AAO Foundation Award Final Report

Principal Investigator	Bhavna Shroff
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Secondary Investigators	
Award Type	Biomedical Research Award
Project Title	Osteoclasts Function During Tooth Eruption in the c-fos knockout Murine Model
Project Year	2002
Institution	University of Maryland – Transferred toVirginia Commonwealth University
Summary/Abstract (250 word maximum)	Tooth eruption is a complex and multifactorial process that is precisely timed during normal development. Deviations from the normal process of tooth eruption are challenging to treat orthodontically when they are generalized to the dentition. Delayed in the eruption of teeth can also prolonge treatment. The availability of transgenic animal models has provided a very powerful model to study several areas of normal development. The c-fos knock out mouse was described by Johnson et al. (1992), Wang et al. (1992) and Grigoriados et al. (1994) as an osteopetrotic mouse presenting altered hematopoiesis and a lack of tooth eruption. The purpose of this study was to evaluate to distribution of osteoclasts in the dental follicle of homozygous and heterozygous animals during the process of eruption. Mandibles were dissected from 2, 5, 9 and 11 days old homozygous and heterozygous animals and immediately fixed in 10% formalin. Specimens were embedded and paraffin sections were obtained for immunohistochemical staining. Monoclonal antibodies directed to tartrate resistant acid phosphatase (TRAP) were used to identify the enzyme activity in the cells of dental follicle and the surrounding bony crypt. The results of our study showed that there was a significant difference in the staining pattern between the heterozygous and homozygous animals at 2 days postnatal. In the heterozygous mice, positive staining for TRAP was observed in the bone surrounding the developing tooth, concentrated in specific cells and in the dental follicle. Cells within the alveolar bone also stained positive for TRAP. In the homozygous mice, no positive staining for TRAP was observed in the dental follicle or in the alveolar bone surrounding the developing tooth. Our results showed that no osteoclasts (or precursors cells) were present during the pre-eruptive phase of eruption in the homozygous mice whereas osteoclasts or their precursor cells were identified in the heterozygous animals. Our results support the hypothesis that the homozygous c-fos mouse presents with a severely decreased number of osteoclasts and that bone resorption is severely affected in these animals that develop osteopetrosis as part of their phenotype.
Were the original,	The first aim of the study was completed successfully. The second

specific aims of the proposal realized?	aim of the project was attempted but we were not successful at isolating and culturing osteoclasts because we could not obtain enough homozygous animals to harvest osteoclasts. The animals colony produced heterozygous and wild type animals primarily. Homozygous animals were very difficult to obtain in sufficient numbers.
Were the results published? If not, are there plans to publish? If not, why not?	The results were published as follows: B, Gaffari A, Grossman K, Lindauer SJ: Osteoclast distribution in the c-fos knock out mouse during tooth eruption. Biological mechanisms of Tooth Eruption, Resorption, and Movement Ed. Davidovitch Z., Mah J., and Suthanarak S, p 11-17, Harvard Society for the Advancement of Orthodontics, Boston, MA, 2006.
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?	Grossman K, Shroff B, Chellaih M, Lindauer SJ: Osteoclasts Distribution during Eruption in the c-fos knock out Mouse. Abstract to the 82nd Session of the IADR/AADR, *J Dent Res*, #3905, 83, Special issue A, 2004. Shroff B, Ghaffari A, Grossman K, Lindauer, SJ: Osteoclasts Function and metalloproteinases (MMP) Distribution in the c-fos knock out Mouse during Tooth Eruption. Abstract to the 8th Conference on biological mechanisms of tooth eruption, resorption and movement, 2005. Ghaffari A, Shroff B, Grossman K, Massey D, Lindauer SJ: Colocalization of Actin and TRAP during Eruption in the c-fos knock out Mouse: Abstract to the 84th Session of the AADR, *J Dent Res*, #754, 85: A. 2006