AAO Foundation Award Final Report

Principal Investigator	Robert Hinton
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Award Type	Biomedical Research
Project Title	"Expression of Growth Factors and Their Receptors in the Mandibular Condylar Cartilage in Response to Biomechanical and Hormonal Stimuli" (1999-2002 with no-cost extensions)
Project Year	1999
Institution	Baylor College of Dentistry
Summary/Abstract	Growth hormone (GH) appears to play an important role in overall growth of the craniofacial skeleton, with its main effects on cartilaginous tissues. It is well established in limb cartilage that GH regulates proliferation and differentiation of growth plate chondrocytes, most likely via stimulation of local mediators such as insulin-like growth factor 1 (IGF-1) or fibroblast growth factor-2 (FGF-2). Surprisingly little is known of the mechanisms underlying growth regulation in secondary cartilages such as the mandibular condylar cartilage (MCC), especially at postnatal growth ages in the mixed dentition or adolescent stages that are typically the targets of therapeutic intervention. We have documented the tissue localization of receptors for IGF-1 (IGF-1r) and FGF-2 (Fgfr1, Fgfr2, and Fgfr3) in the mandibular condylar cartilage of prepubescent 30 day-old rats, demonstrated that these growth factors regulate proliferation in the MCC, and that gene expression for IGF-1 and FGF-2 changes in the MCC during the transition to puberty (Fuentes et al., *47(9): 643-654, 2002*). Using an intraoral appliance that forces the mandible into crossbite (producing a differential alteration in condylar position), we have shown that gene expression for IGF-1, FGF-2, and their receptors in the MCC changes within 3 days following appliance placement and changes further over 14 days, and that the change is typically in opposite directions in the protruded side and retruded side condyles (*Fuentes et al., Am. J. Orthod. Dentofac. Orthoped. , 123:153-159, 2003; Fuentes et al., Am. J. Orthod. Dentofac. Orthoped., 123: 160-166, 2003*). Alterations in gene expression of IGF-1, FGF-2, and their receptors following appliance placement are very similar to changes seen in MCC explants following treatment with exogenous GH. In order to further explore the effect of hormonal stimulus on MCC growth, we have used a mutant strain of

	rats in which GH secretion is 6-10% of normal, but in which all other pituitary hormones are unaffected. Baseline longitudinal cephalometric studies of craniofacial growth in these animals indicated that all dimensions were smaller than same strain controls, but that some dimensions were affected differently than others. Those dimensions most strongly affected by the lack of GH were the least mature (i.e., with the greatest growth potential). While many growth curves were linear, others were second (quadratic) or third order curves (*VandeBerg et al., Archs. Oral Biol., 49: 477-484, 2004; VandeBerg et al., Anat. Rec., 278A: 561-570, 2004*.). We are now completing a study comparing mandibular growth in GH-normal and GH-deficient rats with and without the crossbite appliance (*VandeBerg, J. Dent. Res. 82 (Spec Iss A): abstract #26186, 2003*). Finally, we have shown that supplementation of GH-deficient rats with GH produces differential increases in growth rate of the craniofacial complex that are inversely proportional to the relative maturity of the various craniofacial measures (*Singleton et al., Am. J. Orthod. Dentofac. Orthoped., in press).* We are proud that this paper won the 2004 Milo Hellman Award. <u>The results of these studies extend, and in some instances initiate, our knowledge of how mandibular condylar cartilage growth can be regulated by hormonal input and biomechanical stimuli, and lay the foundation for studies of the interaction of these factors.</u>