

Mutual Interaction between Subepithelial Fibroblasts and Afferent Neurons via ATP and Substance-P in Intestinal Villi

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Subepithelial fibroblasts of the intestinal villi, which form a contractile network beneath the epithelium, are in close contact with epithelial cells, neurons, capillaries, smooth muscles and immune cells, and secrete extracellular matrix, growth factors and cytokines. Cultured subepithelial fibroblasts of the rat duodenal villi display various receptors such as ETs, ATP and substance-P (sub-P), and release ATP in response to mechanical stimulation.

Here, the presence of functional NK1 receptors (NK1R) was pharmacologically confirmed in primary culture and the effects of sub-P were measured in an acute preparation of epithelium-free duodenal villi using a two-photon laser microscope. Sub-P elicited an increase in the intracellular Ca^{2+} and contraction of the subepithelial fibroblasts in culture and the isolated villi. The localization of NK1R and sub-P in the villi was examined by light and electron microscopic immunohistochemistry. NK1R-like immunoreactivity was intensely localized on the plasma membrane of villous subepithelial fibroblasts. These villous subepithelial fibroblasts form synapse-like structures with both sub-P-immunopositive and -immunonegative nerve varicosities. We propose that villous subepithelial fibroblasts and afferent neurons interact mutually via sub-P and ATP, and these interactions play important roles in the functions of intestinal villi such as villous movement, nutrient absorption and intestinal maturation.