Modulation of gene expression in human aortic smooth muscle cells by Porphyromonas gingivalis - a possible association between periodontitis and atherosclerosis

av

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Akademisk avhandling

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Abstract


*Porphyromonas gingivalis* is a gram-negative, rod-shaped, and anaerobic bacterium that is involved in the pathogenesis of periodontitis. *P. gingivalis* produces a variety of virulence factors including gingipains and fimbriae. These virulence factors not only have a detrimental effect on bacteria adhesion, invasion, and colonization but also affect the host cell inflammatory response. *P. gingivalis* is also considered to play a role in the development of other diseases, such as atherosclerosis and cancer. Smooth muscle cells are the main components of vascular walls and regulate the width of the blood vessels in the body. To understand the mechanisms underlying the association between periodontitis and atherosclerosis we have, in the studies involved in this thesis, treated human aortic smooth muscle cells (AoSMCs) with wild type, gingipain mutant, and fimbriae mutant strains of *P. gingivalis*. Using a human whole genome microarray, quantitative real time PCR, Western blotting, ELISA, confocal microscopy, and cellular function experiments, we found that *P. gingivalis* invades AoSMCs, regulates the expression of thousands of genes, and increases cell proliferation by activating the TGFbeta/Notch signaling pathway. The results also show that *P. gingivalis* increases the ratio of angiopoietin 2 (Angpt2) / angiopoietin 1 (Angpt1) in AoSMCs, which determines the regulatory role of angiopoietins in angiogenesis and their involvement in the development of atherosclerosis. Moreover, we also found that *P. gingivalis* can induce interleukin-1β (IL-1β) production in AoSMCs, while inhibiting the expression of NLRP3 inflammasome components. Gingipains, especially arginine gingipain, play a fundamental role in *P. gingivalis*-induced modification of AoSMCs. These findings further support an association between periodontitis and cardiovascular disease.

*Keywords*: Microarray, Angiopoietin, Smooth muscle cells, TNF, Periodontitis, Atherosclerosis, Porphyromonas gingivalis, Cancer, Inflammasome

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