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Auto/Cross-Regulation of *Hoxb3* Expression in Posterior Hindbrain and Spinal Cord

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Abstract

The complex and dynamic pattern of *Hoxb3* expression in the developing hindbrain and the associated neural crest of mouse embryos is controlled by three separate cis-regulatory elements: element I (region A), element IIIa, and the r5 enhancer (element IVa). We have examined the cis-regulatory element IIIa by transgenic and mutational analysis to determine the upstream trans-acting factors and mechanisms that are involved in controlling the expression of the mouse *Hoxb3* gene in the anterior spinal cord and hindbrain up to the r5/r6 boundary, as well as the associated neural crest which migrate to the third and posterior branchial arches and to the gut. By deletion analysis, we have identified the sequence requirements within a 482-bp element III482. Two Hox binding sites are identified in element III482 and we have shown that *in vitro* both Hoxb3 and Hoxb4 proteins can interact with these Hox binding sites, suggesting that auto/cross-regulation is required for establishing the expression of *Hoxb3* in the neural tube domain. Interestingly, we have identified a novel GCCAGGC sequence motif within element III482, which is also required to direct gene expression to a subset of the expression domains except for rhombomere 6 and the associated neural crest migrating to the third and posterior branchial arches. Element III482 can direct a higher level of reporter gene expression in r6, which led us to investigate whether *kreisler* is involved in regulating *Hoxb3* expression in r6 through this element. However, our transgenic and mutational analysis has demonstrated that, although kreisler binding sites are present, they are not required for the establishment or maintenance of reporter gene expression in r6. Our results have provided evidence that the expression of *Hoxb3* in the neural tube up to the r5/r6 boundary is auto/cross-regulated by *Hox* genes and expression of *Hoxb3* in r6 does not require *kreisler*.

Keywords

Hoxb3; hindbrain; rhombomere; *kreisler*; neural crest; cis-regulation

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