Biomedical Research Award

Dr. Rishma Shah, University of North Carolina at Chapel Hill

Biography and Synopsis of Project

Biography

Dr. Rishma Shah is a tenured Associate Professor at the University of North Carolina, Adams School of Dentistry. In addition to working in the Orthodontic Unit, she is a member of the UNC Craniofacial Center team. She completed her BDS with honors (DDS equivalent) at the United Medical and Dental Schools of Guy's and St. Thomas' Hospitals, London. Dr. Shah received her MS in Orthodontics with distinction and her PhD in Biomaterials and Tissue Engineering from the University of London, England. She has also completed Fellowships in Dental Surgery and in Orthodontics at the Royal College of Surgeons. She is experienced in the management of complex craniofacial and interdisciplinary cases. Her research complements her clinical interests.

Project Synopsis: *"Profiling of MicroRNAs and Inflammatory Cytokines in Patients with External Cervical Root Resorption"*

External cervical root resorption (ECRR) is a destructive condition associated with loss of cementum and dentin due to odontoclastic action. The etiology is unclear, although orthodontic treatment has been frequently implicated in addition to trauma associated with surgical procedures and periodontal therapy. Treatment often involves surgical exposure and repair of the lesion in addition to possible root canal treatment. In severe cases, tooth loss occurs potentially leading to devastating effects on oral function, aesthetics, and self-esteem. ECRR is difficult to prevent and treat due to limited knowledge regarding its pathophysiology.

Recently in dentistry, there has been interest in evaluating microRNA (miRNA) activity and association with various disease states. miRNAs are non-coding RNA molecules involved in regulation of various cellular functions through their ability to modify gene expression. Altered miRNA activity has been associated with oral diseases including cancer and periodontitis. miRNA therapeutics, with therapeutic molecules being delivered within optimal delivery systems, is fast becoming a reality for treatment of cancer and other diseases. In a pilot study, we investigated miRNA expression in ECRR lesions, and found downregulation of miR-20a-5p, miR-210–3p, and miR-99a-4p, and upregulation of miR-122–5p. Using bioinformatics analysis, the differentially expressed miRNAs were found to have human mRNA targets involved in inflammatory or immune responses.

There is paucity of research into miRNAs in ECRR, limiting both our understanding of the disease as well as its management and development of targeted therapeutics. Therefore, our proposed study objective is to undertake a larger clinical study of miRNA expression in ECRR lesions, and supplement this with concurrent sampling of gingival crevicular fluid (GCF) from affected and non-affected sites to determine the presence of miRNAs, cytokines and inflammatory mediators[16-17]. We hypothesize there are differences in the expression of miRNAs and inflammatory cytokines between ECRR-affected teeth and control teeth. The study outcomes will provide valuable information to support our long-term objectives to develop diagnostic and/or prognostic tests and novel miRNA-targeted therapies for ECRR.

How Orthodontic Education Will Benefit from the Award

Our proposed novel study will provide valuable information on miRNA and inflammatory cytokine expression in a poorly studied disease, ECRR, that is often linked to orthodontic treatment. In addition, the inflammatory

pathways in this disease will be eluded providing much needed evidence as to the pathophysiology and possible ways to diagnose and treat ECRR.

Why the Foundation is Important to the Project

The Foundation is an important advocate of the project and its long-term implications for the orthodontic patient. The funding provided by the Foundation is essential for the generation of preliminary data to support future funding applications. Furthermore, the new knowledge learned from this project has the potential to support novel, less invasive and cost-effective therapies to manage ECRR.

How Foundation Funding Might Help Advance Your Career

I am grateful to the Foundation for the award of this funding. The generation of preliminary data from this project funded by the Foundation will support future funding applications to the NIH/NIDCR. As a tenured Associate Professor, the award of research funding from institutions, such as the NIH/NIDCR, will be important for advancing my career as a clinician-scientist-educator in the field of orthodontics.