AAO Foundation Award Final Report

Principal Investigator	Bhavna Shroff
Co-Investigator	
Secondary Investigators	John J. Sauk Elaine R. Romberg
Award Type	Biomedical Research
Project Title	**Follicular Apoptosis and Collagenase Expression during Eruption**
Project Year	1997
Institution	University of Maryland
Summary/Abstract (250 word maximum)	Tooth eruption is a complex, multifactorial growth process which is precisely timed and sequenced during normal development. Experimental evidence strongly supports that growth factors such as Epidermal Growth Factor (EGF) have a key role as regulators of tooth eruption (Cohen, 1965; Thesleff et al., 1987; Partanen, 1990) and potential initiators for apoptosis in other organ systems (Guenette and Tenniswood, 1994). We hypothesize that growth factors such as EGF are involved in the initiation of apoptosis and the differential regulation of collagenase gene products in the coronal aspect of the dental follicle and the adjacent enamel organ during tooth eruption. We also hypothesize that the initiation of apoptosis in cells of the coronal dental follicle and cells of the enamel organ is triggered by an increase in the levels of EGF. This induction of apoptosis in the dental follicle will be accompanied by an increase in the expression of proteins such as collagenases that are involved in the latter stages of apoptosis. This includes a significant increase of collagenase gene expression in cells of the coronal dental follicle and enamel organ at the onset of tooth eruption. Furthermore, we hypothesize that the EGF induced initiation of apoptosis and subsequent up regulation of the expression of collagenase gene product are mediated by the transcriptional induction of nuclear proto-oncogenes such as c-fos which may act as a "third messenger" (Kerr et al., 1988) and will directly alter transcription of collagenase and genes involved in apoptosis. The goals of this project are to establish in vivo the spatial and temporal expressions of endogenous EGF, EGF-R. Also, this study proposed to establish *in vivo* the presence of apoptosis in cells of the coronal dental follicle and enamel organ using *in situ* tunnel staining techniques and to characterize these cells for the presence of

	apoptosis markers (bcl-2, ICE, P53, c-myc, FAS/APO) in the CD-1mouse. The results of our study showed that there is a temporal and spatial distribution of EGF and EGF-r in the dental follicle. Our results also demonstrated that apoptosis started in later days of development in the coronal aspect of dental follicle. Our results also demonstrated that proapoptotic and antipoptotic genes were present in the dental follicle and in the coronal epithelium during the follicular growth stage and the pre-emergent eruptive state of tooth eruption. Our findings support that apoptosis may be an important physiological process involved in the formation of the eruption canal.
Were the original, specific aims of the proposal realized?	The original specific aims of the proposal were achieved.
Were the results published? If not, are there plans to publish? If not, why not?	The results of the study were published as follows: Shroff B, Rothman JR, Norris K, Hebert C: Follicular Apoptosis during Tooth Eruption: Second International Conference on Biological Mechanisms of Tooth Eruption, Resorption, Replacements by Implants, 1997, Ed. Zeev Davidovitch and James Maah 71-29. Rothman JR, Shroff B, Norris K, Herbert C, Sumbilla JC, Xu B: Apoptosis in the dental follicle during tooth eruption. Abstract of the 75th Session IADR, *J Dent Res*, #2808,76, 364, 1997. Wilson TG, Norris K, Shroff B: Immunohistichemical distribution of EGF and EGF-R in the dental follicle. Abstract of the 75th IADR, J *Dent Res*, #2809, 76, 365, 1997.
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?	The results were presented at: Apoptosis in the dental follicle during tooth eruption. J.R. Rothman, B. Shroff, K. Norris, C. Herbert, J.C. Sumbilla, B. Xu: 75th General Session of the IADR, 1997. Immunohistochemical distribution of EGF and EGF-R in the dental follicle. T.G. Wilson, K. Norris, B. Shroff: 75th Session of the IADR, 1997