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Review

Conservation and Diversity in the *cis*-Regulatory Networks That Integrate Information Controlling Expression of *Hoxa2* in Hindbrain and Cranial Neural Crest Cells in VertebratesStefan Tümpel^a ... Robb Krumlauf^{a1} **Show more**<https://doi.org/10.1006/dbio.2002.0665>[Get rights and content](#)Under an Elsevier [user license](#)[open archive](#)


Abstract






The *Hoxa2* and *Hoxb2* genes are members of paralogy group II and display segmental patterns of expression in the developing vertebrate hindbrain and cranial neural crest cells. Functional analyses have demonstrated that these genes play critical roles in regulating morphogenetic pathways that direct the regional identity and anteroposterior character of hindbrain rhombomeres and neural crest-derived structures. Transgenic regulatory studies have also begun to characterize enhancers and *cis*-elements for those mouse and chicken genes that direct restricted patterns of expression in the hindbrain and neural crest. In light of the conserved role of *Hoxa2* in neural crest patterning in vertebrates and the similarities between paralogs, it is important to understand the extent to which common regulatory networks and elements have been preserved between species and between paralogs. To investigate this problem, we have cloned and sequenced the intergenic region between *Hoxa2* and *Hoxa3* in the chick *HoxA* complex and used it for making comparative analyses with the respective human, mouse, and horn shark regions. We have also used transgenic assays in mouse and chick embryos to test the functional activity of *Hoxa2* enhancers in heterologous species. Our analysis reveals that three of the critical individual components of the *Hoxa2* enhancer region from mouse necessary for hindbrain expression (Krox20, BoxA, and TCT motifs) have been partially conserved. However, their number and organization are highly varied for the same gene in different species and between paralogs within a species. Other essential mouse elements appear to have diverged or are absent in chick and shark. We find the mouse r3/r5 enhancer fails to work in chick embryos and the chick enhancer works poorly in mice. This implies that new motifs have been recruited or utilized to mediate restricted activity of the enhancer in other species. With respect to neural crest regulation, *cis*-components are embedded among the hindbrain control elements and are highly diverged between species. Hence, there has been no widespread conservation of sequence identity over the entire enhancer domain from shark to humans, despite the common function of these genes in head patterning. This provides insight into how apparently equivalent regulatory regions from the same gene in different species have evolved different components to potentiate their activity in combination with a selection of core components.

Keywords




Hoxa2; *Hoxb2*; hindbrain; neural crest cells; segmentation; regulation; conservation; gene expression; vertebrates; evolution




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