

# **Lipoteichoic Acid-Induced Cyclooxygenase-2 Expression Requires Activations of p44/42 and p38 Mitogen-Activated Protein Kinase Signal Pathways.**

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## **Abstract**

This study investigated the role of p44/42 and p38 mitogen-activated protein kinase (MAPK) in cyclooxygenase-2 expression caused by lipoteichoic acid in human pulmonary epithelial cell line (A549). Lipoteichoic acid-induced increases in cyclooxygenase activity and cyclooxygenase-2 expression were attenuated by tyrosine kinase inhibitors (genistein and tyrphostin AG126), a MAPK/extracellular signal-regulated protein kinase (MEK) inhibitor [2V-amino-3V-methoxyflavone] (PD 98059) and a p38 MAPK inhibitor [4-(4-fluorophenyl)-2-(4-methylsulfinylphenyl)-5-(4-pyridyl)1H-imidazole] (SB 203580). Lipoteichoic acid-induced p44/42 MAPK activation was inhibited by protein kinase C (PKC) inhibitors

12-(2-cyanoethyl)6,7,12,13-tetrahydro-13-methyl-5-oxo-5H-indolo(2,3-a)pyrrolo(3,4-c)-carbazole] (Go 6976)and

{3-[1-[3-(amidinothio)propyl-1H-indol-3-yl]-3-(1-methyl-1H-indol-3-yl)maleimide]} (Ro 31-8220), genistein and PD 98059. Lipoteichoic acid-induced increase in p38 MAPK activity was inhibited by Go 6976, Ro 31-8220, genistein and SB 203580. Lipoteichoic acid-mediated formation of nuclear factor- $\kappa$ B (NF- $\kappa$ B)-specific DNA-protein complex was inhibited by genistein, tyrphostin AG126, PD 98059 and SB 203580. These results suggest that the activations of both p44/42 and p38 MAPK by lipoteichoic acid result in stimulation of NF- $\kappa$ B-specific DNA-protein binding and subsequent cyclooxygenase-2 expression in A549 cells. Both events required activation of upstream tyrosine kinase and PKC.