AAO Foundation Award Final Report

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Award Type	Faculty Development Fellowship Award
Project Title	ROLE OF OSTEOBLASTIC HIF SIGNALING AS AN UPSTREAM FACTOR IN OSTEOCLAST MATURATION-ACTIVATION
Project Year	2008
Institution	University of Oklahoma
Summary/Abstract (250 word maximum)	**Background:** Tooth movement is a slow process and both patient and orthodontist desire a more expedient way to move the teeth to their final position. The molecular mechanisms underlying the process, however, have yet to be elucidated. It was the purpose of this project to highlight the role of compression-induced hypoxia on soluble factor release from osteoblasts and on the functional conversion of monocytes to osteoclasts. **Objective:** The objective of this project was to demonstrate the role played by HIF in promoting osteoclast development from circulating monocytes. **Material & Methods:** Human monocytes were co-cultured with/without osteoblasts and either subjected to 2.5% hypoxia or normoxic conditions and with/without anti HIF agents for 17 days. Supernatant was collected and levels of hypoxia inducible factor (HIF), vascular endothelial growth factor (VEGF) and RANKL were measured. OC development was measured using TRAP and osteologic discs. **Results:** We observed upregulation of HIF, VEGF and RANKL under hypoxia but not in normoxic conditions. These cytokines were not observed when anti-HIF agents were added. OC were observed in the hypoxic conditions only and when co-cultured with osteoblasts. OC development was correlated to VEGF and RANKL. **Conclusion:** HIF is an upstream factor in osteoclast development and possibly plays a critical role in osteoclast production during orthodontic compression of the PDL.
Were the original, specific aims of the proposal realized?	The project was designed to address two specific aims: **1. Do osteoblasts (OB) respond to hypoxia by induction of HIF signaling and production of osteoclast cytokines?** All cytokines under investigation were observed in hypoxic situations. **2. Does hypoxia result in elevated levels of remodeling OC?** Functional osteoclasts were observed in hypoxic conditions only. Functionality was confirmed via resorption assays.
Were the results published? If not, are there plans to publish? If not, why not?	Manuscript is under review. Based on the findings from this project, grant writing is in progress for funding to proceed to clinical studies.
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?	Results have been presented at several meetings to include the 1. University of Oklahoma Orthodontic Biennial meeting, Key West, FL; October 2009; 2. University of Michigan at Ann Arbor, July 2009. 3. Based on these findings, we are submitting a grant application due December 2009 and February 2010.