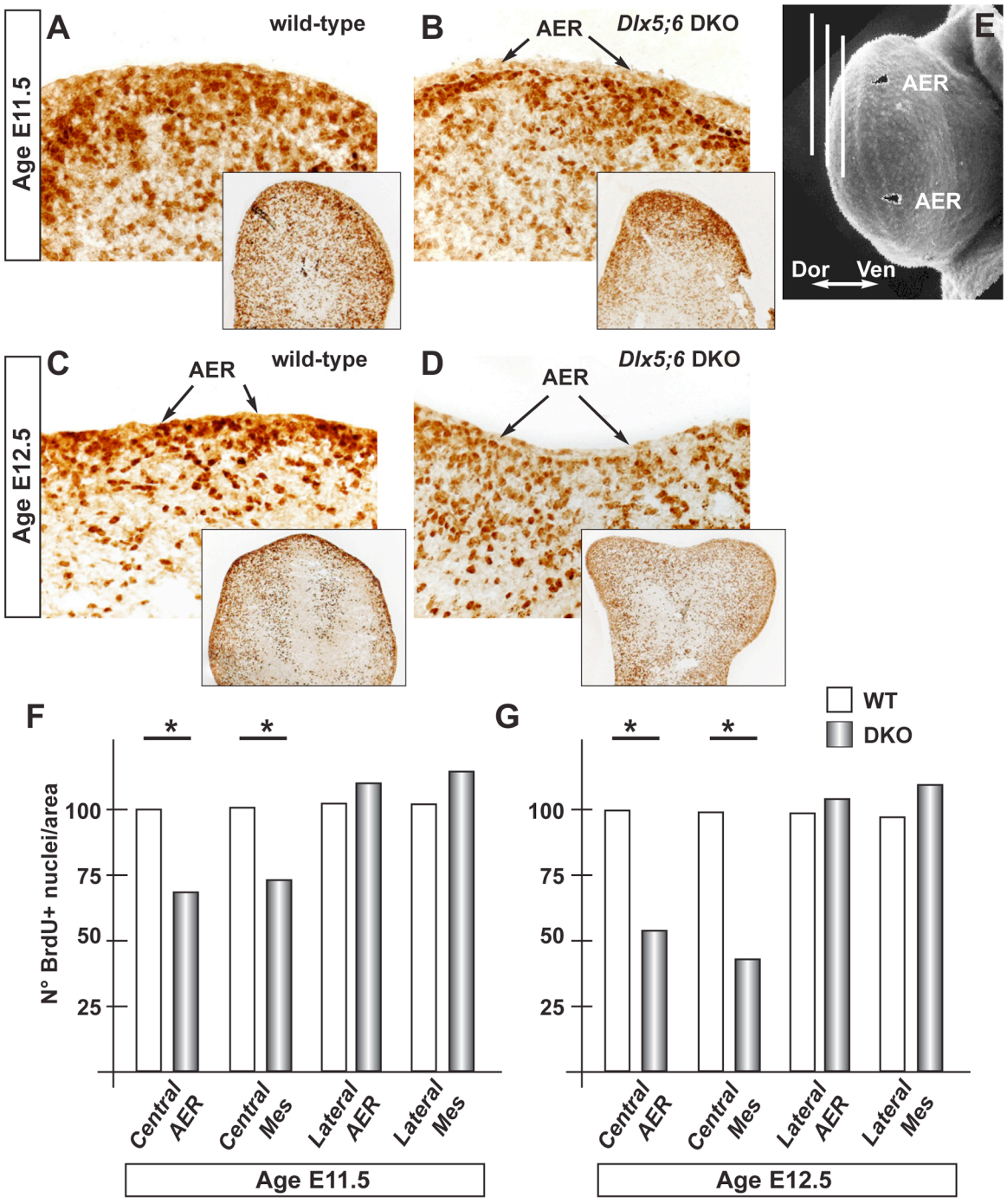
