Dr. Eugene Seidner Student Scholarship Program

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Low-Power Laser-Generated ROS Species Can Activate Latent TGF-β1 and Direct Dental Stem Cell Differentiation

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Introduction
The use of low-power lasers in clinical dentistry is becoming increasingly popular, which calls for a better understanding of the molecular mechanism(s) underlying photobiomodulation. We have previously reported on one of the potential mechanisms, activation of a latent growth factor complex, Transforming Growth Factor-β (TGF-β), as a key mediator in oral wound healing.

Objectives
The purpose of this study was to investigate the precise photochemical and photobiological interactions of low-power lasers and TGF-β activation, and to investigate the potential utility of laser treatment in promoting dental stem cell differentiation to a mineralized odontogenic phenotype.

Method
An 810-nm GaAlAs diode laser was used in all experiments, with various fluorescent dyes to assess generation of specific reactive oxygen species (ROS). The ability of the laser-generated ROS to activate Latent TGF-β1 (LTGFβ-1) was confirmed using an enzyme-linked immunosorbent assay (ELISA) and reporter assay. We also assessed structural and biochemical changes to the latent complex during the activation process. To assess odontogenic differentiation, dental stem cells were isolated from extracted teeth specimens, cultured in a poly(lactide-co-glycolide) 3-D scaffold system, and irradiated with lasers. Differentiation to specific odontogenic phenotype was assessed by using biomineralization assays, molecular assays, and elemental analysis for mineralization.

Results
A robust increase in various ROS species was observed with increasing lasers doses (0.3 to 30 J/cm^2). These ROS species were capable of activating LTGFβ-1 and this process involved oxidation of a specific amino acid residue, resulting in a conformational change in the complex that resulted in TGF-β activation. Further, laser irradiation resulted in differentiation of dental stem cells into a mineralized odontogenic phenotype as assessed by activation of intracellular signaling, extracellular matrix production, and calcium deposition. The causal relationship between ROS activation and odontogenesis was confirmed by using mutant TGF-β and inhibitors of ROS.

Conclusions

We demonstrated the ability of low-power lasers to direct differentiation of dental stem cells, and have elucidated the precise molecular mechanism linking ROS generation by lasers and LTGF-β1 activation. Ongoing studies in animal models will further validate the utility of the low-power laser as an innovative, noninvasive clinical tool in dental applications.

This presentation discusses investigational devices that have not yet received U.S. FDA approval or clearance for the specified clinical indications, or describes off-label uses.

Biography: *Dr. Praveen Arany is trained as a dentist and oral pathologist. He is presently completing a joint PhD residency program at Harvard University and his research is focused on molecular mechanisms of laser photobiomodulation. His main interests are in understanding and applying the regulatory cues that regulate regeneration versus tumor formation.*

Disclosure: *Dr. Arany has no has no commercial or financial interest relative to this presentation*

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