Roles of ion transport in clearance of lung fluid in fetal lung

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Summary

To study a cAMP-mediated signaling pathway in regulation of amiloride-sensitive Na^+ transport in rat fetal distal lung epithelial (FDLE) cells, we measured an amiloride sensitive short-circuit current (Na^+ transport). FDLE had two types of amiloride-sensitive Na^+-permeable cation channels: nonselelctive cation (NSC) and Na^+ channels. Only the NSC channel responded to cAMP, but the Na^+ channel did not. This indicates that the NSC channel is responsible to cAMP-stimulation of amiloride-sensitive Na^+ transport in FDLE. Forskolin, which increases the cytosolic cAMP concentration, stimulated the Na^+ transport. Forskolin also activated cAMP dependent protein kinase (PKA). A ß-adrenergic agonist and cAMP mimicked the forskolin action. KT5720, a PKA inhibitor, did not influence the forskolin action, suggesting that forskolin stimulates the Na^+ transport through a PKA-independent pathway. Moreover, tyrosine phosphorylation of ~70-80, ~97 and ~110-120 kDa proteins was increased by forskolin. A protein tyrosine kinase (PTK) inhibitor, tyrphostin A23 abolished the forskolin action. Further, 5-nitro-2-(3-phenylpropylamino)-benzoate (NPPB, a Cl^- channel blocker) prevented the stimulatory action of forskolin on the Na^+ transport by abolishing the forskolin-induced cell shrinkage and tyrosine phosphorylation. Based on these results, we conclude that forskolin (and cAMP) stimulates the Na^+ transport in a PTK-dependent but not a PKA-dependent pathway by causing cell shrinkage that activates PTK in rat FDLE cells.