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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