

Divergent Gene Expression of *Hoxb3b* in Teleost Fishes is Due to Divergence of Upstream *Cis*-Regulatory Elements

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Hox genes are developmental regulatory genes that function to pattern the cranial nerves that are derived from the rhombomeres (r) during vertebrate embryonic development. *Hoxb3*, in particular, has been shown to be expressed in r5-7 in several tetrapod species, including mouse (*Mus musculus*). Over the course of evolution, teleost fish have undergone a whole genome duplication, and several species have retained both duplicate *Hoxb3* genes, *hoxb3a* and *hoxb3b*. These genes are expressed differently from each other, such that while *hoxb3a* is expressed in r4-7 in many teleost fish species, *hoxb3b* is expressed solely in r4. The *cis*-regulatory elements (CREs) that are responsible for directing *hoxb3b* expression in r4 are currently unknown. We used several software programs, including VISTA and CLUSTAL, to identify conserved sequences upstream of *hoxb3b* in the Japanese medaka (*Oryzias latipes*), Nile tilapia (*Oreochromis niloticus*), Atlantic salmon (*Salmo salar*), and Japanese pufferfish (*Takifugu rubripes*). From these analyses, we observed the presence of several CREs that are similar in sequence to those that direct other *Hox* genes in r4, including *Hoxb1*, *Hoxa2*, and *Hoxb2*. We also used these software programs to understand if the conserved sequences upstream of *hoxb3b* were present for *hoxb3a* in the same teleosts mentioned above, as well as *hoxb3a* in zebrafish (*Danio rerio*), *Hoxb3* in the spotted gar, a species of bony fish that predates the teleost-specific genome duplication, and *Hoxb3* of the dogfish shark (*Scyliorhinus canicula*), coelacanth (*Latimeria chalumnae*), mouse, and human (*Homo sapiens*). Interestingly, we did not observe the presence of the teleost *hoxb3b*-specific sequences for any *Hoxb3* or *hoxb3a* gene. These results suggest that the whole genome duplication in teleost fishes has allowed for the divergence in expression and function of *hoxb3b*.