Short Communication

Semaglutide, a GLP-1 Agonist Like Ozempic, and Its Potential Role as a Preventive Anti-Cancer Agent

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This research note explores the potential of Semaglutide, a GLP-1 agonist similar to Ozempic, as a preventive anti-cancer agent. It discusses shared pathophysiological features between cancer and diabetes, including insulin resistance, inflammation, oxidative stress, and adipokine imbalance. The note highlights GLP-1's role in diabetes prevention, its mechanisms, and ongoing research. It also touches upon the promising relationship between GLP-1 receptor agonists and cancer treatment, focusing on their impact on cell proliferation, apoptosis, and angiogenesis regulation. Finally, it emphasizes the importance of establishing optimal dosages for GLP-1 agonists and their potential to address both diabetes and cancer prevention.

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The intricate interplay between cancer and diabetes unfolds through a complex web of shared pathophysiological and physiological features, engendering a compelling area of investigation in the realm of medical science. Despite the seemingly disparate nature of these diseases, they converge on several fronts, marking an intersection where obesity, insulin resistance, chronic inflammation, oxidative stress, and adipokine imbalance serve as common denominators. [1] Insulin resistance, a pivotal factor in the pathogenesis of both diabetes and cancer, is underpinned by intricate molecular mechanisms. In the context of diabetes, aberrant signaling cascades stemming from impaired insulin receptor substrate (IRS) phosphorylation and activation disrupt the phosphatidylinositol 3-kinase (PI3K)-Akt pathway. This disruption hampers glucose transporter 4 (GLUT4) translocation, diminishing cellular glucose uptake. [2] Concurrently, in cancer, hyperinsulinemia fosters insulin-like growth factor 1 (IGF-1) signaling, promoting cell proliferation through the activation of the mitogen-

activated protein kinase (MAPK) pathway. These parallel disruptions in insulin signaling pathways culminate in elevated blood glucose levels and sustained cellular proliferation. [3] Chronic inflammation in diabetes and cancer is orchestrated by complex molecular cascades. In diabetes, the nuclear factor-kappa B (NF-κB) pathway is activated due to heightened levels of pro-inflammatory cytokines like tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6). NF-κB activation triggers the transcription of inflammatory genes, perpetuating an inflammatory microenvironment. [4] Similarly, in cancer, the tumor microenvironment is shaped by infiltrating immune cells and pro-inflammatory cytokines, sustaining a chronic inflammatory state. The Janus kinase-signal transducer and activator of transcription (JAK-STAT) pathway also plays a crucial role in mediating inflammatory responses in both diseases. [5]

Oxidative stress, a common denominator in diabetes and cancer, unfolds through intricate molecular mechanisms. In diabetes, prolonged hyperglycemia contributes to the overproduction of reactive oxygen species (ROS) via multiple pathways, including the polyol pathway and advanced glycation end-products (AGEs) formation. This ROS excess induces cellular damage, contributing to insulin resistance. [6] In the context of cancer, increased metabolic activity and mitochondrial dysfunction result in elevated ROS levels, promoting genomic instability and tumor progression. [7] Both diseases share a pro-oxidant milieu, accentuating the role of oxidative stress in their pathogenesis. The delicate equilibrium between adipokines plays a crucial role in the pathogenesis of diabetes and cancer. In diabetes, adipose tissue secretes adipokines such as adiponectin and leptin. Reduced adiponectin levels impair insulin sensitivity, while elevated leptin exacerbates inflammation and insulin resistance. [8] Similarly, in cancer, adipokines contribute to the intricate crosstalk between adipose tissue and tumors. Adiponectin exerts anti-inflammatory effects, inhibiting tumor growth, while leptin promotes angiogenesis and cancer cell survival. [9] The imbalance in adipokine secretion in both diseases underscores the importance of restoring this equilibrium as a potential therapeutic strategy.

