
The new biology of gastrointestinal hormones

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Abstract
The classic concept of gastrointestinal endocrinology is that of a few peptides released to the circulation from endocrine cells, which are interspersed among other mucosal cells in the upper gastrointestinal tract. Today more than 30 peptide hormone genes are known to be expressed throughout the digestive tract, which makes the gut the largest endocrine organ in the body. Moreover, development in cell and molecular biology now makes it feasible to describe a new biology for gastrointestinal hormones based on five characteristics. 1) The structural homology groups the hormones into families, each of which is assumed to originate from a common ancestral gene. 2) The individual hormone gene is often expressed in multiple bioactive peptides due to tandem genes encoding different hormonal peptides, alternative splicing of the primary transcript, or differentiated processing of the primary translation product. By these mechanisms, more than 100 different hormonally active peptides are produced in the gastrointestinal tract. 3) In addition, gut hormone genes are widely expressed, also outside the gut. Some are expressed only in neuroendocrine cells, whereas others are expressed in a multitude of different cells, including cancer cells. 4) The different cell types often express different products of the same gene, "cell-specific expression." 5) Finally, gastrointestinal hormone-producing cells release the peptides in different ways, so the same peptide may act as an acute blood-borne hormone, as a local growth factor, as a neurotransmitter, and as a fertility factor. The new biology suggests that gastrointestinal hormones should be conceived as intercellular messengers of general physiological impact rather than as local regulators of the upper digestive tract.