GLP-1 Biomarkers in the Development of Metabolic Disorders

Subjects: Others

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Metabolic illnesses, including obesity and type 2 diabetes, have become worldwide epidemics that have an effect on public health. Clinical investigations and further exploration of these mechanisms could lead to innovative, effective, and personalized treatment strategies for individuals. It is important to screen biomarkers in previous studies to discover what is missing. Glucagon-like peptide-1′s role in insulin secretion and glucose control highlights its diagnostic and therapeutic potential. In validating these biomarkers, it will be easier to reflect pathophysiological processes, and clinicians will be able to better assess disease severity, monitor disease progression, and tailor treatment strategies.

diabetes obesity GLP-1 biomarkers

1. Introduction

Type 2 diabetes (T2D) and obesity are common civilian diseases and two interconnected metabolic disorders that have reached epidemic proportions worldwide. Roughly 90% of all instances of diabetes are type 2, making it the most common form. Insulin resistance is a characteristic that causes the body to react to insulin less effectively. Rising blood glucose levels prevent insulin from working properly, which leads to the release of more insulin. This may cause the pancreas to gradually wear out in some type 2 diabetic people, which will lead to the body producing less and less insulin and even higher blood sugar levels (hyperglycemia) [1][2]. Additionally, diabetes has a substantial burden on individuals and healthcare systems due to its high prevalence, economic costs, and increased risk of complications, and comorbidities. For instance, cardiovascular diseases, such as coronary artery disease and stroke, are complications of diabetes, leading to significant morbidity and mortality [3]. Chronic kidney disease, another complication of diabetes, contributes to end-stage renal disease and requires costly treatments like dialysis or transplantation [4][5]. Biomarker identification is crucial as it enables early detection, accurate diagnosis, and monitoring of disease progression and treatment response. Scientific examples include circulating microRNAs and glycated hemoglobin (HbA1c) as diagnostic and prognostic markers [6][7][8]. This method has some limitations, such as individual variability in the relationship between average blood glucose levels and HbA1c. Some people may have higher or lower HbA1c levels for a given average glucose concentration due to factors such as age, race, and genetic differences. Relying solely on HbA1c without considering other indicators may lead to misinterpretation. However, by identifying new reliable biomarkers, healthcare professionals can enhance risk assessment, tailor treatment strategies, and ultimately mitigate the burden of metabolic disorders on public health.

Obesity, on the other hand, is a condition characterized by excessive accumulation of body fat understood as the accumulation of triacylglycerols in adipocytes, which results in an increased number of those cells and thus higher body weight in patients [1][2]. Obesity has also become a global epidemic, presenting a significant public health challenge in recent years. Defined as an excess accumulation of body fat, obesity is a complex multifactorial disorder influenced by genetic, environmental, and behavioral factors [9][10]. Understanding the etiology and consequences of and potential interventions for obesity is of the utmost importance in addressing this pressing health issue. The pathogenesis of obesity involves a dysregulation of energy balance, characterized by an imbalance between energy intake and expenditure [11]. Adipose tissue is now understood to be an active endocrine organ that secretes a variety of bioactive chemicals known as adipokines. It was previously thought to be a passive energy (triacylglycerides) storage organ, but this view is changing. These adipokines are essential for maintaining insulin sensitivity, energy homeostasis, inflammation, and appetite regulation [12]. To effectively combat obesity and its associated health complications, it is essential to identify reliable biomarkers that can aid in early detection, risk assessment, and monitoring of treatment outcomes.

