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ACTIVATION OF P38 MAP KINASE AND AP-1 DURING THE PROMOTION OF NEURITE EXTENSION OF PC-12 CELLS BY 15-DEOXY- Δ 12,14-PROSTAGLANDIN J2

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15-Deoxy- Δ 12,14-prostaglandin J2 (15-deoxy-PGJ2), a naturally occurring ligand activates the peroxisome proliferator-activated receptor- γ (PPAR- γ). It was known to have promoting ability of nerve growth factor(NGF)-induced neurite extension. However, it is not clear yet as to what signaling pathway is involved in its promoting ability of neurite extension. Since MAP kinase classes as well as transcription factors have been known to be implicated in neuronal cell differentiation, we investigated whether 15-deoxy-PGJ2 exert its ability to promote cell differentiation through up-regulation of MAP kinase classes and the activation of transcription factors. PC 12 cells treated with 15-deoxy-PGJ2 (0.2 to 1.6 μ M) alone showed measurable neurite extension and expression of neurofilament, markers of cell differentiation. However much greater extent of neurite extension and expression of neurofilament was observed in the presence of NGF (50 ng/ml). In parallel with its increasing effect on the neurite extension and expression of neurofilament, 15-deoxy-PGJ2 enhanced NGF-induced p38 MAP kinase expression and its phosphorylation in addition to the activation of transcription factor AP-1 in a dose dependent manner. Moreover, pretreatment of SD 203580, a specific inhibitor of p38 MAP kinase inhibited the promoting effect of 15-deoxy-PGJ2 (0.8 μ M) on NGF (50 ng/ml)-induced neurite extension. This inhibition correlated well with the ability of SB203580 to inhibit the enhancing effect of 15-deoxy-PGJ2 on NGF-induced the expression of p38 MAP kinase and activation of AP-1. These data demonstrate that activation of p38 MAP kinase in conjunction with AP-1 signal pathway may play an important role in the promoting activity of 15-deoxy-PGJ2 on the NGF-induced differentiation of PC12 cells.

keyword : p38 MAP kinase , AP-1 , PC-12 , 15-deoxy-PGJ2 , neurite extension