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Midgut endocrine cells

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3.1 EVOLUTIONARY ASPECTS

3.1.1 Gastrointestinal hormones and their sources: a lesson from the research in mammals

At the beginning of this century, Bayliss and Starling (1902) described a product of intestinal mucosa that stimulated secretion of pancreatic juice. The product was named secretin and its discovery led to the concept of hormones as circulating regulators derived from specific endocrine cells or glands. Several other mammalian gastrointestinal hormones were subsequently identified as extracts eliciting certain physiological effects. The peptidic nature of these hormones was soon recognized, but their amino acid sequence could be determined only in the last 30 years. Today we know structures of nearly three dozen hormones produced in the digestive tract of mammals. Most of them are straight-chain peptides consisting of less than 40 amino acids, few are biogenic amines. Similar compounds were detected in the gut wall of all Chordata (Rawdon and Andrew, 1990). Immunohistochemical techniques revealed that they are produced in the neurons of neural plexuses located chiefly in the gut musculature and/or in the endocrine cells that are scattered in gut mucosa (McGuigan, 1968).

Electron microscopy techniques showed that the gastrointestinal endocrine cells (GEC) are distinguished from other cells of the digestive tract by the presence of peptidergic secretory granules (150–450 nm in
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diameter). There are two morphologically distinct types of GEC. The apical end of the ‘open type’ GEC reaches the gut lumen and is folded into a brush border, whereas the ‘closed type’ GEC are embeded in the epithelium and lack the luminar contact. Both cell types sometimes contain one or more basal cytoplasmic processes, which are indicative of paracrine function (secretion acting on the neighbouring cells). The digestive tract of humans contains at least 18 kinds of GEC differing in their hormonal secretions (Desbuquois, 1990). Coexistence of several peptides, biogenic amines, and/or peptides and amines in a single GEC or an enteric neuron is common. Most GEC do not contain amines but all appear to possess enzymes for the decarboxylation of neuroamine precursors. They also contain a neuron-specific isoform of the glycolytic enzyme enolase.

The histochemical properties of GEC encouraged speculation that they are of neuroectodermal origin. According to the APUD (amine precursor uptake and decarboxylation) theory, GEC are immigrants from the neural plate (Pearse, 1969). The term paraneuron was coined to embrace all cells producing regulators similar to those in neurons, and to accentuate the neuroectodermal origin of these cells. ‘Paraneurons’ are found in various organs, occurring in largest numbers and variety in the digestive tract as GEC (Fujita et al., 1988). For GEC it was proven, however, that they originate from the same precursor cells as the digestive epithelium and are thus of endodermal origin (Fontaine and LeDouarin, 1977; Andrew, 1981).

The enteric nervous system (ENS) and GEC are interlinked and jointly control gut movements, production of digestive fluids, rate of replacement of the gut epithelium and blood flow to the gut (Dockray, 1988). According to Fujita et al. (1988), GEC function as primary sensors, those of the open type registering the nutrient contents of the gut, and those of the closed type complementing nervous perception of the gut wall tension. Hormones are liberated upon direct sensory stimulation, or in response to circulating regulators or nervous stimuli. Most hormones probably act in the immediate vicinity of the releasing sites. These paracrine secretions act on the adjacent muscle cells, digestive cells, and apparently also on the nerve termini in the subepithelial nervous reticulum, by which the humoral signal is transduced into nervous stimuli and eventually causes changes in the nervously controlled functions, including behaviour. There is evidence that gastrin, somatostatin and secretin are also released into the gut lumen and possibly act on the apical site of the digestive cells. Finally, some GEC products enter the body circulation and exert hormonal effects on distal targets. Owing to the various routes of action, a single hormone can exert a variety of effects. For example, cholecystokinin controls gall bladder contractions,