

Publication

Attenuated sensing of SHH by Ptch1 underlies evolution of bovine limbs

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The large spectrum of limb morphologies reflects the wide evolutionary diversification of the basic pentadactyl pattern in tetrapods. In even-toed ungulates (artiodactyls, including cattle), limbs are adapted for running as a consequence of progressive reduction of their distal skeleton to symmetrical and elongated middle digits with hoofed phalanges. Here we analyse bovine embryos to establish that polarized gene expression is progressively lost during limb development in comparison to the mouse. Notably, the transcriptional upregulation of the Ptch1 gene, which encodes a Sonic hedgehog (SHH) receptor, is disrupted specifically in the bovine limb bud mesenchyme. This is due to evolutionary alteration of a Ptch1 cis-regulatory module, which no longer responds to graded SHH signalling during bovine hand-plate development. Our study provides a molecular explanation for the loss of digit asymmetry in bovine limb buds and suggests that modifications affecting the Ptch1 cis-regulatory landscape have contributed to evolutionary diversification of artiodactyl limbs.

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