The intricate interplay of metabolic illnesses is shown by the link between diabetes and obesity. Obesity and diabetes, especially type 2 diabetes, are commonly linked in both directions, creating a synergistic hub of metabolic dysregulation. Insulin resistance, a condition wherein cells in the body lose their sensitivity to insulin and blood glucose levels rise, is a feature shared by both disorders [1][3]. Obesity, especially visceral adiposity, is a significant risk factor for insulin resistance and type 2 diabetes. The similarities lie in the underlying mechanisms of inflammation and metabolic dysfunction, wherein adipose tissue plays a central role [11][12]. Despite these shared aspects, differences exist in the temporal progression and manifestation of these disorders. Biomarkers are measurable indicators that can reflect the presence, progression, or response to treatment of a disease. In the context of T2D and obesity, biomarkers hold immense potential for improving early detection, risk stratification, and personalized treatment approaches [1]. Firstly, T2D is often diagnosed in the late stages, after significant damage has occurred, leading to increased morbidity and mortality rates. Additionally, obesity, a major risk factor for T2D, is a complex condition with diverse underlying mechanisms and phenotypes. Biomarkers specific to obesity can aid in understanding its heterogeneity, allowing for targeted interventions and personalized approaches [1][3]. Secondly, biomarkers play a crucial role in monitoring disease progression and assessing treatment response. Traditional clinical parameters, such as blood glucose levels or body mass index, have limitations in capturing the multifaceted aspects of T2D and obesity [2]. Lastly, biomarkers have the potential to facilitate the development of innovative treatment therapies. Moreover, they can help identify possible treatment targets by clarifying the biological processes and mechanisms involved in T2D and obesity [12]. Notably, markers such as glucagon-like peptide-1 (GLP-1), glucose-dependent insulinotropic peptide (GIP), monocyte chemoattractant protein-1 (MCP-1), and insulin-like growth factor-binding protein 7 (IGFBP-7), while implicated in both diabetes and obesity, may exhibit distinct patterns and quantitative variations at different stages. Gaining an understanding of the complex roles played by these indicators in the complex landscapes of obesity and diabetes can help identify commonalities and differences between these related metabolic disorders [1][3][7][11][12][13].

2. GLP-1 Biomarkers in the Development of Metabolic Disorders

GLP-1 is a biomarker that has been extensively studied and identified as a potential factor associated with the development of metabolic disorders, including T2D and obesity. GLP-1 is an incretin hormone secreted by the intestinal L-cells in response to food intake. It plays a crucial role in regulating glucose homeostasis and insulin secretion.

2.1. GLP-1 and Its Impaired Function in T2D Patients

In individuals with type 2 diabetes, there is often a deficiency or impaired function of GLP-1, leading to reduced insulin secretion and impaired glucose control (**Figure 1**) [13][14]. Numerous scientific studies have investigated the role of GLP-1 in metabolic disorders. For example, a study by Drucker et al. demonstrated that GLP-1 receptor agonists such as exenatide and liraglutide improve glycemic control and promote weight loss in patients with type 2 diabetes [15]. These agonists mimic the action of endogenous GLP-1 and enhance insulin secretion, suppress glucagon release, delay gastric emptying, and promote satiety [16][17]. Another study by Nauck et al. showed that GLP-1 receptor agonists not only improve glycemic control but also have beneficial effects on cardiovascular outcomes, reducing the risk of major adverse cardiovascular events [18].

