

Pathological mechanisms in diabetes: A comprehensive insight

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Received: 10-Apr-2023, Manuscript No. FMDM-23-100905; **Editor assigned:** 12-Apr-2023, PreQC No. FMDM-23-100905 (PQ); **Reviewed:** 28-Apr-2023, QC No. FMDM-23-100905; **Revised:** 08-May-2023, Manuscript No. FMDM-23-100905 (R); **Published:** 15-May-2023, DOI: 10.37532/1758-1907.2023.13.488-489



Description

Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels resulting from impaired insulin secretion, insulin resistance, or a combination of both. The prevalence of diabetes has reached epidemic proportions globally, posing a significant burden on healthcare systems and individuals alike. Understanding the pathological mechanisms underlying diabetes is crucial for the development of effective therapeutic strategies. This article aims to delve into the intricate web of pathological mechanisms contributing to the development and progression of diabetes.

■ Insulin resistance

Insulin resistance lies at the heart of type 2 diabetes, the most prevalent form of the disease. In individuals with insulin resistance, the body's cells become less responsive to the action of insulin, leading to impaired glucose uptake. This resistance is primarily attributed to obesity, sedentary lifestyle, genetic predisposition, and chronic low-grade inflammation. Adipose tissue-derived pro-inflammatory cytokines, such as Tumor Necrosis Factor-alpha (TNF- α) and Interleukin-6 (IL-6), play a significant role in insulin resistance by interfering with insulin signaling pathways.

■ Beta cell dysfunction

In type 2 diabetes, beta cells, located in the islets

of Langerhans within the pancreas, fail to secrete adequate amounts of insulin to overcome insulin resistance. Several factors contribute to beta cell dysfunction, including chronic hyperglycemia, lipotoxicity, glucotoxicity, oxidative stress, and inflammation. These factors collectively impair beta cell function, reduce insulin synthesis and secretion, and eventually lead to beta cell apoptosis or death.

■ Chronic inflammation

Chronic low-grade inflammation is a prominent feature in both type 1 and type 2 diabetes. In type 1 diabetes, autoimmune destruction of pancreatic beta cells triggers an inflammatory response. In type 2 diabetes, adipose tissue inflammation and the release of pro-inflammatory cytokines contribute to systemic inflammation. This chronic inflammatory state further exacerbates insulin resistance, impairs beta cell function, and promotes the development of complications associated with diabetes.

■ Oxidative stress

Oxidative stress, characterized by an imbalance between the production of reactive oxygen species and the body's antioxidant defense mechanisms, plays a pivotal role in diabetes pathogenesis. Elevated glucose levels promote the generation of ROS, causing cellular damage and impairing insulin signaling pathways. Moreover, oxidative stress-induced DNA damage can lead to genetic mutations and further contribute to

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the development and progression of diabetes.

■ Endoplasmic reticulum stress

The endoplasmic reticulum is responsible for protein synthesis, folding, and quality control. In conditions of chronic nutrient overload, such as obesity and diabetes, the ER becomes overwhelmed, leading to ER stress. ER stress activates the unfolded protein response pathway, aiming to restore cellular homeostasis. However, prolonged or unresolved ER stress can lead to beta cell dysfunction, insulin resistance, and cell death.

■ Advanced glycation end products

The non-enzymatic reaction between glucose and proteins results in the formation of advanced glycation end products. AGEs accumulate in various tissues, contributing to the pathogenesis of diabetes and its complications. AGEs can induce oxidative stress, inflammation, and endothelial dysfunction, impairing vascular health and promoting the development of diabetic complications, including nephropathy, retinopathy, and neuropathy.