



Monocyte and Neutrophil Inflammatory Responses to the Periodontopathogen *Porphyromonas gingivalis*

av

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Abstract

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Periodontitis is one of the most common adult infections. During bacteremia in healthy individuals or patients with chronic periodontitis, a number of oral bacteria such as *Porphyromonas gingivalis* encounter inflammatory cells in the blood eg. platelets, neutrophils and monocytes. Although several studies have suggested an association between periodontitis and cardiovascular diseases, the infection and inflammatory mechanisms are poorly understood. Hence, the aim of this thesis was to elucidate the mechanisms that are involved in *P. gingivalis* interaction with blood leukocytes, in order to further understand the molecular pathogenesis that renders periodontitis as a risk factor for several systemic conditions. We have demonstrated that *P. gingivalis* induces ROS production in neutrophils, THP1 cells and in whole blood, through activation of pattern recognition receptors, such as toll-like receptors, nuclear oligomerizing domains and protease-activated receptors. Besides, we have also shown that monocytes secrete IL-1 β and CXCL8 in response to *P. gingivalis*. Both these cytokines prime neutrophils, endothelial cells and other vascular cells in an autocrine and paracrine manner. *P. gingivalis* has a plethora of virulence factors of which gingipains are very unique. In addition to activating inflammatory signalling pathways in cells, gingipains also regulate CXCL8 and IL-1 β , thereby curtailing the host defence strategies. We demonstrated that oxidized LDL, but not native LDL, induces IL-1 β release and CD36 expression on THP1 cells. Furthermore, LDL mildly modifies *P. gingivalis*-induced inflammatory responses as well as CD36 expression in THP1 cells. We also observed that *P. gingivalis* is eliminated mainly by phagocytosis in neutrophils. In summary, these studies clarify the mechanisms of interaction between *P. gingivalis* and leukocytes, which can increase the understanding of the pathogenesis of periodontitis and associated systemic disorders.

Keywords: Monocytes, Neutrophils, *Porphyromonas gingivalis*, Gingipains

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