Modulation of inducible nitric oxide synthase induction by prostaglandin E2 in macrophages: distinct susceptability in murine J774 and RAW 264.7 macrophages.

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摘要

Abstract

Prostaglandin E2 (PGE2) is the major cyclooxygenase metabolite in macrophages with complex proinflammatory and immunoregulatory properties. In the present study, we have compared the modulatory role of PGE2/cAMP-dependent signaling on induced nitric oxide (NO) production in two murine macrophages, J774 and RAW 264.7. With no effect on NO release by itself, PGE2 co-addition with lipopolysaccharide (LPS) resulted in a concentration-dependent enhancement in NO release and inducible NO synthase induction in J774, but not in RAW 264.7, macrophages. The potentiation effect of PGE2 in J774 cells was still seen when applied within 9 h after LPS treatment. Whereas RAW 264.7 macrophages release PGE2 with greater extent than J774 macrophages in response to LPS, indomethacin and NS-398, upon abolishing LPS-induced PGE2 release, caused a more obvious inhibition of NO release from J774 than RAW 264.7 cells. Thus, we suggest a higher positive modulatory role of PGE2—either endogenous or exogenous—on NO formation in J774 cells. Supporting these findings, exogenous PGE2 triggers cAMP formation in J774 cells with higher potency and efficacy. Of interest, dBcAMP also elicits higher sensitivity in potentiating NO release in J774 cells. We conclude that the opposite effect of PGE2/cAMP signaling on macrophage NO induction depends on its signaling efficacy and might be associated with the difference in endogenous PGE2 levels