OPINION

Hepatic Glucagon Receptor (GCGR) Signaling to Drive Alpha Cell Hyperproliferation and Pancreatic Neuroendocrine Tumor Formation

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ABSTRACT

Hypoglycemia causes the pancreatic alpha cells to produce glucagon, which promotes hepatic glucose synthesis. Deregulated glucagon secretion is linked to type 2 diabetes, and elevated glucagon levels contribute to diabetic hyperglycemia. Endocrine cells of the pancreatic islets are known as alpha cells (α-cells). They make up to 20% of human islet cells, which synthesize and secrete the peptide hormone glucagon, which raises blood glucose levels.

INTRODUCTION

In reaction to low blood glucose, α-cells produce glucagon. Glucagon's main purpose is to release glucose from the liver's glycogen stores. Each of the three primary cell types found in pancreatic islets produces a different endocrine product: The hormone glucagon is secreted by Alpha cells (α-cells). Beta cells (β-cells) are the most common islet cells and produce insulin.

Hepatic Glucagon Receptor (GCGR) Signaling

A Glucagon protein-coupled receptor in the liver, kidney, intestinal smooth muscle, brain, adipose tissue, heart, pancreatic -cells, and placenta transmits glucagon action. Animal models using genetically engineered Glucagon and its Receptor (Gcgr) have revealed new information regarding the involvement of Glucagon and its Receptor (Gcgr) in areas other than glucose regulation. Sweet taste responsiveness, inotropic and chronotropic effects in the heart, satiety, glomerular filtration rate, insulin, cortisol, ghrelin, GH, glucagon, and somatostatin secretion, and hypothalamic signalling to reduce hepatic glucose synthesis have all been linked to glucagon action. Under specific conditions, glucagon (α) cells can transdifferentiate into insulin (β) cells. These data indicate that glucagon signalling is crucial in a variety of organs. As a result, therapy options for diabetics that prevent Gcgr activation may have repercussions beyond glucose homeostasis [1].

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Signaling to Alpha Cell Hyperproliferation

Despite the lack of evidence from clinical trials, beverages and supplements made from mangosteen fruit are claimed to enhance gut health and immunity. We recently discovered that the most prevalent xanthone in mangosteen fruit, -mangostin (-MG), changed the intestinal microbiome, increased dysbiosis, and worsened colitis. The cecal and colonic microbiotas of all four mouse strains were dramatically affected by dietary -MG, encouraging a drop in commonly presumed beneficial bacterial groups while increasing the abundance of pathogenic bacteria. Firmicutes were found to be less abundant and Proteobacteria were found to be more abundant when -MG was consumed. Dietary -MG was also linked to an increase in colonic epithelial cell proliferation, immune cell infiltration, and stool fluid content. These findings imply that ingesting pharmacologics may be harmful [2].

Signaling to Pancreatic Neuroendocrine Tumor Formation

Tumor-associated macrophages have lately emerged as a significant regulatory cell type during cancer progression, with the bulk of research to far finding that they increase tumour malignancy. CD68(+) macrophages are positively correlated with tumour grade and liver metastasis in human pancreatic neuroendocrine tumours, according to this study (PNETs). We crossed the RIP1-Tag2 (RT2) mouse model of pancreatic islet cancer with colony-stimulating factor-1 (CSF-1)-deficient Csf1(op/op) mice, which have less tissue macrophages, to study the various mechanisms by which macrophages enhance PNET growth. The cumulative tumour burden in Csf1(op/op) RT2 animals was significantly reduced, which was due to a considerable decrease in angiogenic switching and tumour number rather than an effect on tumour growth [3].

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Impact of Hepatic Glucagon Receptor (GCGR) Signaling

Nutritional elements that influence the endocrine metabolic regulation of chickens could open up new avenues for increasing animal health and production. The purpose of this study was to see how dietary cereal type (Wheat-Based (WB) *vs.* Maize-Based (MB) diets), crude protein level (normal (NP) *vs.* lowered (LP), and sodium (n-)butyrate (1.5 g/kg diet) supplementation (*vs*. no butyrate) influenced the responsiveness of the hepatic glucagon receptor (GCGR), insulin receptor beta (IR), and mammalian On day 21, liver samples were taken from Ross 308 broiler chickens for quantitative real-time polymerase chain reaction and Western blot analysis [4].

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