

Inhibition of Glucagon Secretion by Insulin

Overview

Glucagon and **insulin** are two key hormones secreted by the **pancreas** that work **antagonistically** to regulate **blood glucose levels**:

- **Insulin** (from β -cells of Islets of Langerhans): Lowers blood glucose by promoting uptake and storage.
- **Glucagon** (from α -cells): Raises blood glucose by promoting glycogenolysis and gluconeogenesis.

Insulin not only lowers blood sugar but also plays a **paracrine role** in **inhibiting glucagon secretion**.

Mechanism: How Insulin Inhibits Glucagon Secretion

◆ 1. Paracrine Signaling in the Pancreatic Islets

- In the **islets of Langerhans**, α -cells (glucagon), β -cells (insulin), and δ -cells (somatostatin) are **closely positioned**.
 - **Insulin is secreted from β -cells**, and it acts **locally** (paracrine effect) on **neighboring α -cells** to **suppress glucagon release**.
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◆ 2. Direct Inhibition Mechanism

- **Insulin binds to insulin receptors** on α -cells.
 - This activates **intracellular signaling** (PI3K-Akt pathway).
 - Leads to:
 - **Hyperpolarization** of α -cell membrane.
 - **Inhibition of voltage-gated Ca^{2+} channels**.
 - $\downarrow$ Calcium influx $\rightarrow \downarrow$ **Glucagon exocytosis**.
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◆ 3. Indirect Inhibition

Insulin also inhibits glucagon via **indirect pathways**:

a. Increased Somatostatin Release

- Insulin promotes release of **somatostatin** from δ -cells.
- Somatostatin strongly inhibits glucagon secretion from α -cells.

b. Lowering Blood Glucose

- As insulin lowers blood glucose, it **removes the stimulus** for glucagon secretion (which is hypoglycemia).
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What Happens in Diabetes?

- In **Type 1 diabetes mellitus (T1DM)**:
 - $\downarrow$ Insulin $\rightarrow$ **uncontrolled glucagon secretion** $\rightarrow$ worsens **hyperglycemia**.

- In **Type 2 diabetes mellitus (T2DM)**:
Insulin resistance or β -cell dysfunction $\rightarrow$ **reduced inhibitory effect** on α -cells $\rightarrow$ **elevated glucagon**.

Summary Table

Hormone	Source	Function	Effect on Glucagon
Insulin	β -cells	$\downarrow$ Blood glucose	Inhibits glucagon via direct and indirect pathways
Glucagon	α -cells	$\uparrow$ Blood glucose	Opposes insulin

