Original Scientific Article

Human periodontal ligament fibroblasts synthesize C-reactive protein and Th-related cytokines in response to interleukin (IL)-6 trans-signalling

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Aim

To characterize the potential of human periodontal ligament fibroblasts (HPLF) to synthesize CRP and Th-related cytokines in response to IL-6 in periodontal health and apical inflammation.

Methodology

Primary HPLF stimulated with IL-6, soluble(s) IL-6 receptor (R) and controls were assayed for CRP, Th1, Th2, Th17 and Treg-related cytokines by quantitative real-time PCR and ELISA, respectively. IL-6R mRNA expression and its soluble protein levels were screened in HPLF cultures, and *ex vivo* samples of healthy periodontal ligaments (n = 5) and apical lesions (n = 13). Data were analysed with ANOVA or unpaired t-test.

Results

0.5 ng mL^{-1} IL-6 plus 1 ng mL^{-1} of its soluble receptor (sIL-6R) for 24 h was effective in inducing CRP production. IL-6 alone had a mild dose-dependent effect; co-stimulation with sIL-6R significantly enhanced this effect, whereas it was completely abolished by the addition of IL-6R blocking antibody ($P < 0.05$). Similarly, higher mRNA expression and protein levels of Th1, Th17 and partially Treg-related cytokines were found for IL-6 combined with its soluble receptor versus the nonstimulated group and IL-6R antibody ($P < 0.05$). IL-6R mRNA expression was slightly induced by IL-6 compared to THP-1 cells, but sILR-6 protein could not be detected in HPLF. High sIL-6R levels were detected in apical lesions and were immunolocalized to mononuclear inflammatory cells and proliferating epithelium.

Conclusion

IL-6 trans-signalling induced Th1 and Th17-related cytokines and represents an extra-hepatic mechanism for PCR synthesis in human periodontal ligament fibroblasts, contributing to explain the bone-destructive phenotype of apical lesions and eventually its systemic complications.