

## Insulin Synthesis

Insulin is a hormone that is produced by beta cells in the pancreas. Insulin's functions are critical to cell survival and growth. Insulin starts as a single polypeptide called preproinsulin. Removal of the signal peptide sequence from preproinsulin in the rough endoplasmic reticulum yields proinsulin. Proinsulin undergoes modifications in the Golgi apparatus to yield insulin and C-peptide, which are packaged in endosomes ready for exocytosis. Beta cells release insulin and C-peptide when stimulated by calcium influx. Clinically, insulin and C-peptide levels are elevated in insulinoma while only insulin levels are elevated in surreptitious (exogenous) insulin use.



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## Synthesis

## Preproinsulin

### Pre-tattoo on Pro-bodybuilder with Insect-syringe

Preproinsulin is a proinsulin molecule with a signal peptide attached to its N-terminus. It is a biologically inactive precursor of insulin.

## Rough Endoplasmic Reticulum

## Rough-ER Building

Removal of the signal peptide from preproinsulin results in the formation of proinsulin in the rough endoplasmic reticulum of pancreatic beta cells.

## Proinsulin

## Pro-bodybuilder with Insect-syringe

Removal of the signal peptide from N-terminus of preproinsulin results in the formation of proinsulin.

## Golgi Body

## Golgi Post-office

Processing of proinsulin in the Golgi apparatus results in the formation of biologically active insulin. This processing involves the removal of the C-peptide and connection of the A- and B-chains through disulfide bonds.

## Beta Cells Release Insulin

### Beta-fish with Insect-syringe

Synthesis, storage, and release of insulin mainly take place in beta cells of the pancreas. Pancreatic beta cells are located in the islets of Langerhans. They make up the majority of the cells in the islets.

### Beta Cells Release C-peptide

## Beta-fish with Cat-pimp-tie

C-peptide is a short polypeptide that connects insulin's A-chain to its B-chain in the proinsulin molecule. C-peptide is released with insulin after the cleavage of proinsulin. Hence, C-peptide is a byproduct of endogenous insulin synthesis. This is important clinically as increased C-peptide levels reflect an increased endogenous production of insulin (e.g., insulinoma, sulfonylurea use). In contrast, exogenous insulin administration (e.g., a patient who overdosed on injected insulin) won't result in the elevation of C-peptide levels as exogenous insulin lacks C-peptide.

## Clinical Relevance

## Insulinoma

Insect-syringe-gnome Up-arrow Insect-syringe Up-arrow Cat-pimp-tie

An insulinoma is a tumor of the pancreas that is derived from the beta cells of the pancreas. This tumor secretes excessive amounts of insulin and can result in hypoglycemia. As the insulin is synthesized endogenously, C-peptide levels will be elevated.

### **Sulfonylureas**

[Sulfur-funnel-U-rainbow](#) [Up-arrow](#) [Insect-syringe](#)

Sulfonylureas (e.g. glyburide, glipizide) are medications used to treat diabetes mellitus. These drugs help to increase endogenous pancreatic secretion of insulin so insulin and C-peptide levels in a patient taking sulfonylureas should be high-normal or elevated.

### **Surreptitious Insulin Use**

[Syrup-tissues](#) [Insect-syringe](#) [Up-arrow](#) [Insect-syringe](#) [Down-arrow](#) [Cat-pimp-tie](#)

Surreptitious insulin use is characterized by high insulin levels and low C-peptide levels. Exogenous insulin doesn't contain C-peptide, and its ingestion results in increased total insulin levels, which suppresses the production of endogenous insulin due to feedback inhibition, hence C-peptide levels will be low.