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Nerve growth factor stimulates glioblastoma proliferation through Notch1 receptor signaling

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Notch receptors are heterodimeric transmembrane proteins that regulate cell fate, such as differentiation, proliferation, and apoptosis. Dysregulated Notch pathway signaling has been observed in glioblastomas, as well as in other human malignancies. Nerve growth factor (NGF) is a member of neurotrophin family and is essential for cell growth and differentiation in the nervous system. Recent reports suggest that NGF stimulates glioblastoma proliferation. However, the relationship between Notch1 and NGF in glioblastomas remains unknown. In this study, we evaluated the expression of the Notch1 receptor in human glioblastoma and the U87-MG cell line, and the relationship between NGF and Notch1 signaling. Notch1 expression was higher in the glioblastoma than in the adjacent or in control brain tissue. The effect of NGF- β on the U87-MG human glioblastoma cell line was evaluated by MTT assay and showed that NGF stimulates U87-MG cells in a dose-dependent manner ($p=0.005$). To determine whether this proliferation by NGF was associated with the Notch 1 signaling pathway, the Notch1 and Hes1 protein were evaluated by RT-PCR and Western blot analysis, which demonstrated that Notch1 and Hes1 expression were increased by NGF in a dose-dependent manner ($p=0.044$, $p=0.020$, respectively). After transfection with Notch1 siRNA, there was no significant difference in cell proliferation between control and 100 nM NGF- β treatments ($p=0.887$), which means that U87-MG cell proliferation was suppressed by Notch1 siRNA. These results indicate that NGF stimulates glioblastoma cell proliferation in a dose-dependent manner via the Notch1 receptor, and that NGF induces up-regulation of Notch1 signaling.

Biography

In Bok Chang has completed his MD from Cheon Buk National University and PhD from Kangwon National University. He has been serving as an Associate Professor of Department of Neurosurgery of Hallym University Sacred Heart Hospital.

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