most critical genes involved in development of neural circuits underlying a simple behaviour.

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Regulatory elements controlling the expression of short-stature (Shox) genes during development
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The murine Shox2 (mShox2) gene is required for development of the proximal limbs, palate, jaws and heart. Deficiencies of the closely related human SHOX (hSHOX) gene cause the limb abnormalities associated with Turner, Léri–Weill and Langer syndromes. Some Léri–Weill and Langer patients have an intact hSHOX coding region, but deletions far downstream of the gene, suggesting that long-range enhancer elements are required for hSHOX expression in limbs. To begin to understand the regulation of Shox genes, we used transgenic mouse embryos to analyze the regulation of mShox2 and hSHOX. First we analyzed the regulatory potential of sequences near each gene by inserting a LacZ reporter at the start codon of each coding sequence on an appropriate bacterial artificial chromosome (BAC). Transgenic embryos produced from the mShox2 construct revealed the presence of regulatory elements driving expression in proximal limbs, sensory neurons and the hindbrain. Further analysis revealed that sensory neuron expression is associated with sequences close to the Shox2 gene, whereas limb and hindbrain expression requires an evolutionarily conserved region approximately 35 kb downstream. In contrast transgenic embryos containing the hSHOX-LacZ BAC showed expression only in the first pharyngeal arch, a known expression domain of hSHOX. Therefore we are now searching for hSHOX limb enhancers on BACs mapping further downstream of the gene. One prominent candidate is a conserved sequence with homology to the mShox2 limb/hindbrain enhancer region.

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