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Increase of Cdk5 and p35 during Retinoic Acid-Induced Neuronal Differentiation of SK-N-BE(2)C cells

Jong-Hee Lee* and Kyung-Tai Kim

Department of Life Science, Pohang University of Science and Technology, Pohang 790-784, Republic of Korea

Cdk5, a neuronal Cdc2-like kinase, exhibits a variety of functions in neuronal differentiation and neurocytoskeleton dynamics as well as neuronal degeneration and cell death. However, its role in retinoic acid (RA)-induced differentiation has not been reported yet. We newly found that RA treatment of SK-N-BE(2)C, human neuroblastoma, increased expression of Cdk5 concomitantly with a neuronal specific activator, p35. Inhibition of Cdk5 activity by using a specific inhibitor, roscovitine and by transfecting cells with a dominant negative form of Cdk5 caused dramatic decrease of RA-induced differentiation. When SK-N-BE(2)C cells were over-expressed with p35 or Cdk5, the rate of RA-induced differentiation was increased. The results suggest that Cdk5 plays an important role in the RA-induced neuronal differentiation. A previous report indicated that activation of ERK is involved in the induction of p35 in PC12 cells. This result was confirmed in our study in which expression of p35 was decreased in SK-N-BE(2)C cells when activity of ERK was inhibited by PD98059. On the other hand, the mechanism involved in increase of Cdk5 expression is not defined yet. We detected increased expression of c-fos and acitivation of CREB upon RA treatment. Possible involvement of c-fos and CREB in the induction of Cdk5 is now under investigation.