

Role of proinsulin: Therapeutic strategies in diabetes management

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Description

Proinsulin is a precursor hormone to insulin, playing a crucial role in the regulation of blood sugar levels in the body. While insulin is the primary hormone responsible for lowering blood sugar, proinsulin serves as its precursor, undergoing processing to form mature insulin within the pancreatic beta cells.

Proinsulin is a single-chain polypeptide hormone synthesized within the pancreatic beta cells in response to elevated blood glucose levels. It consists of three regions: The A chain, B chain, and C peptide. During synthesis, proinsulin undergoes proteolytic cleavage, resulting in the formation of insulin and C-peptide. Insulin is then released into the bloodstream, where it acts to lower blood sugar levels by promoting glucose uptake by cells. Two proteases work together to convert proinsulin to insulin during the maturation of secretory vesicles, and ionophores that interfere with intracellular H⁺ gradients prevent this conversion from happening. Patients with islet cell tumors (insulinomas), which produce insulin, may have high amounts of proinsulin. These patients experience hypoglycemia episodes as a result of the tumors' improper insulin secretion.

■ Role in diabetes

In individuals with diabetes, abnormalities in proinsulin processing and insulin secretion can occur, leading to impaired blood sugar control.

Elevated proinsulin levels: Insulin resistance and beta cell dysfunction in type 2 diabetes can

result in increased production and secretion of proinsulin relative to insulin. Elevated proinsulin levels are indicative of impaired beta cell function and insulin resistance.

Altered proinsulin-to-insulin ratio: Changes in the ratio of proinsulin to insulin may serve as a marker of beta cell dysfunction and insulin resistance in both type 1 and type 2 diabetes. An elevated proinsulin-to-insulin ratio is associated with poorer glycemic control and increased risk of diabetes-related complications.

Diagnostic marker: Measurement of proinsulin levels or the proinsulin-to-insulin ratio may be used in conjunction with other markers to assess beta cell function, insulin resistance, and diabetes risk. However, its clinical utility in diagnosis and management remains an area of ongoing research.

Beyond glucose regulation: In addition to its role in blood sugar control, proinsulin may have broader implications for health and disease:

Cardiovascular health: Emerging evidence suggests that proinsulin levels may be associated with cardiovascular risk factors, including hypertension, dyslipidemia, and endothelial dysfunction. Elevated proinsulin levels have been linked to an increased risk of cardiovascular disease independent of traditional risk factors.

Obesity and metabolic syndrome: Proinsulin levels are often elevated in individuals with obesity and metabolic syndrome, reflecting underlying insulin resistance and beta cell dysfunction. Targeting proinsulin processing



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pathways may hold promise for therapeutic interventions aimed at improving metabolic health.

Neurological disorders: Recent studies have explored the potential role of proinsulin in neuroprotection and synaptic plasticity within the central nervous system. Dysregulation of proinsulin processing has been implicated in neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease, highlighting its multifaceted roles beyond glucose metabolism.

Proinsulin serves as a critical precursor to insulin, playing a pivotal role in the regulation of blood sugar levels and overall metabolic health. Abnormalities in proinsulin processing and secretion are associated with diabetes, cardiovascular disease, obesity, and neurological disorders, underscoring its significance in health and disease. Further research into the mechanisms underlying proinsulin action may uncover novel therapeutic targets for the prevention and treatment of diabetes and its complications, as well as other related conditions.