Principal Investigator	Margarita Zeichner-David
Co-Investigator	Hong Beom Moon Julia Reyna Vivial Maung Mohamed Panarpour
Secondary Investigators	
Award Type	
Project Title	Characterization Of Molecules Associated With Tooth Movement And/Or Root Resorption
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Institution	University of Southern California
Summary/Abstract	Although many clinical and histological studies have been carried out to elucidate the etiology and pathogenesis of external root resorption, the molecular events leading to this process during orthodontic tooth movement are still unknown. In this study we proposed to test the hypothesis that by comparing the expression of mRNAs in the periodontium subjected to orthodontic forces (experimentally determined to produce resorption) maintained for different time periods, and teeth were no forces were applied, we can identify the molecules involved in the sequence of events leading to root resorption. To test this hypothesis, experiments were designed using a rat animal model for root resorption and DNA microarrays technology. Wistar rats *(45-50)* days old were used. A continuous force of 9Ogr was applied to the left maxillary molars, and rats were sacrificed after 1, 2, 3, 4 and *5* days (previous studies have determined that by day *5* root resorption was quite noticeable). Total RNA obtained from left molars (experimental) and right molars (control) was converted into cDNA, labeled with P^{32} and hybridized to identical Rat 1.2 and 1.2 II microarrays (containing more than 2000 genes, Clontech, CA). Analysis of the arrays was done using the Atlaslmage 2.0 software from Clontech. Our results indicate that after 24 hours of the application of the force there is already a considerable increase in the expression of several different types of proteins ranging from transcription factors, signal transducer, growth factors, cytokines, proteases etc. Particularly noteworthy was a 2-3-fold increase in the heat shock protein 60-kda, beta-nerve growth factor, macrophage migration inhibitory factor and cathepsin K. Other major changes found between days 2-4 where in the reduction of expression of genes like the c-myc responsive gene, several transport carrier proteins and adhesion proteins while genes for several proteases were induced. Particularly interesting was the increase in stromelysin, cathepsin K and L and matrix metalloproteinase 13, thus confirming the important role of proteases in root resorption. We also found more than a two fold increase in the expression of Osteonectin, Bone Gla protein (BGP) and Dentin Sialophosphoprotein (DSPP) suggesting that the application of an orthodontic force induces the expression of

	secondary dentin. Although the significance of these findings still remains to be determined, our results suggest that the rat model together with the microarray technology provide a valuable means to identify differentially expressed genes resulting from the application of orthodontic forces.