The exploration of GLP-1 as a potential guardian against the onset of diabetes opens a fascinating chapter in the quest for innovative therapeutic strategies. GLP-1, a hormone secreted by the intestine in response to nutrient intake, exerts multifaceted effects on glucose homeostasis. Its role in preventing diabetes stems from its ability to orchestrate a finely tuned symphony of physiological responses. At the forefront of GLP-1's anti-diabetic prowess is its impact on insulin secretion and glucose regulation. GLP-1 enhances pancreatic beta-cell function, stimulating insulin release in a

glucose-dependent manner. Moreover, it acts as a brake on glucagon release, preventing excessive glucose production by the liver. The combined effect promotes glucose clearance and maintains blood glucose levels within a narrow, healthy range. [10] Delving into the realm of research, numerous studies have sought to unravel the optimal dosage of GLP-1 for its prophylactic effects against diabetes. These investigations have meticulously examined varying doses, probing the intricate balance between efficacy and potential side effects. Notably, the dosage explored in these studies has been tailored to mimic physiological GLP-1 levels, avoiding fluctuations that could compromise its therapeutic potential.[11] The mechanistic underpinnings of GLP-1's diabetes-preventive action involve a cascade of events. GLP-1 engages its receptor, GLP-1R, on pancreatic beta cells, initiating a signaling cascade that enhances insulin biosynthesis and secretion. Simultaneously, it suppresses glucagon secretion, curtailing hepatic glucose output. Beyond the pancreas, GLP-1 modulates gastric emptying, curbing postprandial glucose spikes. Furthermore, GLP-1 promotes satiety, influencing dietary patterns and weight management. [12]

These findings underscore the intricate dance of GLP-1 in orchestrating a comprehensive defense against diabetes. The ongoing research endeavors, scrutinizing dosage nuances and mechanistic intricacies, hold the promise of refining GLP-1-based interventions, potentially reshaping the landscape of diabetes prevention. As the scientific community unravels the molecular tapestry of GLP-1's actions, the prospect of harnessing its preventive potential against diabetes becomes increasingly tantalizing.[13][14]

The intersection between GLP-1 receptor agonists and cancer treatment introduces a compelling narrative in the pursuit of innovative therapeutic avenues. Research has unveiled a promising relationship, positioning GLP-1 receptor agonists as potential agents in the battle against cancer. This paradigm shift prompts a nuanced exploration of the mechanistic underpinnings that render these agonists not only as diabetes management tools but also as promising contenders in the oncological landscape. [15] At the heart of this relationship lies the ability of GLP-1 receptor agonists to modulate crucial cellular processes within cancer cells. Activation of GLP-1 receptors initiates a cascade of intracellular events that culminate in a multifaceted response. One key facet involves the inhibition of cancer cell proliferation, a hallmark of tumorigenesis. [16] The intricate signaling pathways affected by GLP-1 receptor activation, notably the cAMP-PKA pathway, act as molecular brakes on uncontrolled cell division, thereby impeding the relentless expansion of malignant cells.[17]

Additionally, GLP-1 receptor agonists exhibit the remarkable capacity to induce apoptosis, the programmed cell death vital for maintaining tissue homeostasis. This phenomenon serves as a strategic intervention in cancer treatment, where evading apoptosis is a characteristic feature of malignant cells. The molecular dialogues orchestrated by GLP-1 receptor activation tilt the balance towards programmed cell death, thereby curbing the survival and persistence of cancer cells. [18]

Furthermore, the anti-cancer potential of GLP-1 receptor agonists extends to the regulation of angiogenesis, the process by which new blood vessels form to nourish growing tumors. By interfering with pro-angiogenic factors, these agonists create an inhospitable microenvironment for tumor growth, undermining the critical support network required for sustained malignancy.[19][20]

Guiding Dosage and Clinical Considerations: Establishing a guiding dosage for exenatide in preventive interventions demands a meticulous balance between efficacy and safety. Clinical trials investigating eventide's preventive potential against diabetes typically commence with a standardized dosage, commonly **0.5 mg once** weekly, with subsequent adjustments based on individual responses. This nuanced approach adheres to the overarching principle of mirroring physiological GLP-1 levels to optimize therapeutic benefits while minimizing potential side effects. As this journey progresses, the guiding dosage of exenatide becomes a beacon for future research endeavors exploring its dual potential in diabetes prevention and as an anticancer agent. The delicate interplay between glycemic control and cancer modulation underscores the interconnectedness of these diseases, propelling exenatide into the spotlight as a promising agent in the landscape of preventive medicine. As ongoing studies unravel the full spectrum of exenatide's preventive prowess, the prospect of a unified therapeutic approach to combat diabetes and cancer continues to captivate the scientific community. [21]

Statements and Declarations

The authors declare that there are no conflicts of interest.

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Declarations

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