# Potentiation of lipopolysaccharide-induced IL-6 release by uridine triphosphate in macrophages: cross interaction with cyclooxygenase-2-dependent prostaglandinE2 production.

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## 摘要

## Abstract

Our previous study has demonstrated the potentiation by uridine triphosphate (UTP) of nitric oxide (NO) and prostaglandin E2 (PGE2) production in lipopolysaccharide (LPS)-stimulated murine J774 macrophages. In this study, we found that the amount of interleukin-6 (IL-6) release in response to LPS stimulation was greatly enhanced in the presence of UTP. This enhancement exhibited concentration dependence and occurred after 8 h of treatment with LPS. RT-PCR analysis indicated that the steady-state level of IL-6 mRNA induced by LPS was apparently increased upon co-addition of UTP. The potentiation by UTP was inhibited by the treatment with U73122 (a phosphatidylinositol-phospholipase C inhibitor), BAPTA/AM (an intracellular Ca2+ chelator), KN-93 (a selective inhibitor of calmodulin-dependent protein kinase) or PDTC (a nuclear factor B inhibitor). To understand the cross-regulation among NO, PGE2 and IL-6, all of which are dramatically induced after LPS stimulation, the effects of L-NAME (a nitric oxide synthase inhibitor), indomethacin (a cyclooxygenase inhibitor), NS-398 (a cycloxygenase-2 inhibitor) and IL-6 antibody were tested. The results revealed the positive regulation between PGE2 and IL-6 synthesis because NS-398 and indomethacin inhibited LPS plus UTP-induced IL-6 release, and IL-6 antibody attenuated LPS plus UTP-induced PGE2 release. Taken together these results reinforce the role of UTP as a regulatory element in inflamed sites by demonstrating the capacity of this nucleotide to

potentiate LPS-induced release of inflammatory mediators..

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