

# The Biochemistry of Hunger Stimulating Hormone: Why Understanding This Cascade In Hypothalamus Is Beneficial

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## Abstract

Ghrelin is the key hormone responsible for our hunger stimulate to food intake in body system. At present a huge number of people suffer from obesity, so understanding the mechanisms by which various hormones and neurotransmitters have influence on energy balance has been a subject of current research in neuroscience. At present ghrelin is the only known gastrointestinal hormone that increases food intake where Plasma ghrelin levels are inversely correlated with body weight and rise following weight loss in humans. It is a natural ligand of the growth hormone (GH) secretagogue (GHS) receptor type 1a (GHS-R1a). The GHS-R is highly expressed in the hypothalamus, but is also found in the brainstem, pituitary, GI tract, adipose tissue and other peripheral tissues. Ghrelin is still recognized as a potential drug target for weight regulation. The main objective of this is to summarize the current knowledge and optimize about the physiology and pathophysiology of ghrelin in food intake regulation.

**Keywords:** Ghrelin; Growth hormone; Neurotransmitter; Neuroscience

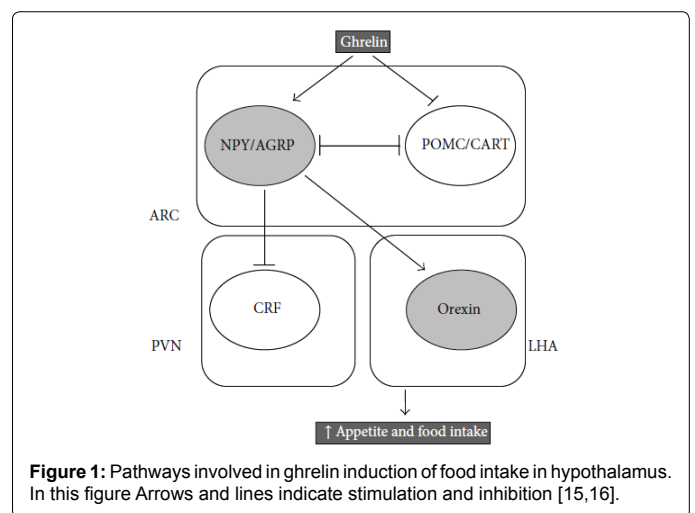
## Editorial

Ghrelin, the hunger hormone is a type of peptide hormone secreted by the ghrelinergic cells located throughout the GIT mostly from stomach & a lesser extent from duodenum. It acts as a neuropeptide in the CNS. Besides regulating appetite it also plays a significant role in regulating distribution and rate of use of energy. Ghrelin act as G-protein coupled receptor (GPCR) named Growth hormone secretagogue receptor (GHSR) or ghrelin receptor. It has 28 amino acids and containing an *n*-octanoyl group in the serine residue at position 3 [1-6]. It is reported that ghrelin is performed its action into various types of tissues such as duodenum, jejunum, ileum, colon, lung, heart, pancreas, kidney, testis, pituitary, and hypothalamus in the body system, moreover in the CNS system it expressed at low level [7-9].

Recent findings revealed that administration of ghrelin to rats induces food intake and reduction of energy expenses [10-14]. The major physiological and biological function of ghrelin includes growth hormone secretion, stimulation of food intake, gastric acid secretion, regulation of motility and the regulation of the endocrine and exocrine pancreatic secretions.

After crossing the blood-brain barrier ghrelin reaches in brainstem [17], and transmits its signal through the vagal nerve [18]. In hypothalamus, it activates the arcuate nucleus (ARC), paraventricular nucleus (PVN), dorsomedial region, central nucleus of amygdala, and the nucleus of solitary tract [19-20]. By stimulating the activity of NPY/AGRP neurons and decreasing the activity of POMC and CART neurons, ghrelin increases appetite and food intake [21-23]. AMPK is regulates the fuel availability by stimulating ATP producing pathways and inhibiting ATP consuming pathways [24]. After ATP depletion, AMP rises and induces the activation of AMPK by phosphorylation [25]. Activated AMPK then induces the phosphorylation of acetyl-CoA

carboxylase (ACC), which leading to the inhibition of ACC activity and the decrease in malonyl-CoA levels and finally resulting in increased fatty acid oxidation via the activation of carnitine-palmitoyl transferase 1 (CPT1) [26-27] (Figure 1).

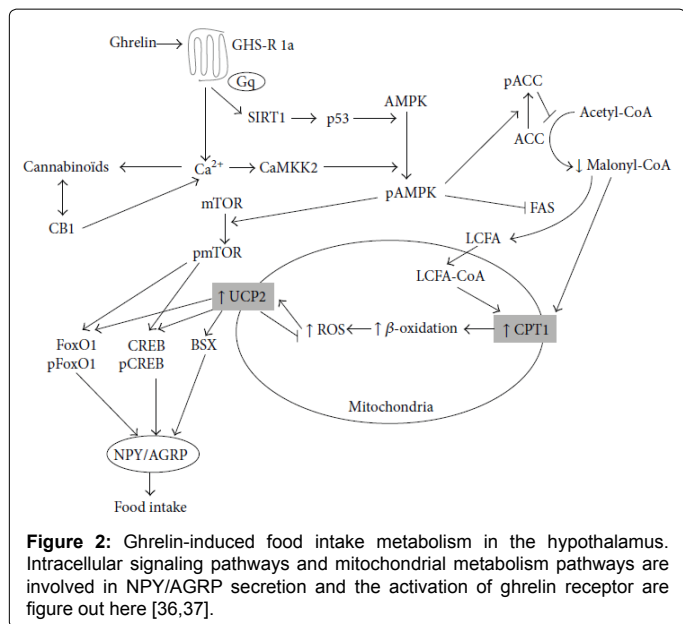


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From the literature review it is reported that, SIRT1 and p53 are required for ghrelin induced AMPK activation [28]. mTOR is regulated by the cellular AMP/ATP ratio; mTOR activity decreases when AMP/ATP is increases. On the other hand, mTOR activity increases when AMP/ATP ratio decreases [29] and is activated by AMPK [30]. Activated mTOR phosphorylates S6-kinase-1 (S6K1), S6 ribosomal protein (S6), and initiation factor 4E-binding protein (4E-BP1) [31-32]. It has been shown that hypothalamic mTOR signaling mediates the orexigenic action of ghrelin [33-34]. Then ghrelin-mediated mTOR activation induces the increase of CREB-pCREB, FoxO-pFoxO1, and BSX transcription factors which in turn activate NPY and AGRP synthesis and finally leading to food intake in body systems [35] (Figure 2).

## Summary

It is to be concluded that in the field of neuroscience ghrelin has attracted tremendous interest in research. This is the key hormone in regulation of energy homeostasis in human body. Current evidences show that ghrelin affects GH release, food intake, energy and glucose homeostasis, gastrointestinal, cardiovascular and immune functions, cell proliferation and differentiation, and cognitive behavior. Ghrelin is still recognized as a potential drug target for weight regulation. For its unique molecular structure, in near future it's possible to find out a breakthrough in the regulation of hunger stimulate, weight control and proper management of food intake in obese and anorexia patient by understanding its biochemical and pathophysiological mechanism.

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