Effect on Periodontitis through Modulating Macrophages: Ameliorate Alveolar Bone Loss and Improve Anti-Inflammatory Activity

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Outline

I. Introduction

II. Human β-defensin 3 inhibits periodontitis development by suppressing inflammatory responses in macrophages.

III. Anti-inflammatory effect of IL-1ra-loaded dextran/PLGA microspheres on *Porphyromonas gingivalis* lipopolysaccharide-stimulated macrophages *in vitro* and *in vivo* in a rat model of periodontitis.

IV. Conclusion

Abstract

Periodontitis is an infectious disease caused by *Porphyromonas gingivalis.* It will extend deep into periodontal tissues and cause the destruction of connective tissue and the loss of alveolar bone. Macrophages, as the innate immune system, play an important role in the pathogenesis of periodontitis. It can be polarized into two phenotypes depending on different microenvironment stimuli: the classical inflammatory M1 type and anti-inflammatory M2 type. Human β-defensins 3 (hBD3s) are cationic peptides with immunomodulatory effects. *In vitro*, hBD3 significantly suppressed TNF-α and IL-6 secretion in RAW 264.7 cells stimulated by the LPS of *Porphyromonas gingivalis* (P.g). Furthermore, hBD3 attenuated the polarization of RAW 264.7 cells into the M1 phenotype, with reduced translocation of nuclear factor-κB (NF-κB). In the mouse periodontitis model, hBD3 inhibited the levels of TNF-α, IL-6, and matrix metalloprotease-9 (MMP-9) in gingival tissues. The interleukin-1 receptor antagonist (IL-1ra) is a glycoprotein that binds to the IL-1 receptor on the cell surface to competitively inhibit the biological activity of IL-1α and IL-1β to modulate inflammatory. Using S/O/W method to prepare dextran/PLGA microspheres loaded IL-1ra to control drug release and prevent degradation immediately. The average particle size of IL-1ra microspheres was 12.76 ± 4.89 μm. Then, the data showed that IL-1ra microspheres decreased pro-inflammatory cytokines both in LPS stimulated RAW264.7 cells and periodontitis rats. Moreover, after IL-ra microspheres treatment significantly alleviates alveolar bone loss. In summary, targeting to switch macrophages to anti-inflammatory phenotype has potential to be a new strategy to treat periodontitis.

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