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Erk activation mediates lipopolysaccharide-induced induction of matrix metalloprotease-9 from rat primary astrocytes.

Woo Jong Lee*, Byung Kwon Yoo, Gyu Hwan Park, and Kwang Ho Ko.

Department of Pharmacology, College of Pharmacy,
Seoul National University, Seoul, Korea

In central nervous system, matrix metalloproteinases (MMPs) are produced by neuron as well as glia and implicated in physiological events such as neurite outgrowth and myelination etc. In addition, MMPs also contribute to the pathogenesis of several CNS diseases such as multiple sclerosis, Alzheimers disease and malignant glioma. In spite of their functional importance, little is known about the signal transduction pathways leading to the induction of MMPs in CNS. Here, we investigated whether the activation of Erk(1/2) is involved in the induction of MMP-9 in LPSstimulated primary astrocytes. The activity, protein and mRNA level of MMP-9 but not those of MMP-2 were increased by LPS treatment, which were assessed by gelatin zymography, immunoblotting and RT-PCR, respectively. LPS treatment induced activation of Erk(1/2) within 30min, which was dose-dependently inhibited by PD98059, a specific inhibitor of the Erk(1/2) kinase (MEK). In this condition, PD98059 blocked the increase in MMP-9 protein and mRNA level as well as gelatin-digesting activity. The treatment of phorbol mirystoyl acetate (PMA) activated Erk(1/2) with concomitant increase in MMP-9 production in a dose-dependent manner. The results from the present study suggest that induction of MMP-9 in rat primary astrocytes by LPS is mediated at least in part by the activation of Erk(1/2). The Erk(1/2)-mediated MMP-9 induction may provide insights into the regulation of MMP-9 production in CNS, which may occur *in vivo* in pathological situations such as CNS inflammation.