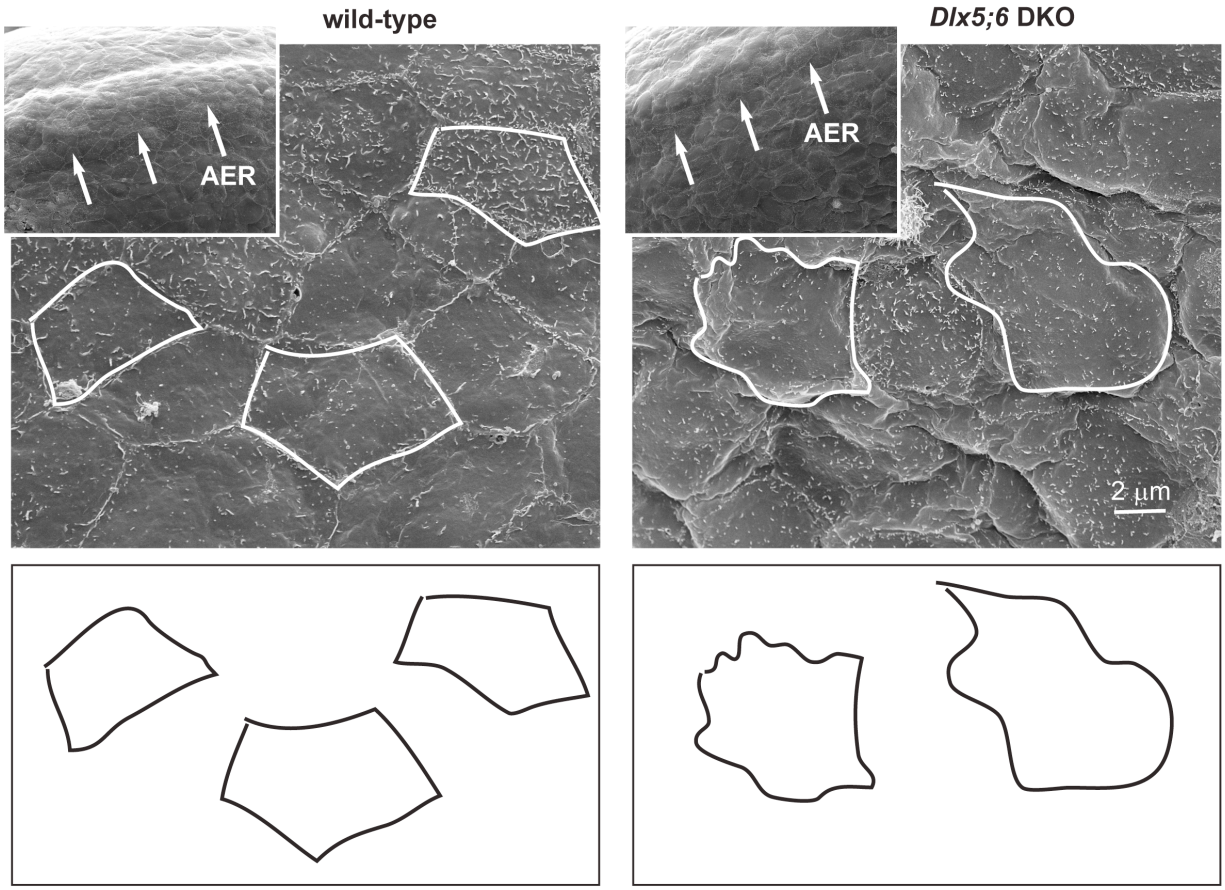
Supplementary Figures

