

The distribution of short-chain fatty acid receptor, GPR43, and the effects of propionate on spontaneous motility of circular muscle in the rat terminal ileum

Hideaki Tazoe

Department of Environmental Health Sciences, Graduate School of Nutritional and Environmental Sciences

In gastro-intestinal (GI) tract, the luminal side is defined as an extracorporeal area. The stimuli from luminal contents to GI tract are classified into chemical ones and physical ones. Focused on the chemical stimuli, short-chain fatty acids (SCFAs) are the major anion in the large intestinal lumen of monogastric mammals, including human. SCFAs are produced during bacterial fermentation of carbohydrates and glycoproteins. SCFAs have various physiological/pathophysiological effects on GI tract with absorption and/or sensing by epithelial cells. The effects of SCFAs in the intestinal lumen are considered to be induced via the activation of specific receptors and/or via absorption in epithelial cells, however, the sensing mechanism of SCFAs in the intestinal lumen is currently unclear.

In 2003, two different groups, Brown et al. and Le Poul et al. simultaneously reported that the SCFA receptors were identified from orphan G-protein coupled receptors (GPCRs), specifically GPR41 and GPR43. We have reported GPR43 was expressed by enteroendocrine cells in rat intestine. In that report, GPR43 immunoreactivity was localized to enteroendocrine cells expressing peptide YY (PYY). Moreover, we investigated the expression of GPR43 in the human colon.

In the present study, we investigated the distribution of GPR43 protein expression in the rat GI mucosa by Western blot analysis. That indicated GPR43 protein was highly expressed in terminal ileum than other small intestinal mucosa. Moreover, we showed propionate, one of the SCFAs, modulated spontaneous motility of circular muscle in the rat terminal ileum. Its modulating effects were composed with a phasic increase, and a continuous decrease in frequency of spontaneous contractions. A phasic increase was appeared via cholinergic pathways, and a continuous decrease was appeared via tetrodotxin insensitive pathways. These results indicated that backward flow of caecal content modulate the ileal spontaneous motility, a phasic increase via cholinergic, and a continuous decrease via tetrodotxin insensitive pathways. (301 words)