Analysis of intracellular calcium signaling pathway by substance P in isolated crypt cells from guinea pig distal colon.

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Summary

Crypt cells play an important role in the chloride secretion. Many neuropeptides including substance P can evoke chloride secretion in epithelial cells. However, mechanism of intracellular signaling pathway of chloride secretion is incompletely understood.

Thus, we have examined intracellular Ca^{2+} signaling pathway in isolated crypt cells from guinea-pig distal colon using confocal laser scanning microscope. In the present studies, tachykinins were used as secretagogues. Substance P increased in $[Ca^{2+}]_i$ in isolated crypt cells in a concentration-dependent manner. Specific NK-1 receptor antagonist, FK888 was antagonized substance P-induced increase in $[Ca^{2+}]_i$. The finding suggests that crypt cells possess NK-1 receptors. In extracellular Ca^{2+} free condition, substance P still evoked increase in $[Ca^{2+}]_i$ similar to that of control. On the other hand, substance P-evoked increase in $[Ca^{2+}]_i$ was significantly decreased by the pretreatment with thapsigargin

From the present results, it is reasonable to speculate that the substance P-induced increases in $[Ca^{2+}]_i$ occurs following steps; 1) substance P binds to NK-1 receptors at basolateral membrane 2) activated-substance P receptors probably activate PLC, and then, 3) Ca^{2+} release occurs from thapsigargin-sensitive Ca^{2+} stores and Ca^{2+} influx from serosal side.