Platelet-derived growth factor (PDGF) regulates Epithelial Na^+ channels *via* ERK1/2

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The epithelial sodium channel (ENaC) plays an important role in reabsorbing Na^+ across epithelia lining the kidney collecting duct, the distal colon, the lung and excretory ducts of salivary and sweat glands. Function of ENaC is, therefore, crucial for the maintenance of Na^+ and fluid homeostasis and in the regulation of plasma volume and blood pressure.

Activity of ENaC is regulated by growth factors. It has been reported that endothelin-1 (ET-1), epidermal growth factor (EGF) and hepatocyte growth factor (HGF) regulate the amiloride-sensitive sodium current *via* mechanisms that involve mitogen activated protein kinases (MAPKs). Platelet-derived growth factor (PDGF) is known as one of serum factors that promote proliferation of arterial smooth muscle cells. PDGF is a strong stimulator of the MAPK signaling cascade, which transfers external signals to generate intracellular responses including proliferation, cell migration, cell cycle progression and differentiation. The role of PDGF in the regulation of ENaC activity is currently unknown.

In this study, we used electrophysiological techniques to investigate the role of PDGF in the regulation of the activity of ENaC. We found that PDGF-BB (20ng/ml) inhibits the amiloride-sensitive short-circuit current in mouse kidney collecting duct (M1) cells and in Fisher rat thyroid (FRT) cells transfected with exogenous ENaC. The inhibitory effect of PDGF on the activity of ENaC in FRT cells was abolished by pre-treating the cell with an ERK1/2 inhibitor (PD98059), suggesting that the cellular signalling pathway by which PDGF inhibits activity of ENaC involves ERK1/2. Moreover, immunoblot analysis in FRT cells revealed that PDGF increased phosphorylation of ERK1/2 in this cell type and that this effect of PDGF was inhibited by PD98059.

Taken together, our data suggest that PDGF is a negative regulator of ENaC that inhibits the channel via an ERK1/2-dependent mechanism.