II-7. The effect of lipopolysaccharides of *A. actinomycetemcomitans* on MMP-8 release through CD14, TLRs, cytosol inhibitors and NF-κB inhibitors

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Background

MMP-8 is a cytosolic protein with collagenolytic action in polymorphonuclear leukocytes and its level increases in some inflammatory diseases, including periodontal diseases, rheumatoid arthritis, and ulcerative colitis. Recently, we found that the lipopolysaccharide of Actinomyces actinomycetemcomitans(A-LPS) induced MMP-8 release from human neutrophils. P-LPS, a major virulence factor of periodontal pathogens, is known to induce the production and release of inflammatory cytokines through CD14, Toll-like receptor(TLR)and nuclear factor κB(NF-κB). In the present study, we investigated whether MMP-8 release by P-LPS is induced via the CD14-TLR-NF-κB pathway and the cellular mechanism of MMP-8 release in human neutrophils.

Methods

Human neutrophils were isolated from the peripheral blood of healthy donors and pre-incubated in medium containing against CD14, TLR2, TLR4 and several inhibitors of microtubules and microfilaments, and NF-κB inhibitor, TPCK and then incubated with P-LPS. The amount of MMP-8 release in culture medium was determined using ELISA

Results

P-LPS increased MMP-8 release from neutrophils and its induction was inhibited by anti-CD14, but not by anti-TLR2 antibodies anti-TLR4 antibodies. NF-κB inhibitor suppressed P-LPS-induced NF-κB binding activity and MMP-8 release. The inhibitor of microfilament polymerization significantly decreased P-LPS-induced MMP-8 release, but the inhibitors of microtubule did not.

Conclusion

These results suggest that MMP-8 release is induced by P-LPS via the CD14-NF-κB signal pathway in human neutrophils and may be dependent on microfilament systems