Induction of cyclooxygenase-2 protein by lipoteichoic acid derived from Staphylococcus aureus in human pulmonary epithelial cells: Involvement of a nuclear factor-kB-dependent pathway.

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Abstract

This study investigated the role of protein kinase C (PKC) and transcription factor nuclear factor-κB (NF-κB) in cyclooxygenase-2 (COX-2) expression caused by lipoteichoic acid (LTA), a cell wall component of the gram-positive bacterium Staphylococcus aureus, in human pulmonary epithelial cell line (A549).

LTA caused dose- and time-dependent increases in COX-2 expression and COX activity, and a dose-dependent increase in PGE2 release in A549 cells. The LTA-induced increases in COX-2 expression and COX activity were markedly inhibited by dexamethasone, actinomycin D or cyclohexamide, but not by polymyxin B, which binds and inactivates endotoxin.

The phosphatidylcholine-phospholipase C (PC-PLC) inhibitor (D-609) and the phosphatidate phosphohydrolase inhibitor (propranolol) reduced the LTA-induced increases in COX-2 expression and COX activity, while phosphatidylinositol-phospholipase C inhibitor (U-73122) had no effect. The PKC inhibitors (Go 6976, Ro 31-8220 and GF 109203X) and NF-κB inhibitor, pyrrolidine dithiocarbamate (PDTC), also attenuated the LTA-induced increases in COX-2 expression and COX activity.

Treatment of A549 cells with LTA caused an increase in PKC activity in the plasma membrane; this stimulatory effect was inhibited by D-609, propranolol, or Go 6976, but not by U-73122.

Exposure of A549 cells to LTA caused a translocation of p65 NF-κB from the cytosol to the nucleus and a degradation of IκB-α in the cytosol. Treatment of A549 cells with LTA caused NF-κB activation by detecting the formation of NF-κB-specific DNA-protein complex in the nucleus; this effect was inhibited by dexamethasone, D-609, propranolol, Go 6976, Ro 31-8220, or PDTC.

These results suggest that LTA might activate PC-PLC and phosphatidylcholine-phospholipase D to induce PKC activation, which in turn

initiates NF-κB activation, and finally induces COX-2 expression and PGE2 release in human pulmonary epithelial cell line.