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Cell and Developmental Biology

Commentary

Enteroendocrine Cell Diversity and Function in Nutrient Detection Hormone Secretion and Systemic Physiological Regulation

Sarah Cooper*

Department of Physiology and Metabolic Science, Imperial College London, London, United Kingdom

DESCRIPTION

Enteroendocrine cells are specialized epithelial cells found throughout the lining of the gastrointestinal tract, playing a pivotal role in regulating digestive physiology, nutrient absorption and systemic metabolism. These cells act as both sensors and secretors, detecting luminal contents such as nutrients, microbial metabolites and hormones and responding by releasing a wide array of signaling molecules that orchestrate local and distant physiological responses. Although they represent only a small fraction of the total epithelial cell population, enteroendocrine cells exert a profound influence on the coordination of digestive processes, appetite regulation, glucose homeostasis and gut-brain communication. Their study is central to understanding gastrointestinal biology, metabolic regulation and the pathophysiology of diseases such as obesity, diabetes and irritable bowel syndrome.

The development and differentiation of enteroendocrine cells are tightly regulated by transcription factors and signaling pathways that determine their lineage from intestinal stem cells. Within the intestinal crypts, pluripotent stem cells give rise to progenitor populations that can differentiate into absorptive enterocytes, secretory goblet cells, Paneth cells, or enteroendocrine cells. Key transcriptional regulators, including neurogenin, achaete-scute homolog and pancreatic and duodenal homeobox, orchestrate the commitment of progenitor cells toward the enteroendocrine lineage. Disruption of these transcription factors impairs enteroendocrine cell formation and function, highlighting their critical role in intestinal development.

Enteroendocrine cells are highly diverse, comprising multiple subtypes that secrete distinct hormones in response to specific stimuli. For example, cells in the proximal small intestine produce cholecystokinin, which stimulates pancreatic enzyme secretion and gallbladder contraction, while cells in the distal ileum and colon secrete peptide YY and glucagon-like, which slow gastric emptying, enhance insulin secretion and modulate appetite. Other enteroendocrine cells produce serotonin, motilin, gastrin, somatostatin and ghrelin, each with unique effects on gut motility, nutrient absorption and neuroendocrine signaling. This functional diversity allows the gastrointestinal tract to respond dynamically to ingested nutrients and microbial metabolites, fine-tuning digestion and energy balance.

The sensing mechanisms of enteroendocrine cells are sophisticated and involve multiple receptors and transporters that detect nutrients, bile acids and microbial products. Glucose, amino acids, fatty acids and short-chain fatty acids are recognized through specific transporters and G protein-coupled receptors, triggering intracellular signaling cascades that culminate in hormone secretion. Recent studies have also shown that enteroendocrine cells can directly communicate with neurons in the enteric nervous system and vagus nerve, forming a gut-brain axis that influences feeding behavior, mood and metabolic homeostasis. This bidirectional communication highlights the integrative role of enteroendocrine cells in linking gastrointestinal function with systemic physiological processes.

Enteroendocrine cell function is influenced by the intestinal microbiome, which produces metabolites such as short-chain fatty acids and secondary bile acids that modulate hormone secretion. Dysbiosis, or imbalance of gut microbial communities, can alter enteroendocrine cell activity and contribute to metabolic disorders, inflammatory bowel disease and gastrointestinal dysfunction. Understanding the interplay between gut microbiota and enteroendocrine cells offers opportunities for therapeutic interventions, including probiotics, prebiotics and dietary modifications that target hormone release and improve metabolic health.

Technological advances have significantly enhanced the study of enteroendocrine cells. Single-cell RNA sequencing has revealed previously unrecognized heterogeneity within enteroendocrine populations, identifying new subtypes with distinct hormonal profiles and developmental origins. High-resolution imaging and lineage-tracing experiments have elucidated the spatial distribution and turnover dynamics of these cells along the gastrointestinal tract. Organoid culture systems, which recapitulate intestinal architecture in vitro, allow researchers to study enteroendocrine differentiation, hormone secretion and

Correspondence to: Sarah Cooper, Department of Physiology and Metabolic Science, Imperial College London, London, United Kingdom, E-mail: s.cooper@imperial.ac.uk

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responses to microbial and nutritional stimuli in controlled laboratory settings.

CONCLUSION

In conclusion, enteroendocrine cells are a important component of the gastrointestinal system, serving as sensors, regulators and mediators of digestive, metabolic and neuroendocrine functions. Their diverse hormonal repertoire enables precise regulation of nutrient digestion, absorption, appetite and energy balance, while their communication with the enteric nervous system and brain integrates local and systemic physiology. Advances in molecular biology, single-cell technologies and organoid models have deepened our understanding of enteroendocrine cell development, function and heterogeneity. Continued research in this field holds promise for developing targeted therapies for metabolic diseases, gastrointestinal disorders and conditions associated with dysregulated gut hormone signaling. The study of enteroendocrine cells not only enhances our comprehension of gut physiology but also provides critical insights into the broader mechanisms that maintain systemic health and homeostasis.