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ROLES OF MAPK PATHWAYS IN GDNF-INDUCED GLIOMA CELL MIGRATION

Hyun Song, Dong June Chung[1], Pill-Hoon Choung[2] and Aree Moon

College of Pharmacy, Duksung Women's University
[1] Sungkyunkwan University
[2] Seoul National University

Glial cell-derived neurotrophic factor (GDNF) is a potent neurotrophic factor that enhances survival of midbrain doparminergic neuron and is a member of the transforming growth factor-b superfamily. GDNF and its receptors are widely distributed in brain and are believed to be involved in the control of neuron survival, proliferation and differentiation. In this study, we examined the effect of GDNF on proliferation and migration of Hs683 human glioma cells. GDNF markedly enhances proliferation and migration of Hs683 cells in a dose-dependent manner. Since involvement of mitogen-activated protein kinases (MAPKs) in the cellular effect of GDNF has been suggested, we wished to investigate the activation of JNK, ERK-1,2 and p38 by GDNF treatment in Hs683 cells. GDNF (80 ng/ml) prominently increased phosphorylated form of p38 without affecting total p38 level. A kinetic study of GDNF-induced p38 activation showed that p38 was maximally activated within 30 min after GDNF treatment and decreased at 1 hr in the Hs683 cells. Activation of other MAPKs, JNK and ERK-1,2, was also detected upon GDNF treatment, to a lesser degree compared to p38. Our data suggest that the enhancing effect of GDNF on glioma cell migration may possibly be mediated by activation of MAPKs, especially p38.

Keyword : GDNF,MAPK