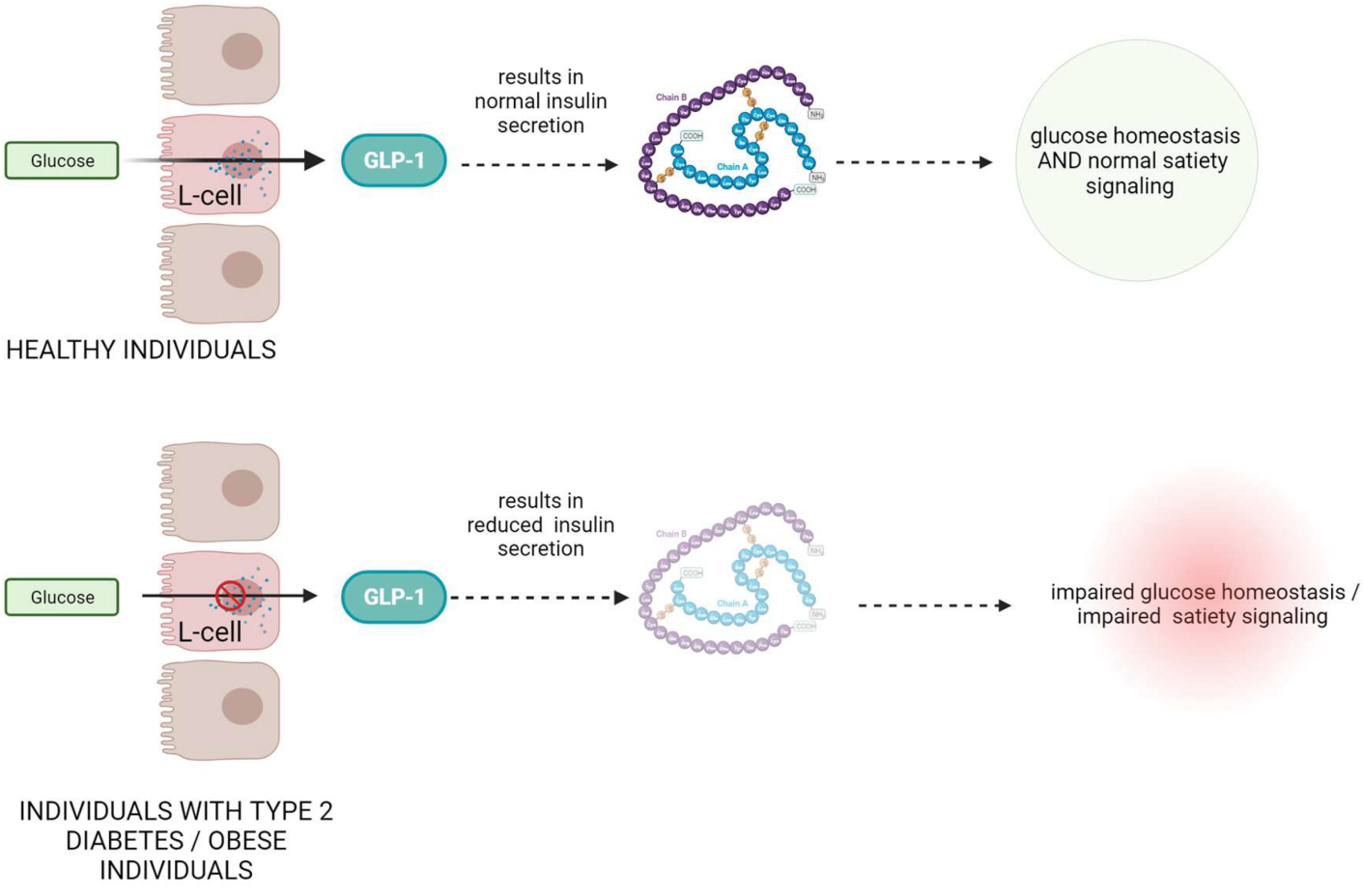

Figure 1. The role and mechanism of action of GLP-1 protein in healthy subjects and in patients with type II diabetes and obesity.

2.2. Dysregulated GLP-1 Secretion in Obese Patients

Moreover, GLP-1 has also been found to play a role in obesity. In obese individuals, GLP-1 secretion is often dysregulated, leading to reduced GLP-1 levels and impaired satiety signaling [19]. Research by Ard et al. demonstrated that administration of GLP-1 to obese individuals resulted in reduced food intake and increased feelings of fullness [20].

2.3. GLP-1 as a Therapeutic Hope

Additionally, GLP-1-based therapies have shown promising results in clinical trials. The LEADER trial, conducted by Marso et al. demonstrated that the GLP-1 receptor agonist liraglutide reduced the risk of major adverse cardiovascular events and cardiovascular mortality in patients with type 2 diabetes [21]. Another study by Davies et al. showed that exenatide, a GLP-1 receptor agonist, led to significant improvements in glycemic control and weight reduction in obese individuals with type 2 diabetes [22]. Further, they emphasize the potential of GLP-1 as an important biomarker for early diagnostics and therapeutic intervention in metabolic disorders [23][24][25][26].

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