

AAO Foundation Award Final Report

Principal Investigator	Sundaralingam Premaraj
Co-Investigator	
Secondary Investigators	
Award Type	Biomedical research award
Project Title	Role of Parathyroid-Hormone-related-Protein (PTHrP) in Orthodontic Tooth Movement
Project Year	2012
Institution	University of Nebraska Medical Center
Summary/Abstract (250 word maximum)	<p>Orthodontic tooth movement occurs when periodontal ligament (PDL) cells convert mechanical forces into chemical signals. When the PDL is compressed by the action of orthodontic forces, RANKL is upregulated, which promotes the differentiation and activation of osteoclasts. Osteoclasts resorb the alveolar bone on the compression side, allowing the tooth to move. Here, we show that direct compression of human PDL cells induces expression of PTHrP between two to four hours after application of a static compressive load. This upregulation is detected with very light force levels as low as 0.2 g/cm². After this initial spike, PTHrP levels reduce, but remain above background for 24 hours. Jagged1 and RANKL follow the same expression pattern. Analysis of compressed PDL cells indicates that Jagged1 is expressed on a subset of these cells, although RANKL appears more uniformly expressed. Transfection of siRNA specific for PTHrP reduces PTHrP mRNA as well as Jagged1. Greater reduction of PTHrP expression tended towards greater reduction in Jagged1. Likewise, addition of soluble PTHrP resulted in an increase in Jagged1. A negative feedback mechanism appears to play a role in regulation, as addition of soluble PTHrP resulted in a decrease of endogenous PTHrP mRNA expression. Under all conditions tested, RANKL mRNA levels also correlated directly with PTHrP and Jagged1 expression levels. We report that direct compression of PDL fibroblasts initiates an upregulation of PTHrP. PTHrP then upregulates Jagged1 expression on a subset of PDL fibroblasts. Jagged1 is a known ligand of Notch capable of RANKL upregulation, osteoclast differentiation and bone resorption, allowing orthodontic tooth movement.</p>
Were the original, specific aims of the proposal realized?	Yes
Were the results published? If not, are there plans to publish? If not, why not?	No, manuscript is in preparation
Have the results of this proposal been presented? If so, when and where? If not, are there plans to do so? If not, why not?	<ol style="list-style-type: none"> 1. Corwyn Hopke, DDS, MS, Master's thesis defense presentation - Contribution of PTHrP to orthodontic loading induced alveolar bone modeling, University of Nebraska, November 2013. 2. An abstract has been submitted to IADR annual meeting