Protein Kinase C may play a role in lubiprostone’s mechanism on the activation of CFTR in airway epithelial cells.

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Abstract
Cystic fibrosis remains a highly prevalent hereditary disease, caused by loss-of-function mutations in the CFTR channel. Lubiprostone is known to activate CFTR in airway cells indirectly through targeting EP4 prostanoid receptors (Cuthbert, 2010). On the other hand, protein kinase C (PKC) was shown to inhibit EP4 receptor responses, albeit in the context of EP4-mediated chemotaxis of eosinophil; its effect upon CFTR activation is not known (Luschnig-Schrat et al., 2011). The role of PKC in lubiprostone’s activation of CFTR in human bronchial epithelial cell line 16HBE14o- was investigated using the Ussing chamber method. Transepithelial potential difference (Vte) and short-circuit current (Isc) were recorded to reflect the transepithelial ion exchange. Specific CFTR inhibitor was used to ensure that lubiprostone’s effect focuses on CFTR channels. Day-matched control was ensured, with alternating control trials (n=14) and trials with PKC inhibitor added (n=15). Values are mean ± SD. The effect of lubiprostone and CFTR inhibitor on both the Vte and Isc was significant (p<0.05). This ascertains the effect of lubiprostone in activating Cl− secretion, and CFTR inhibitor’s effect in reducing such secretion. Additionally, PKC inhibitor significantly decreased the effect of lubiprostone in causing an increased transepithelial potential difference (p<0.05). On the contrary, the effect of CFTR inhibitor on both the Vte and Isc was not significantly different between PKCinh trials and control trials; this is also true for lubiprostone’s effect on Isc (0.05). Of note, however, the p-values of all four comparisons were within 0.10. From these data, the role of the PKC pathway was not confirmed, as only one out of the four dataset comparisons was statistically significant. However, the low p-values encourage for further work in this direction.

References