D109 Role of Hyperpolarization Attained by Linoleic Acid in Chick Myoblast Fusion.

Jae-Yong Park*, Doyun Lee, Kyungjin Kim, and Man-Sik Kang
Department of Molecular Biology and Research Center for Cell Differentiation, Seoul National University

Our previous report has suggested that hyperpolarization generated by reciprocal activation of calcium-activated potassium ($K_{(Ca)}$) channels and stretch-activated channels induces calcium influx that triggers myoblast fusion. Here we show that linoleic acid is involved in the process of generating hyperpolarization in cultured chick myoblasts and hence in promotion of the cell fusion. Linoleic acid dramatically hyperpolarized the membrane potential from -14 +/- 3 to -58 +/- 5 mV within 10 min. This effect was partially blocked by 1 mM tetraethylammonium (TEA) or 30 nM charybdotoxin, a selective $K_{(Ca)}$ channel inhibitor, and completely abolished by 10 mM TEA. Single-channel recordings revealed that linoleic acid activates TEA-resistant potassium channels as well as $K_{(Ca)}$ channels. Furthermore, linoleic acid induced calcium influx from extracellular solution, and this effect was partially blocked by 1 mM TEA and completely prevented at 10 mM, similar to the effect of TEA on linoleic acid-mediated hyperpolarization. Since the valinomycin-mediated hyperpolarization promoted calcium influx, hyperpolarization itself appears capable of inducing calcium influx. In addition, gadolinium prevented the valinomycin-mediated increase in intracellular calcium level under hypotonic conditions, revealing the involvement of stretch-activated channels in calcium influx. Furthermore, linoleic acid stimulated myoblast fusion, and this stimulatory effect could completely be prevented by 10 mM TEA. These results suggest that linoleic acid induces hyperpolarization of membrane potential by activation of potassium channels, which induces calcium influx through stretch-activated channels, and thereby triggers myoblast fusion.

D110 Dexamethasone, a Synthetic Glucocorticoid, Inhibits PDGF-induced Neurite Outgrowth of Hippocampal Progenitor Neuronal Cell Line, HiB5

Gi Hoon Son, Dong Ho Geum and Kyungjin Kim
Department of Molecular Biology and Research Center for Cell Differentiation, College of Natural Science, Seoul National University, Seoul 151-742, KOREA

Hippocampus is one of the most sensitive brain regions to stress hormones such as glucocorticoid (GC) during development and in adulthood. The present study intended to investigate the effect of GC on the differentiation of hippocampal progenitor neuronal cell line, HiB5. Treatment of dexamethasone (DEX), a GC agonist, inhibited neurite outgrowth in platelet-derived growth factor (PDGF)-induced differentiation of HiB5 cells via GC receptor (GR). During differentiation process, expression of differentiation marker genes such as nestin and mid-size neurofilament was altered. DEX promoted the fast dephosphorylation of extracellular signal–regulated MAP kinase (ERK) after PDGF treatment. Blockade of ERK signaling pathway with PD098959 blocked neurite outgrowth of HiB5 cells. The fast dephosphorylation of ERK by DEX was blocked by sodium orthovanadate and actinomycin D. The effect of DEX is mediated by tyrosine phosphatase and one possible mediator is SHPTP1. SHPTP1 but not SHPTP2 mRNA levels were induced by DEX and this induction was evidently blocked by RU486, a GR antagonist. These results indicate that GC inhibits ERK signaling pathway by induction of a tyrosine phosphatase activity and as a result of failure in sustained activation of ERK signaling, subsequently inhibits PDGF-induced differentiation of HiB5 cells.