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Phosphatidylinositol-3 Kinase (PI-3K) Mediates Epinephrine-Induced Survival and Differentiation of PC12-α_2 Cells

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AIM

The three known subtypes of α_2-adrenergic receptor are heptahelical transmembrane receptors coupled to G-proteins (GPCRs) and mediate part of the physiological actions of the hormones-neurotransmitters epinephrine & nor-epinephrine in vascular smooth muscle cells, in kidneys, in the Central Nervous System etc. PC12 cells are a cell line derived from rat pheochromocytoma, which differentiates to sympathetic neurons in presence of NGF (Nerve Growth Factor), and, for this reason, it constitutes a model system for the study of differentiation in vitro.

Recent studies in our laboratory showed that PC12 cells expressing, following transfection, subtypes of α_2-adrenergic receptor (PC12-α_2) differentiate into a neuronal phenotype after exposure to epinephrine. In the present study, we investigated the role of Phosphatidylinositol-3 Kinase (PI-3K) and of the effector molecule Akt/PKB in the survival and neuronal differentiation of PC12-α_2 cells.

MATERIALS AND METHODS

We employed the Western blotting method with antibodies against phosphorylated and non-phosphorylated Akt and against the neuronal differentiation marker peripherin in differentiated and non-differentiated PC12-α_2 cells, after stimulation with epinephrine in the presence or absence of the inhibitor LY294002, and the DNA fragmentation technique.

RESULTS

Epinephrine activates Akt/PKB in PC12-α_2 cells and induces peripherin expression during differentiation of these cells, as well as their survival. The expression of peripherin and the survival of PC12 cells are PI3K-dependent, since they are inhibited by LY294002.

CONCLUSIONS

Epinephrine promotes survival and differentiation of PC12 cells via its α_2 receptors, and these actions are mediated by PI-3K. This study indicates that epinephrine might act as a neurotrophic factor in vivo, alone or in combination with other agents.