

Fig. S1. Inactivation of HoxA and HoxD genes does not abrogate *Bmp4* expression in the limb mesenchyme. (A-D) Whole-mount in situ hybridization showing *Bmp4* expression at E9.5 (A,B) and E10.5 (C,D) in control (A,C), *HoxA;D* null (B) and *HoxAc*^{-/-};*D*^{-/-} (D) limb buds. In Hox mutants, *Bmp4* expression is impaired in the AER but not in the mesenchyme.

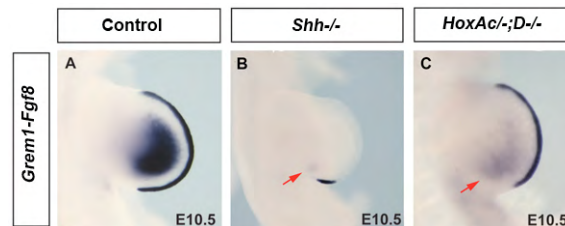


Fig. S2. Residual *HoxA* transcript is sufficient for *Grem1* activation in conditional *HoxA;D* mutants (A-C) Expression pattern of *Grem1* and *Fgf8* at E10.5 in control (A) *Shh*^{-/-} (B) and *HoxAc*^{-/-};*HoxD*^{-/-} (C) limb buds. Arrows in B,C indicate *Grem1* expression. *Fgf8* is expressed in the entire AER in *HoxAc*^{-/-};*HoxD*^{-/-} buds

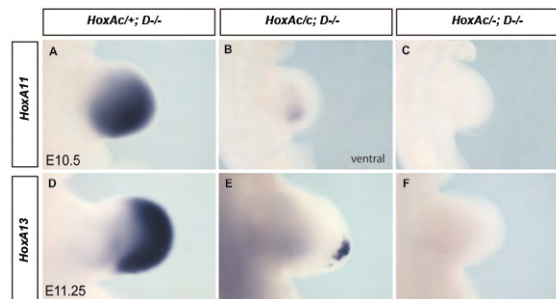


Fig. S3. Transient *HoxA* expression due to the kinetics of the *Prx1*-Cre activity. (A-C) *HoxA11* expression in *HoxAc*^{+/+};*D*^{-/-} (A), *HoxAc*^{c/c};*D*^{-/-} (B) and *HoxAc*^{-/-};*D*^{-/-} (C) E10.5 limb buds. (D-F) *HoxA13* expression in *HoxAc*^{+/+};*D*^{-/-} (D), *HoxAc*^{c/c};*D*^{-/-} (E) and *HoxAc*^{-/-};*D*^{-/-} (F) E10.5 limb buds. Completion of the Cre-mediated deletion is delayed when both HoxA alleles are conditional instead of one.

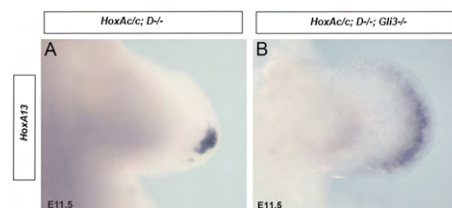


Fig. S4. Transient *HoxA13* expression is observed in the anterior mesenchyme when *Gli3* is inactivated. (A,B) *Grem1* expression pattern in *HoxAc*^{c/c};*D*^{-/-} (A) and *HoxAc*^{c/c};*D*^{-/-};*Gli3*^{-/-} (B) at E11.5.

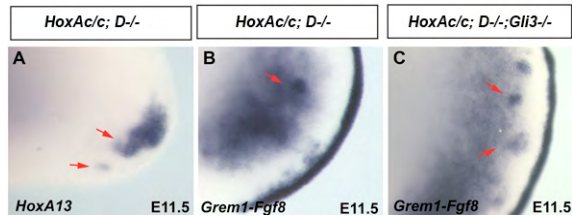


Fig. S5. Mosaic *Hoxa13* expression correlates with patchy *Grem1* expression. (A) Mosaic *HoxA13* expression in *HoxAc/c;D^{-/-}* limb buds is associated with non-uniform Cre-mediated deletion among mesenchymal cells. Red arrows in A indicate the cell clusters expressing *HoxA13*. (B,C) Whole-mount *in situ* hybridization showing *Grem1* and *Fgf8* expression in *HoxAc/c;D^{-/-}* (B), *HoxAc/c;D^{-/-};Gli3^{-/-}* (C). *Grem1* expression is non-uniform and red arrows in B,C indicate different cell clusters strongly expressing *Grem1* that correlates with mosaic *HoxA13* expression (A).

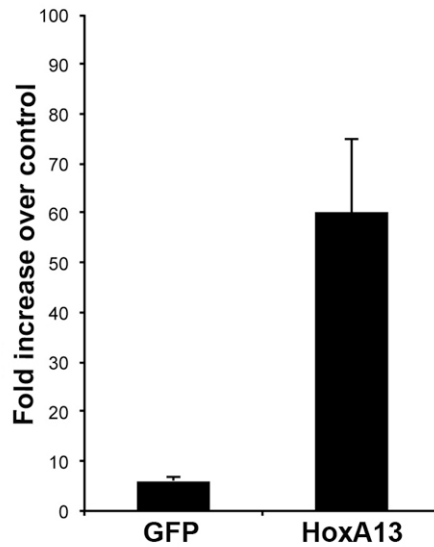


Fig. S6. *Hoxa13* triggers the activity of *Grem1* limb enhancers in P19 cells. Transcription assays in P19 cells co-transfected with *Grem1* enhancer linked to luciferase-coding sequences and the GFP or *Hoxd9*-expressing vector. Luciferase activity is indicated as fold change over luciferase activity in absence of the *Grem1* enhancer. Bars indicate s.d.

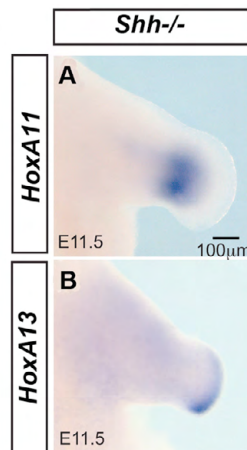


Fig. S7. *Hoxa11* and *Hoxa13* remain expressed in *Shh^{-/-}* limb buds. (A,B) Whole-mount *in situ* hybridization showing *Hoxa11* (A) and *Hoxa13* (B) expression in *Shh^{-/-}* limb buds at E11.5.