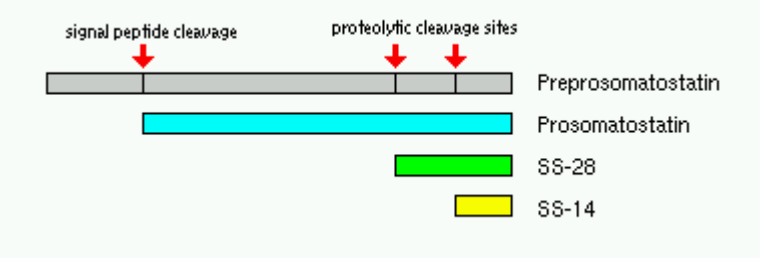
Endocrine Index Glossary

Somatostatin

Somatostatin was first discovered in hypothalamic extracts and identified as a hormone that inhibited secretion of growth hormone. Subsequently, somatostatin was found to be secreted by a broad range of tissues, including pancreas, intestinal tract and regions of the central nervous system outside the hypothalamus.

Structure and Synthesis

Two forms of somatostatin are synthesized. They are referred to as SS-14 and SS-28, reflecting their amino acid chain length. Both forms of somatostatin are generated by proteolytic cleavage of prosomatostatin, which itself is derived from preprosomatostatin. Two cysteine residules in SS-14 allow the peptide to form an internal disulfide bond.



The relative amounts of SS-14 versus SS-28 secreted depends upon the tissue. For example, SS-14 is the predominant form produced in the nervous system and apparently the sole form secreted from pancreas, whereas the intestine secretes mostly SS-28.

In addition to tissue-specific differences in secretion of SS-14 and SS-28, the two forms of this hormone can have different biological potencies. SS-28 is roughly ten-fold more potent in inhibition of growth hormone secretion, but less potent that SS-14 in inhibiting glucagon release.

Receptors and Mechanism of Action

Five stomatostatin receptors have been identified and characterized, all of which are members of the G protein-coupled receptor superfamily. Each of the receptors activates distinct signalling mechanisms within cells, although all inhibit adenylyl cyclase. Four of the five receptors do not differentiate SS-14 from SS-28.

Physiologic Effects

Somatostatin acts by both endocrine and paracrine pathways to affect its target cells. A majority of the circulating somatostatin appears to come from the pancreas and gastrointestinal tract. If one had to summarize the effects of somatostatin in one phrase, it would be: "*somatostatin inhibits the secretion of many other hormones*".

Effects on the Pituitary Gland

Somatostatin was named for its effect of inhibiting secretion of growth hormone from the pituitary gland. Experimentally, all known stimuli for growth hormone secretion are suppressed by somatostatin administration. Additionally, animals treated with antisera to

somatostatin show elevated blood concentrations of growth hormone, as do animals that are genetically engineered to disrupt their somatostatin gene.

Ultimately, growth hormone secretion is controlled by the interaction of somatostatin and growth hormone releasing hormone, both of which are secreted by hypothalamic neurons.

Effects on the Pancreas

Cells within pancreatic islets secrete insulin, glucagon and somatostatin. Somatostatin appears to act primarily in a paracrine manner to inhibit the secretion of both insulin and glucagon. It also has the effect in suppressing pancreatic exocrine secretions, by inhibiting cholecystokinin-stimulated enzyme secretion and secretin-stimulated bicarbonate secretion.

Effects on the Gastrointestinal Tract

Somatostatin is secreted by scattered cells in the GI epithelium, and by neurons in the enteric nervous system. It has been shown to inhibit secretion of many of the other GI hormones, including gastrin, cholecystokinin, secretin and vasoactive intestinal peptide.

In addition to the direct effects of inhibiting secretion of other GI hormones, somatostatin has a variety of other inhibitory effects on the GI tract, which may reflect its effects on other hormones, plus some additional direct effects. Somatostatin suppresses secretion of gastric acid and pepsin, lowers the rate of gastric emptying, and reduces smooth muscle contractions and blood flow within the intestine. Collectively, these activities seem to have the overall effect of decreasing the rate of nutrient absorption.

Effects on the Nervous System

Somatostatin is often referred to as having neuromodulatory activity within the central nervous sytem, and appears to have a variety of complex effects on neural transmission. Injection of somatostatin into the brain of rodents leads to such things as increased arousal and decreased sleep, and impairment of some motor responses.

Pharmacologic Uses

Somatostatin and its synthetic analogs are used clinically to treat a variety of neoplasms. It is also used in to treat giantism and acromegaly, due to its ability to inhibit growth hormone secretion.

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