FINAL REPORT

Title of Project: The Role of Osteoclast Differentiation Factors (RANK, RANKL, and OPG) in Tooth Movement.

Principal Investigator: Daniel C. Nguyen, DDS

Mentors: James Mah, DDS, PhD
Peter M. Sinclair, DDS, MSD

Institution: University of Southern California School of Dentistry
Department of Orthodontics/ Center for Craniofacial Molecular Biology

Summary:

Orthodontic tooth movement is the result of the mechanical forces applied to the tooth and alveolar bone attachment complex. Numerous studies have shown that factors which alter remodeling within the attachment apparatus respond to applied mechanical stress. Although much knowledge has been gained in our understanding of bone homeostasis under normal conditions, bone remodeling as a biologic response to orthodontic application is still unclear. Recently, three proteins have been isolated and shown to be involved in the interaction between stromal/osteoblastic cells and osteoclast progenitor cells leading to osteoclast differentiation and proliferation. Osteoclast differentiation factor, also called RANKL (receptor activator of NF-κB ligand), is a protein produced and localized on the surface of osteoblast cells. RANKL binds to a receptor called RANK on the surface of hematopoietic osteoclast precursor cells resulting in these cells differentiating into mature osteoclasts. The purpose of our study was to determine the role of mechanical force on the expression of RANKL, its receptor RANK, and osteoprotegerin (OPG), a potent inhibitor of osteoclast differentiation. Using a modified Brudvik and Rygh (1993) in vivo system in which orthodontic force was applied to Wistar rat molars, we found that mechanical *compression* that occurs during force application resulted in higher expression of RANK and RANKL proteins as detected by immunohistochemical staining of tooth sections with antibodies specific for these proteins. The increased expression RANK and RANKL led to increased osteclastogenesis, thus, resulting in resorption of the alveolar bone surrounding the compression side of the tooth socket. In contrast, mechanical *tension* resulted in an increase in expression of OPG, leading to inhibition of osteoclast proliferation and differentiation, resulting in bone deposition on the tension side of the tooth. This research, made possible by the support of the AAOF, has promoted better understanding of the molecular and cellular regulation of tooth movement. A better understanding of the molecular controls of tooth movement will undoubtedly lead to improved treatment modalities for orthodontic patients in the future.