

AAO Foundation Award Final Report

Principal Investigator	Robert J. Hinton
Co-Investigator	Anthony Iacopino David S. Carlson
Secondary Investigators	
Award Type	Biomedical Research Award
Project Title	AAOF Biomedical Research Award “TGF- β in the Mandibular Condylar Cartilage Following Functional Protrusion in Growing and Non-Growing Rats” (1995-1999 with no-cost extensions)
Project Year	1995
Institution	Baylor College of Dentistry
Summary/Abstract	<p>Although ‘functional’ orthopedic appliances are in widespread use, the biologic mechanisms underlying their action are still poorly understood. While it is presumed that these appliances influence the growth rate and direction of the mandibular condylar cartilage, the specific changes in functionally important molecules (cytokines, proteoglycans) present in the cartilage matrix during such treatment remain essentially unknown. Likewise, little is known of age-related changes in these molecules, although it is generally agreed that chronological age is a significant determinant of the efficacy of orthodontic treatment. The TGF-β family of cytokines has been implicated in a host of biological processes in cartilage, including matrix synthesis, collagen synthesis, and cell proliferation, and is likely involved in the remodeling response that takes place following protrusion of the lower jaw in experimental animals. Moreover, preliminary data from our laboratory indicates that the TGF-β isoforms TGF-β1, β2, and β3 differ markedly in expression and spatial distribution with age in porcine condylar cartilage, often in conjunction with changes in Type II collagen. This proposal was designed to test the following hypotheses: (1) isoforms of TGF-β vary considerably in their expression and spatial distribution in the rat mandibular condyle over the growth period and during aging; (2) changes in distribution and expression of TGF-β in the condylar cartilage are induced following placement of an intraoral appliance that forces protrusion of the lower jaw upon closing.</p> <p style="text-align: center;">A tangible outcome of this funding was the completion and publication of a study on the distribution of TGF-β isoforms in the condylar cartilage of the pig (<i>Moroco et al., Cell Tiss. Res., 289: 119-124, 1997</i>). After repeated but ultimately unsuccessful attempts</p>

to utilize a 'Twin block' type appliance to prompt anterior mandibular posturing in rats, the intraoral appliance part of the study was undertaken using an intraoral appliance that forces the mandible into a crossbite (producing a differential alteration in condylar position). By this time (circa 1997), we had concluded that members of the fibroblast growth factor (FGF) and insulin-like growth factor (IGF) families were of more interest as potential modulators of condylar cartilage growth rate. The remaining funds from this grant were used to initiate studies on IGF and FGF localization and gene expression in the condylar cartilage in normal and crossbite animals. These studies were completed with the help of a subsequent AAOF Biomedical Research Award (1999), and published as *Fuentes MA et al. Archs. Oral Biol.*, 47(9): 643-654, 2002, *Fuentes MA et al. Am. J. Orthod. Dentofac. Orthoped.*, 123:153-159, 2003, and *Fuentes MA et al. Am. J. Orthod. Dentofac. Orthoped.*, 123: 160-166, 2003.

Progress on this 1995 grant was less impressive than we hoped, although it helped lay the groundwork for a more prolific output to emerge from the 1999 AAOF grant (4 additional papers, several abstracts, and the winner of the 2004 Milo Hellman Award from the AAO). Taken together, the two grants have funded research that extends, and in some instances initiates, our knowledge of how mandibular condylar cartilage growth can be regulated by hormonal/growth factor input and biomechanical stimuli.