

**Stony Brook University
The Graduate School**

Doctoral Defense Announcement

Abstract

The Impact of the Diabetic State on Gingival Tissues: The Role of Tetracyclines in
Disease Management

By

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Chronic hyperglycemia is associated with the development of numerous long-term diabetic complications, some directly affecting oral health, such as delayed wound healing and periodontitis. These conditions, in part, are due to the heightened immuno-inflammatory response reported in diabetics, driven primarily by the development of advanced glycation end-products (AGEs). This dissertation investigates the contribution of resident fibroblasts, exposed to glycated matrices, to inflammatory processes *in vitro*. Elevated levels of pro-inflammatory mediators have been detected in the gingival crevicular fluid (GCF) of type 1 diabetics with periodontitis. A randomized controlled clinical trial was designed to determine the impact of periodontal therapy on local inflammatory processes *in vivo*.

In vitro experiments demonstrated that dermal and gingival fibroblasts cultured on AGE modified collagen secrete increased amounts of IL-6, IL-8 and MCP-1 compared to cells cultured on unmodified collagen. Thus, resident fibroblasts may significantly contribute to periodontal destruction and delayed wound healing by recruiting and priming inflammatory cells capable of secreting additional pro-inflammatory cytokines and proteinases into the tissues of diabetic individuals.

The effect of periodontal therapy on local biochemical markers of inflammation in diabetics was determined in a 15-month, double-blind, placebo-controlled clinical study. 18 subjects received scaling and root planing (SRP) and were randomized to either a sub-antimicrobial dose of doxycycline (SDD) or placebo for 9-months. Periodontal measurements and GCF were obtained at 3-month intervals. GCF samples collected at baseline, 3- and 9-months were analyzed for collagenase activity and inflammatory cytokines. Both groups experienced a significant improvement in clinical parameters over time. Patients treated with SDD and SRP had a statistically significant decrease in collagenase activity, IL-1 β , IL-8 and VEGF as early as 3 months and maintained at 9 months for collagenase, IL-1 β and VEGF. Reductions in these markers obtained with SRP alone at 3 months rebounded to baseline levels or above at 9 months. The results demonstrated that a 9-month regimen of SRP and SDD significantly improved clinical parameters and biochemical markers in type I diabetics with periodontitis. The sustained reductions in pro-inflammatory mediators in the SDD group may help to make clinical responses more predictable in diabetics.

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