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OPINION

Gastrointestinal Tract, a Sensory Organ Sensing the External Environment in the Body

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Summary

Gastrointestinal (GI) tract seems to be the organ in the body; however, its lumen is external environment because opening to the external environment from mouth and anus. Moreover, it cannot be thought of the place where there are more than 1,000 species and 100-trillion numbers of microorganisms as an internal environment. Many multicellular animals including humans' separates between internal environment and external environment by special tissues called epithelia. Barrier functions of epithelia prevent invading of luminal antigens, harmful substances, and microorganisms, etc, so that all the other cells excepting epithelial cells can leave from expose of them. However, on the ground of function of nutrient ingestion, the structure of the epithelium lining the lumen of the GI tract can strengthen not so much and consists of only one-layer of epithelial cells called simple columnar epithelium, different from the epidermis consisting of a strong barrier called stratified squamous epithelia. Therefore, the GI tract must have special host-defense functions making up for the weak barrier simultaneously to conduct the contradictory functions of nutrient ingestion and prevention from invasion of harmful substances and microorganisms.

Mucosal immune system in the GI tract consists of three predominant lymphoid tissues/cells called Gut-Associated Lymphoid Tissue (GALT) including Peyer's patch, Isolated Lymphoid Follicle (ILF) and intraepithelial lymphocytes in the GI mucosa. In short, the function of GALT is to surveillant the GI luminal antigens and to induce suitable immune responses including production of antigen-specific secretory Immunoglobulin A (IgA) [1]. It is considered that mucosal immune system maintains the symbiotic ecosystem in the intestinal lumen by interaction between microbiota and host [2].

In addition to the mucosal immune system, the GI tract employ surveillant systems for the external environment out of the body, which are olfactory and taste sensing systems. In 1991, Buck and Axel identified Olfactory Receptors (ORs) [3], and in 1999, Taste Receptors (TRs) were identified [4]. It was not long before these receptors were confirmed to express in the GI tract [5]. However, before identifying TRs in 1996, it had been reported that taste sensing-associated G protein, also called gustducin ($G\alpha_{gust}$), expressed in scattered cells, called brush cells or tuft cells, in the GI tract epithelia [6]. Figure 1 shows the $G\alpha_{gust}$-expressed cells in the rat ileal villi (A) and vallate papilla (B). The physiological roles of olfactory substances and tastant sensing in the GI tract have currently unclear yet, but we have first reported that a bitter tastant, 6-n-propyl-2-thiourcil (6-PTU) [7], and an olfactory substance,

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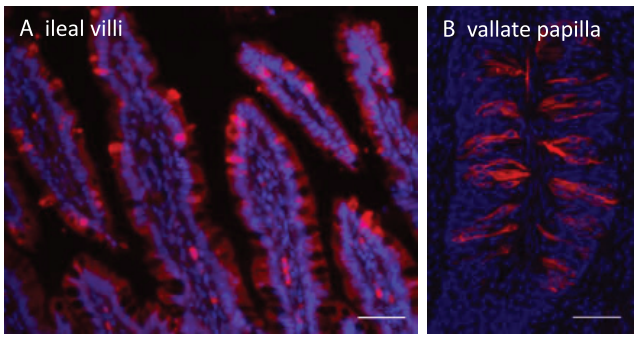

Figure 1 $G\alpha_{gust}$-expressed cells in rat ileal villi.
A). Vallate papilla.
B). Red indicates $G\alpha_{gust}$ immunoreactivity. Blue indicates cell nuclei. Bar = 50 μm.

thymol [8], induces secretory response in the human and rat colonic epithelia. Therefore, it is considered that intestinal olfactory and taste sensing at least have a role inducing mucosal fluid secretion.

In the GI luminal chemical sensing, roles of enteroendocrine cells have been known since the finding of secretin, the first discovered hormone, releasing into blood-circulation from enteroendocrine S cells by duodenal HCl [9]. Following S cells, enteroendocrine I cells releasing Cholecystokinin (CCK) by mainly fatty acids in duodenum and jejunum, L cells releasing Glucagon-Like Peptide-1 (GLP-1) known as incretin, GLP-2 and Peptide YY (PYY), and EC cells releasing serotonin (5-Hydroxytriptamine, 5-HT) by several luminal stimuli including mechanical stimuli, etc are well known as luminal environmental, especially chemical sensory cells.

As described above, GI tract continuously monitors the luminal, that is external environment in the body, and the information might transmit locally and systemically to maintain intestinal and systemic homeostasis. Therefore, it can be considered that the GI tract is a sensory organ sensing the external environment in the body. Recently, evidence about correlation between gut microbiota and host health is accumulated; however, almost all the mechanisms remain unclear yet. One of the mechanisms might be due to the GI luminal sensory system sensing metabolites produced by microbiota. In addition, we propose that these luminal sensory system in the GI tract might be novel target for drug discovery and development of functional foods.

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