

AAO Foundation Award Final Report

Principal Investigator	Dr. Bhavna Shroff
Co-Investigator	John Sauk Elaine Romberg
Secondary Investigators	
Award Type	Biomedical Research Award
Project Title	Follicular Apoptosis and Collagenase Expression during Eruption
Project Year	2000
Institution	University of Maryland
Summary/Abstract (250 word maximum)	<p>Tooth eruption is a multifactorial process that investigators have been examining for over a century. Osteopetrotic animals represent an excellent model for studying this process. These animals demonstrate decreased bone resorption, and delayed or absent tooth eruption, thus providing a model for investigating the relationship between these two events (Marks and Walker, 1976). Recently an Osteopetrotic mouse with a known null mutation in the c-fos gene has been developed (Johnson et al., 1992). This animal is a promising tool in the study of tooth eruption not only because it is a variant of osteopetrosis, but c-fos is also known to participate in several events implicated in tooth eruption including apoptosis, expression of matrix metalloproteinases, and the epidermal growth factor pathway. The purpose of this investigation was to document the effect of a null mutation in the c-fos gene on the chronology of tooth development, as well as the expression of matrix metalloproteinases (MMPs), epidermal growth factor (EGF), and epidermal growth factor receptor (EGFR). Mandibles were obtained from 21, 24, 28 and 30 day old neonate heterozygous and homozygous mice. 70µm thick sections were stained with hematoxylin and eosin, or reacted against antibodies directed against collagenase (MMP-1), stromelysin (MMP-3), gelatinase (MMP-9-1; MMP-9-2), c-fos epidermal growth factor (EGF), and epidermal growth factor receptor (EGF-R). The results indicated that tooth development in the homozygous mutants was slightly delayed compared to their heterozygous littermates. They also showed that expression of MMP-9 and MMP-1 are effected by lack of c-fos, while MMP-3, EGF, and EGF-R are relatively unaffected.</p> <p>Several important conclusions may be made from this study:</p> <ol style="list-style-type: none"> 1. Development of mandibular first molars was slightly delayed

	<p>in homozygous animals when compared to their heterozygous littermates. Overall tooth morphology was normal in both genotypes.</p> <ol style="list-style-type: none"> 2. Expression of MMP-9 in the dental follicle and surrounding structures suggest that monocyte recruitment proceed in a normal fashion in the osteoclast deficient homozygous c-fos knock-out mice. Failure of local activation of osteoclasts is therefore presumably responsible for lack of tooth eruption. 3. Expression of MMP-3, EGF, and EGFR were similar in the homozygous mutants compared to the heterozygous mutants. This suggested that these factors are relatively unaffected by the absence of c-fos. 4. An altered pattern of expression of MMP-1 reflected the strong association between MMP-1 and c-fos.
<p>Were the original, specific aims of the proposal realized?</p>	<p>The original specific aims of the proposed projects were completed.</p>
<p>Were the results published? If not, are there plans to publish? If not, why not?</p>	<p>The results were published as follows:</p> <p>Shroff B, Siegel SM: molecular Basis for Tooth Eruption and its Clinical Implications in Orthodontic Tooth Movement: <i>Seminars in Orthodontics</i>, 2000, vol6, no3, 155-172.</p> <p>Shroff B, Jaffe J: The c-fos knock out Mouse: A New Murine Model for Tooth Eruption. <i>Biological Mechanisms of Tooth Movement and Craniofacial Adaption</i> Ed. Davidovitch. Z and Mah J, p 275-284, Harvard Society for the Advancement of Orthodontics , Boston, MA, 2004.</p>
<p>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?</p>	<p>The results were presented at several AADR/IADR and abstracts are published as listed:</p> <p>Khurana P, Norris K, Hebert C, Shroff B: Follicular Metalloproteinase Expression during Tooth Eruption: Abstract of the 78th Session of the IADR, <i>J Dent Res</i>, #2617, <u>79</u>,471, 2000.</p> <p>Jaffe JP, Shroff B, Bryant N. DiLorenzo C, Subliborski B: Characteristics of Tooth Development in a c-fos knock out Murine Model. Abstract of the 31st Session of AADR/80th Session of IADR, <i>J Dent Res</i>, #3778,<u>81</u>, 463, 2002.</p> <p>Bryant N, Dilorenzo C, hayes n, Ross D, Jaffe JP, Suliborski B, Shroff B: Follicular Apoptosis in a c-fos knock out Murine Model during Tooth Eruption. Abstract of the 31st Session of AADR/80th Session of IADR, <i>J Dent Res</i>, #3779, <u>81</u>, 463, 2002.</p> <p>Jaffe, J, DiLorenzo C, Shroff B: Distributon of Metalloproteinases-9 during Tooth Eruption in the c-fos Knock out Murine model. Abstract</p>

	<p>to the 32nd Session of the AADR, <i>J Dent Res</i>, #410, 82 Special issue A, 2003.</p> <p>Shroff B, DiLorenzo C, Jaffe J: Distribution of Metalloproteinases-1 and -3 during Tooth Eruption in the c-fos Knock out Murine Model. Abstract to the 32nd Session of the AADR, <i>J Dent Res</i>, #411, 82 Special Issue A, 2003.</p> <p>Shroff B, Jaffe J: The c-fos knock out Mouse: A new Murine Model for Tooth Eruption. Poster presentation at the 4th International Conference on Biological Mechanisms of Tooth Movement and Craniofacial Adaptation, 2003.</p>
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