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ATP Modulation of Cloned Rat Brain Large-conductance Ca^{2+} -activated K^+ Channel by Protein Phosphorylation

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Large conductance Ca^{2+} -activated K^+ channels (Maxi-K channel) have been implicated in many important physiological processes such as co-ordination of membrane excitability in neurons. Modulation of these channels are archived by the activity of various protein kinases. The most widely studied example of Maxi-K channel regulation by protein phosphorylation has been obtained using plasma membranes from the rat brain incorporated into lipid bilayers. One type of channel can be up-regulated by ATP by the activity of unidentified endogenous protein kinase, which is closely associated with channel protein (Chung et al., 1991). Here we used cloned α -subunit of rat brain Maxi-K channels (rSlo), which was expressed heterologously in HEK293 cells. Application of ATP (0.1-4 mM) to the intracellular side of inside-out patches produced concentration-dependent activation of the channels. Application of hydrolyzable ATP analog (ATP γ S) mimicked the ATP effect. However, non-hydrolyzable analog (AMPPNP) did not mimic it, implying that ATP effect is due to the activity of endogenous protein kinase in patch membranes. Several protein kinase inhibitors were tested to reverse the effect. It is concluded that rSlo channel activity is subject to modulation by the activity of a closely associated kinase, suggesting that this system may be of physiological importance.