Growth Hormone

Hypothalamus

GHRH, synthesized by neuroendocrine neurons in the hypothalamus, is released in a pulsatile manner into the hypophyseal portal circulation supplying the pituitary gland. Somatostatin, is also synthesized in neurons in the hypothalamus and serves to inhibit GH synthesis and release by the anterior pituitary gland.

GHRH ↓ SST

Anterior pituitary

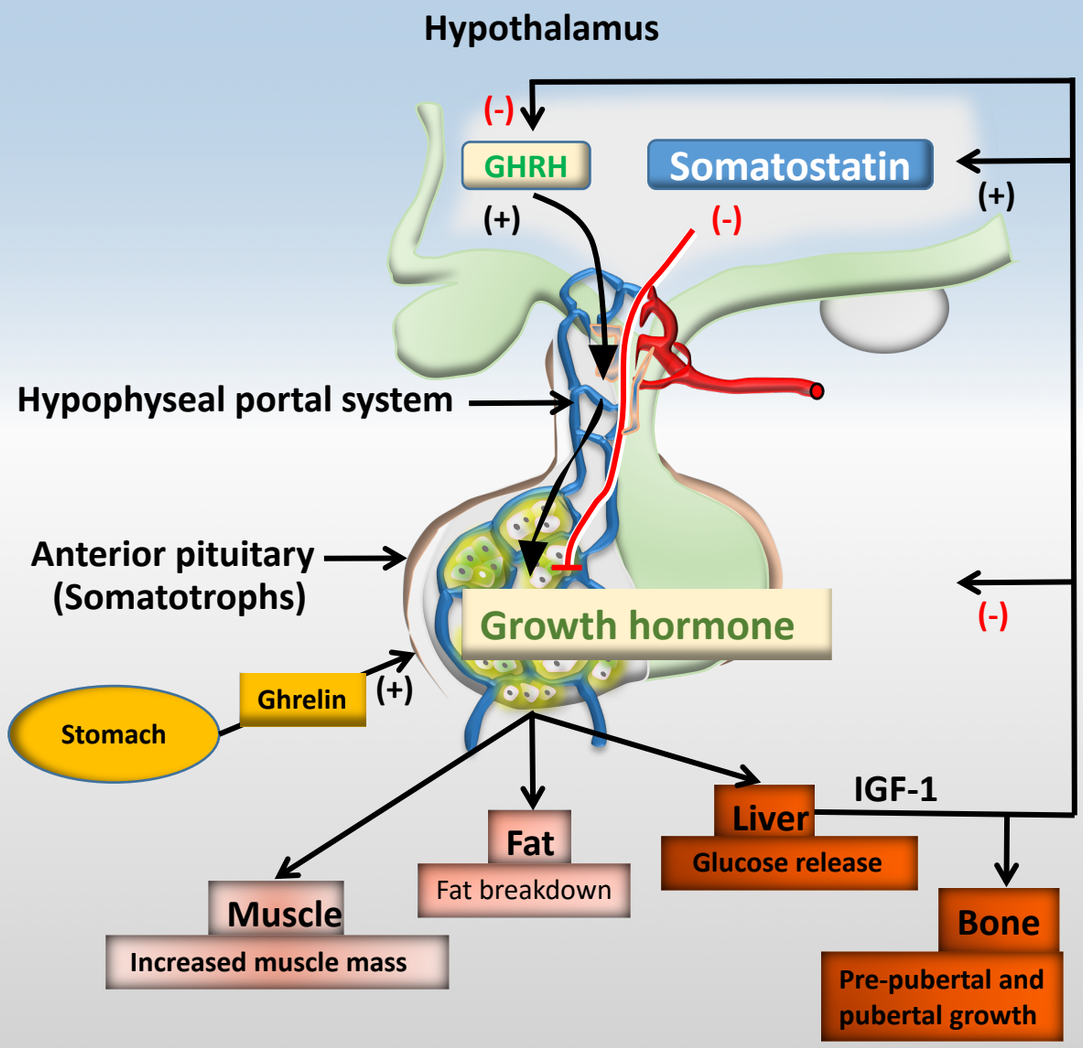
Somatotrophs in the anterior pituitary respond to both the stimulatory and inhibitory actions of GHRH and somatostatin, respectively, to regulate the episodic release of GH. Ghrelin from the stomach also modulates GH secretion, and GH itself has been implicated in auto-regulation by short and ultra-short feedback loops. Pulses of GH secretion typically have higher amplitudes during sleep, and GH pulses increase at puberty but decline with aging.

↓ GH

Target organs

Receptors for GH reside in many cell types throughout the body. In the liver, GH stimulates gluconeogenesis and elevates blood glucose levels. In fat, GH stimulates fat breakdown and in muscle, GH stimulates protein synthesis, leading to increased muscle mass. GH action on bone is largely indirect mediated by IGF-1 release from the liver. IGF-1, also serves as a negative feedback signal regulating GH release acting directly at the pituitary to block GH release and indirectly at the level of the hypothalamus.

GHRH: Growth hormone releasing hormone
SST: Somatostatin
GH: Growth hormone
IGF-1: Insulin-like growth factor 1



GH is released in pulses during development and adulthood, and the amplitudes of these pulses decline with aging. Suppression of GH release has profound effects on growth, energy homeostasis and muscle mass and should be considered a potential mechanism for any toxicant that reduces growth. Additionally, the HPT, HPG and HPA axes are involved in the regulation of growth and development.

It is paradoxical that toxicologists routinely gauge toxicity of xenobiotics by measuring changes in the rate of growth, yet pay little attention to the endocrine mechanisms that govern growth and energy homeostasis throughout life. It is not surprising that prolactin, structurally similar to GH has growth promoting effects in some tissues.

Drs. Grattan and Hovey, who are experts on prolactin, understand the complexity of the relationships between GH and prolactin. Drs. Handa, Cooper and Plant, experts in the HPA, HPT and HPG axes, respectively, understand the coordinated role of GH, thyroid hormone, corticosteroids and sex steroids in regulating growth and development.

Let the experts at QS³ assist you in interpreting the toxicological effects of your chemical on growth and development.