Extracellular Vesicles From the Saliva of Periodontal Patients Modulates Macrophage Function

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Periodontal disease is a chronic inflammatory condition of the gingiva, induced by accumulation of bacterial plaque leading to the destruction of alveolar bone and tooth loss. Clearance of bacterial plaque requires a pro-inflammatory response; however if this process goes unchecked, tissue damage may occur. Macrophages are responsible for the innate immune system's response to infection and tissue healing/repair. Important macrophage functions include cytokine production and phagocytosis. Macrophages regulate cytokine production by utilizing transcription factors. Nrf2 is a transcription factor which blocks pro-inflammatory cytokine production and promotes anti-inflammatory cytokine production. Extracellular vesicles (EVs) are small heterogeneous membrane-enclosed structures that are released by cells and allow for cell-to-cell communication. We hypothesized that EVs are drivers of immune dysfunction in periodontal disease. This study tested how EVs from the saliva of patients with gingivitis affect macrophage phenotype through evaluation of cytokines, macrophage phagocytosis function and Nrf2 translocation to the nucleus. The phagocytosis assay demonstrated that EVs suppress macrophage function by impairing bacterial phagocytosis. The Luminex assay measured cytokine expression and showed that EVs promote a pro-inflammatory cytokine milieu early and late after exposure. The ELISA assay indicated EVs halt nuclear translocation of Nrf2 in macrophages, preventing inflammation suppression. Overall, these findings indicate that EVs from gingivitis patients promote inflammation in the oral cavity. EVs limit phagocytosis and Nrf2 translocation, leading to increased pro-inflammatory cytokine release and the prolongation of the inflammatory response.

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