PHILIPS

Effects of cigarette smoke extract on cell signalling via redox-sensitive transcription factors: The bacterial-oral epithelial-PMNL axis

Fa-ming Chen

Cigarette smoking is a major risk factor for periodontitis, yet mechanisms underpinning the effects of smoking on periodontal inflammation are poorly understood. Studies have found that GCF levels of glutathione (GSH) are 1000-fold those of serum in periodontal health and significantly reduced in periodontitis. Given the pivotal role for GSH in pro-inflammatory gene regulation via NF-κB, and the reported impact of smoking on GSH levels, it is surprising that there is minimal data on the effects of CSE on oral epithelial cell gene transcription and cytokine/chemokine production. On the other hand, the direct effects of cigarette smoking on polymorphonuclear leukocyte (PMNL) reactive oxygen species (ROS) production have also received limited attention. To date, there have been no studies on the effect of smoking on PMNL ROS responses to periodontal bacteria. We hypothesise that smoking (cigarette smoke extract, CSE) affects PMNL function indirectly by upregulating NFκB-stimulated pro-inflammatory gene/protein expression in oral epithelial cells and directly by 1] increasing baseline extracellular PMNL ROS release and/or 2] changing the ROS-response of PMNL to periodontal bacteria. Therefore, this application proposes a series of in-vitro proof of principle studies to explore the effects of aqueous CSE on PMNLs using established methods in the host's laboratories. We intend to determine the effect of CSE on: a] NFκB activation and expression (mRNA and protein) of pro-inflammatory cytokines/chemokines in oral epithelial cells; b] total and extracellular PMNL ROS generation with and without priming/stimulation with cytokines or periodontal bacteria and c] PMNL gene expression of components the NADPH oxidase complex.