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Activation of the Urokinase Plasminogen Activator/ Urokinase Plasminogen Activator Receptor System in Periodontitis: A Case–Control Study

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Introduction: The plasminogen activating (PA) system has a multitude of functions such as wound healing, proteolytic activity, collagen degradation and cell growth, and the role of the urokinase plasminogen activator/urokinase plasminogen activator receptor (uPA/uPAR) system has been studied in many disease states. The aim of this study was to investigate salivary concentrations of uPA, uPAR and uPA activity in patients with periodontitis to identify biomarkers and novel pathogenic relationships.

Methods: Saliva samples were obtained from 169 participants, comprising patients with periodontitis ($n = 103$) and periodontally healthy volunteers ($n = 66$) and analysed for uPA and uPAR with a multiplex protein assay using proximity extension analysis in a subset of samples, followed by validation with ELISA. The protease activity of salivary uPA was quantified using a fluorometric assay.

Results: Patients with periodontitis had a 4.0-fold higher ($p < 0.001$) salivary uPA and a 2.5-fold higher ($p < 0.001$) salivary uPAR concentration in comparison to periodontally healthy participants. The salivary uPA activity (median [IQR]) from patients with periodontitis (123.21 [188.29] U/mL) was 1.6-fold higher ($p < 0.01$) than the salivary uPA activity from periodontally healthy participants (76.83 [98.09] U/mL). Levels of uPA and uPAR were strongly correlated with periodontal indices, whereas only weak correlations were found with BMI and age.

Conclusion: Activation of uPA/uPAR likely plays a role in the pathogenesis of periodontal diseases. uPA/uPAR may have potential utility as candidate salivary biomarkers in periodontal pathogenesis.