

Interactions between the endocrine system and the gastrointestinal tract

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It is well-known that the gastrointestinal tract (GIT) is not a mere site for the absorption of nutrients. Several peptides are synthesized and released from neurons and endocrine cells from the stomach and intestines, which makes the gut the largest endocrine organ in the body (1). These substances interact with different systems, and regulate a variety of processes, such as food intake, energy metabolism, and endocrine balance. The relationship between the GIT and the endocrine system is multidirectional, and hormones released by traditional endocrine organs can also regulate GIT function.

In this special issue, selected world-renowned authors from countries such as Australia, Brazil, Turkey and The Netherlands review the multiple interactions between the endocrine system and the GIT.

Gut-derived peptides act as satiety signals within the brain, and play a crucial role in the regulation of food intake (2), before, during and after weight loss (3). Four decades ago, cholecystokinin was the first gut-derived peptide with effects on the regulation of food intake to be described (4). Nowadays, several other gut peptides with effects on food intake have been discovered, in addition to cholecystokinin. The understanding of the physiology of some of these peptides led to the development of novel therapies, such as glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors, for the treatment of type 2 diabetes (5). In their review, Boguszewski and van der Lely comprehensively describe the mechanisms by which these gut peptides control energy balance. Moreover, they address a very contemporary issue regarding the role of gut microbiota in the pathogenesis of obesity (6).

Among the peptides produced by the gut, the growth hormone secretagogue ghrelin is the only with orexigenic effects (7). Newer research has also demonstrated that ghrelin exerts central and peripheral actions to regulate glucose metabolism (8). Moreover, due to its effects in the control of cell proliferation *in vitro*, ghrelin may also play a role in the pathogenesis of gastrointestinal cancers (9). In this special

issue, authors from Monash University, Australia, present an outstanding review of the biology of ghrelin and its effects in the regulation of energy metabolism. In addition, possible links between ghrelin and gastrointestinal cancer are discussed (10).

Whereas the association between ghrelin and gastrointestinal cancer needs to be further elucidated, it is well-known that the excess of growth hormone, seen in patients with acromegaly, is directly associated with an increased risk for the development of intestinal polyps and colorectal cancer (11). The mechanisms by which this occurs, as well as the recommendations for the management of patients with acromegaly in regards to the screening and treatment of colorectal cancer, are reviewed in a superbly informative manuscript led by Vilar (12).

As an endocrine organ, the gut can also be affected by malignancies influencing neuroendocrine cells. These malignancies affecting the gut and the pancreas secrete a variety of hormones in excess, such as insulin, glucagon, gastrin, vasoactive intestinal peptide, and somatostatin, leading to diverse clinical manifestations. In this issue, authors from Turkey provide a very complete review of the epidemiology, pathophysiology, diagnosis and recent advancements in the treatment of gastroenteropancreatic neuroendocrine tumors (13).

The effects of GIT disorders in the endocrine system are discussed in three exceptional manuscripts in this special issue. First, the role of malabsorptive disorders in the pathogenesis of osteoporosis is reviewed by Franco. In that paper, recommendations for the screening, treatment, and prevention of metabolic bone disease in malabsorptive disorders are comprehensively reviewed (14). Second, another manuscript led by Boguszewski focussed on a highly prevalent malabsorptive disorder among children seeking medical care due to short stature—celiac disease. In that manuscript, the authors demonstrate that celiac disease can determine short stature not only by malnutrition, but also by growth hormone deficiency (15). Last, the

interference of malabsorptive disorders in the adequate control of hypothyroidism is reviewed by de Carvalho and Figuera, raising awareness to the fact that gastrointestinal disorders must be investigated in case of inadequate control of hypothyroidism, despite full adherence to levothyroxine replacement (16).

Traditionally, the liver is not considered as part of the GIT. However, it maintains close anatomical and physiological relationships with the gut. In addition, it has fundamental roles in the control of endocrine homeostasis and metabolism. In this issue, Chitturi addresses very pertinent aspects of obesity-related non-alcoholic fatty liver disease, from epidemiology to treatment (17). Finally, Rodríguez *et al.* review the role of leptin (an adipocyte-derived hormone) in the pathogenesis of lipodystrophy-associated non-alcoholic fatty liver disease, and present evidence for the efficacy of leptin analogues in the treatment of such condition (18).

In summary, the GIT and the endocrine system are closely related, and body homeostasis depends on their proper function and interaction. Researchers and clinicians must be aware of those interactions, promoting the development of safe and effective diagnostic and therapeutic approaches for the management of disorders affecting both systems.

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