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

Alexandre Grimaldi, Thach-Vu Ho, Carolina Parada, and Yang Chai

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.