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IL-1β stimulates urokinase-type plasminogen activator expression and secretion in human dental pulp cells

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ABSTRACT

Plasminogen activator (PA) is the enzyme that converts plasminogen to its active form, plasmin, which is involved in various physiological and pathological phenomena. The conversion is catalyzed by two types of PA, urokinase-type PA (uPA) and tissue-type PA (tPA). We investigated the effect of the inflammatory cytokine interleukin-1β (IL-1β) on PA secretion in human dental pulp cells. When the cells were stimulated by IL-1β, PA activity in the medium was clearly increased in a time- and dose-dependent manner. This PA activity in the medium was reduced after immunoprecipitation with anti-uPA antibody, and uPA protein was detected in the immunoprecipitated fraction by Western blotting. However, no such effect was observed with anti-tPA antibody. In the IL-1β-stimulated cells, expression of uPA mRNA was enhanced whereas expression of tPA mRNA was less. The IL-1β-stimulated uPA mRNA expression and PA activities in the cell lysate and medium were reduced by the tyrosine kinase inhibitors herbimycin A and genistein, and by the NFκB inhibitor pyrolidinedithiocarbamate, and were augmented by the tyrosine phosphatase inhibitor sodium orthovanadate. These observations suggest that IL-1β stimulates uPA production via activation of NFκB and tyrosine phosphorylation, and also secretion of the enzyme, and that the uPA/plasmin system appears to be involved in inflammation in human

dental pulp.

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