Role of Dlx5 in the development of the palatal-pharyngeal region in higher vertebrates

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Distal-less (Dll) genes belong to an evolutionarily conserved family of homeobox transcriptional regulators, which are important for the early embryonic development of bone in the limbs and craniofacial region. Mutations in human Dll orthologs, *Dlx5/6*, cause split-hand/split-foot type 1 malformation (SHFM1) associated with sensorineural deafness, cleft palate, developmental delay, and micrognathia. *Dlx5* mutant mice have craniofacial abnormalities including cleft soft palate and micrognathia. However, the role of *Dlx5* in the palatal-pharyngeal development, which is important for speech, remains unclear. This study examines the role of *Dlx5* in the formation of the soft palate, the Eustachian tube (ET), and the pharyngeal region. Gene expression analysis demonstrates that *Dlx5* is expressed in muscles and osteogenic progenitor cells. Homozygous *Dlx5* mutant mice lack soft palatal muscles including the levator veli palatini (LVP) and palatopharyngeus (PLP). The posterior regions of the hard palate and pterygoid plate are smaller in $Dlx5^{-/-}$ mice than in controls. Morphometric analyses of the premaxilla, maxilla, palatine bone, and mandible show that these bones are smaller in height, width, and length in $Dlx5^{-/-}$ mice compared to controls. Taken together, our data reveal that $Dlx5^{-/-}$ mice recapitulate craniofacial phenotypes similar to those of SHFM patients. Further studies of *Dlx5* expression in the proximal region of the mandible, posterior palate, and pharyngeal region may reveal the mechanism responsible for the pharyngeal morphology. These studies hold potential for improving our understanding of the evolution of speech in the human lineage