Supplementary Figure 1.



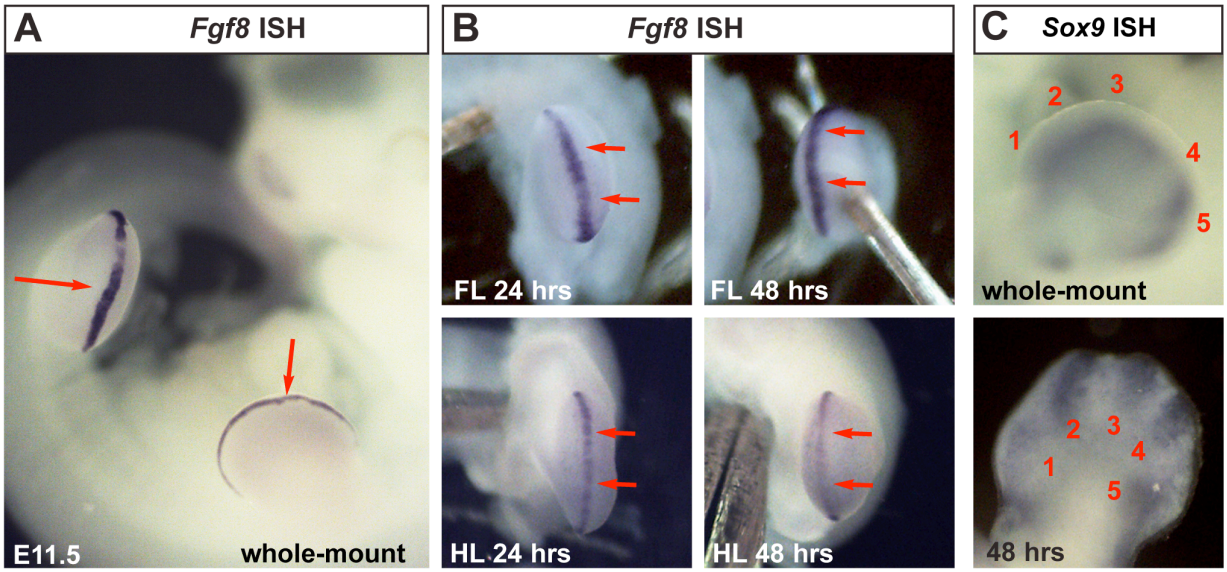
BrdU incorporation in WT and *Dlx5;6* DKO hindlimbs. Two embryonic ages are shown: E11.5 (top) and E12.5 (bottom). **A-D**. WT limbs are on the left, *Dlx5;6* DKO limbs are on the right. **E.** Schematic diagram to show the section plane used for this analysis. The inserts show a low magnification of the same. **F,G.** Quantification of the number of BrdU+ nuclei/area observed in the AER and in the underlying mesenchyme at E 11.5 (F) and E12.5 (G). The central and the lateral sectors were counted separately since ectrodactyly is essentially a middle-ray malformation (see micrograph in D). WT is made =100%. Asterisks indicate statistical significance. Note a significant decrease of proliferation in the AER and mesenchyme of the central sector, and an increase in the lateral mesenchyme.

Supplementary Figure 2.



