

Ghrelin: The Only Known Appetite-Stimulating Hormone

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Ghrelin is a peptide first identified in rat stomach. It is the only known appetite stimulating hormone. Ghrelin not only controls food intake and energy balance but also stimulates Growth Hormone secretion. It may be a further endocrine factor involved in control of steroidogenesis and gonadal functions. This paper includes ghrelin's properties, receptors, its affect on appetite and information to researchers who wants to determine ghrelin levels.
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Growth hormone secretagogues (GHS) stimulate GH secretion via a specific receptor.¹ GHS-receptor(GHS-R) had been cloned² and an endogenous ligand for GHS-R had been purified by Kojima et al. The scientists called the GH-releasing peptide "ghrelin" as ghre is the Proto-Indo-European root of the word "grow". Ghrelin is an acylated 28 amino acid peptide recently identified in rat stomach and its production has also been detected in hypothalamic neurons.³ This peptide which is a natural ligand for the Growth Hormone (GH)-secretagogue receptor, a G-protein coupled receptor primarily expressed in the pituitary and hypothalamus⁴ and has shown to be a potent stimulant of GH secretion.⁵ The peptide acts via activation of NPY/Agouti gene-related protein (AGRP) neurons in the hypothalamic arcuate nucleus.⁶⁻⁸

Apart from GH secretion stimulant effect, ghrelin has attracted attention for its involvement in the control of food intake and energy balance. In rodents, subcutaneous, intracerebroventricular and intraperitoneal administration of ghrelin stimulates feeding, reduces fat utilization and increases body weight.^{6,9-11} Ghrelin has been shown to be orexigenic when administered at approximately physiological doses in rodents.¹² and humans,⁷ suggesting that normal fluctuations of endogenous circulating ghrelin can affect appetite. In other words, ghrelin stands as the only known appetite stimulating hormone.^{6,9,10} As ghrelin is mainly produced in the stomach and major binding sites of ghrelin have been identified in hypothalamic areas, ghrelin might represent an important endocrine signal connecting peripheral mechanisms sensing caloric intake with brain centers controlling energy homeostasis.¹³

Plasma ghrelin levels are lower in obese human subjects,¹⁴ while in lean subjects, plasma ghrelin concentrations

rise progressively during fasting and fall to a nadir within an hour after eating, a pattern reciprocal to that of insulin.¹⁵ This observation supports the possibility that ghrelin may be a "trigger" for meal initiation¹⁶ and might play a role in human obesity.¹⁷ Circulating ghrelin levels increase in several models of negative energy balance, including low-calorie diets,¹⁸ cancer anorexia,¹⁹ cardiac cachexia²⁰ and anorexia nervosa.²¹ These findings suggest that ghrelin may participate in the adoptive response to weight loss and thus in long-term body-weight regulation.

Ghrelin also strongly binds to gonadal and adrenal human tissues.²² Tena-Sempere et al showed that ghrelin affects the chorionic gonadotropin- and cAMP-induced testosterone secretion in rat testis by inhibiting key enzymes of steroidogenesis.²³

In the light of these findings, researchers tried to find out circulating ghrelin levels in polycystic ovary syndrome (PCOS) patients and its change with weight loss. Pagotto et al, studied possible interactions among ghrelin, glucose homeostasis and reproductive system in obese women with PCOS and body mass index-matched controls. They found that obese PCOS women have lower ghrelin levels than those expected based on the presence of obesity. Only in obese-PCOS group, ghrelin levels negatively correlated with insulin sensitivity and regardless of the presence of PCOS, a marked negative correlation exists between ghrelin and androstenedione levels, suggesting an interaction between ghrelin and steroid synthesis or action.²⁴

Further studies are needed to address ghrelin's exact role not only in energy balance and metabolism but also in control of steroidogenesis and gonadal functions as well. Researchers who are willing to work on ghrelin and metabolism must know that radioimmuno assay (RIA) or RIA like Enzyme Linked Immunosorbent Assay (ELISA) commercial kits are available only for research purposes. Because active form of ghrelin molecule is very unstable and labile in serum/plasma due to the nature of octanoyl group on serine-3, blood samples must be collected in tubes containing special solutions which differ according to commercial kit. They must be chilled on ice, centrifuged. Specimens can be stored

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at 4°C if they will be tested within 4 hours. For longer storage, specimens should be aliquot and stored at <-20°C.

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