Involvement of p38 mitogen-activated protein kinase in lipopolysaccharide-induced iNOS and COX-2 expression in J774 macrophages

陳炳常

Chen BC;Chen YH and Lin WW

摘要

Abstract

Both the nitrite and prostaglandin E2 (PGE2) release caused by lipopolysaccharide (LPS) in J774 macrophages are inhibited by SB 203580, a specific p38 mitogen-activated protein kinase (MAPK) inhibitor, in a concentration-dependent manner. The 50% inhibitory concentration (IC50) for nitrite and PGE2 responses was 1μm and 0·5 μm, respectively. Inhibition was marked following simultaneous treatment with SB 203580 and LPS, and was much reduced when SB 203580 was added 6 hr after LPS treatment. In parallel, LPS induction of inducible NO synthase (iNOS) and cyclo-oxygenase-2 (COX-2) proteins and their steady-state levels of mRNA were reduced by SB 203580. LPS activation of nuclear factor-kappa B (NF-κB), activator protein-1 (AP-1) and p38 MAPK was also inhibited by SB 203580. These results suggest a crucial role of p38 MAPK in regulation of the transcriptional level of endotoxin LPS-induced iNOS and COX-2 protein expression.