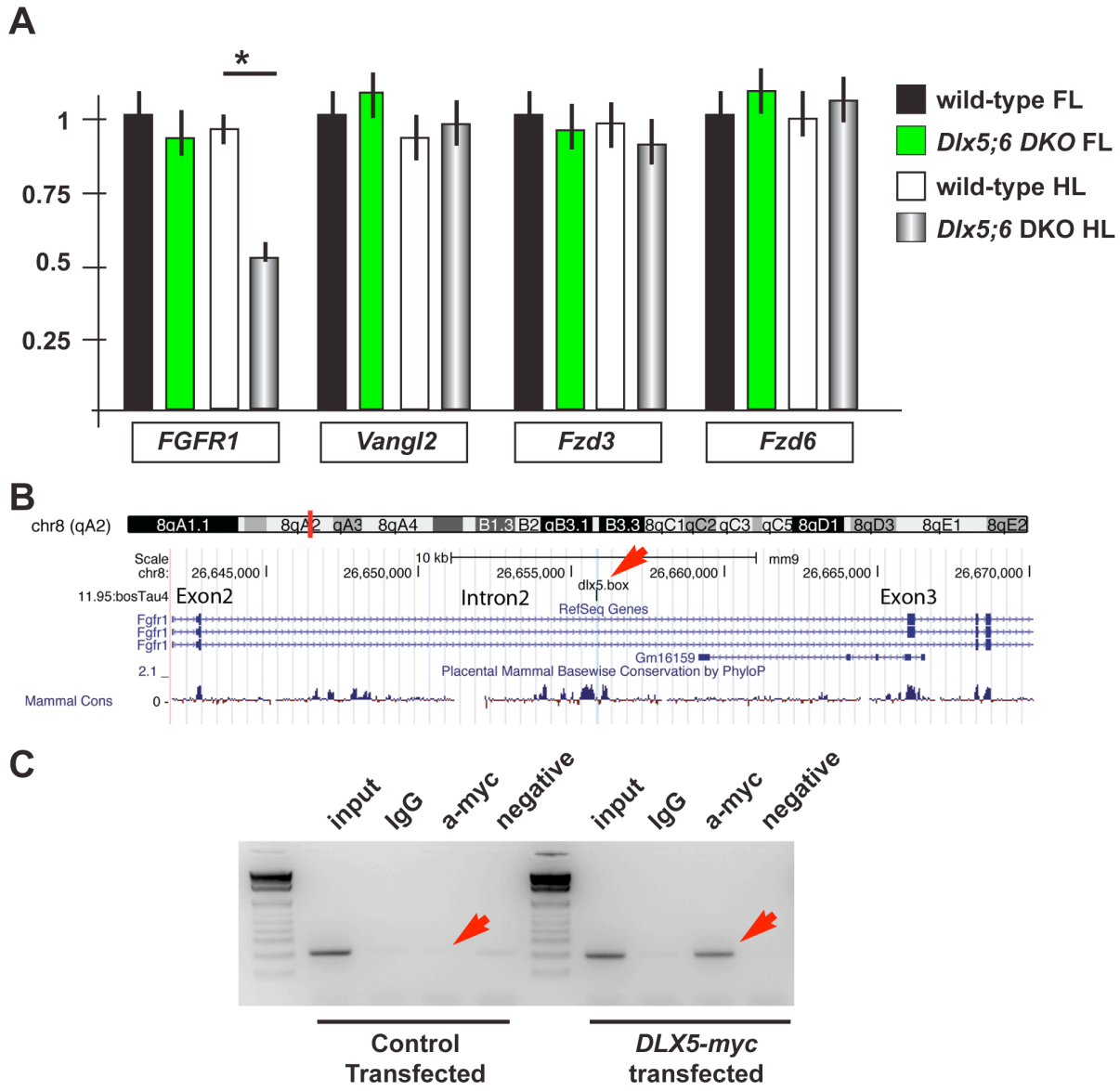
Morphology of AER cells of WT (on the left) and *Dlx5:6* DKO (on the right) hindlimbs, observed by SEM. Inserts report lower magnification of the same. The contour of some of the WT and *Dlx5;6* DKO epithelial cells is reported below.

Supplementary Figure 3.



Ex-vivo cultures of whole limbs maintain the AER and the early mesenchymal condensations. **A.** Whole mount *in situ* hybridization on a WT E11.5 embryos, to detect the *FGF8* mRNA. **B.** Forelimbs (top panels) and hindlimbs (bottom panels) collected at the embryonic age E11, and cultured *ex vivo* for 24 hrs (on the left) or 48 hrs (on the right), hybridized to detect the *FGF8* mRNA. The AER is indicated (red arrows). **C.** Whole mount *in situ* hybridization on hindlimbs collected at the embryonic age E11.5 and cultured *ex-vivo* for 48 hrs, to detect the *Sox9* mRNA. The presumptive digits are indicated (red numbers).

Supplementary Figure 4.



FgfRR1 is a target of Dlx5 and is downregulated in *Dlx5;6* DKO limbs. **A.** Relative abundance of *FgfR1*, *Vangl2*, *Fzd3* and *Fzd6* mRNAs in WT and *Dlx5;6* DKO forelimbs and hindlimbs, by Real-Time qPCR. Asterisks indicate statistical significance. **B**. Predicted DLX5 binding sites in the intron 2 of the *FgfR1* locus, conserved in mammalian species (red arrowheads), annotated on the UCSC mouse genome browser. Exons and mammalian conservation are shown. **C**. ChIP analysis of the *FgfR1* promoter region containing a predicted Dlx5 binding site, in SH-SY5Y cells transfected with WT *DLX5-myc tag* expression vectors. Immunoprecipitation was done with anti-myc antibody. Red arrowheads indicate specific signal.