ROLE OF ASPROSIN IN OBESE CHILDREN AND METABOLIC SYNDROME

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Abstract:
Asprosin is an adipcytokine that target many organs ,stimulate appetite leading to weight gain and influence glucose metabolism and insulin resistance.

Keywords: Asprosin, obesity, metabolic syndrome.

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Introduction:

One recent player in the metabolic game is asprosin. Asprosin is a fasting-induced protein hormone secreted by the adipose tissue and recruited by the liver. Protein hormones are a subclass of hormones that usually use a cell-surface receptor to bind to the target cell, using a secondary messaging system they stimulate rapid signal transduction. Most of protein hormones result from the cleavage of larger proteins; asprosin is the result of the C-terminal cleavage product of profibrillin (encoded by FBN1) and exemplifies a glucogenic protein hormone. It was first described in Neonatal Progeroid Syndrome (NPS), which is associated with FBN1 truncating mutations which results in the ablation of asprosin. Ablation of asprosin is accountable for a distinctive symptom of NPS: subcutaneous lipoatrophy **(1).**

Asprosin circulating levels are increased by fasting as a response to the low plasma glucose concentrations. In the liver, it bounds to a G-protein-coupled receptor—later known to be OLFR734 and activates the G protein-cAMP-PKA pathway resulting in the secretion of hepatic glucose. (Fig.1).

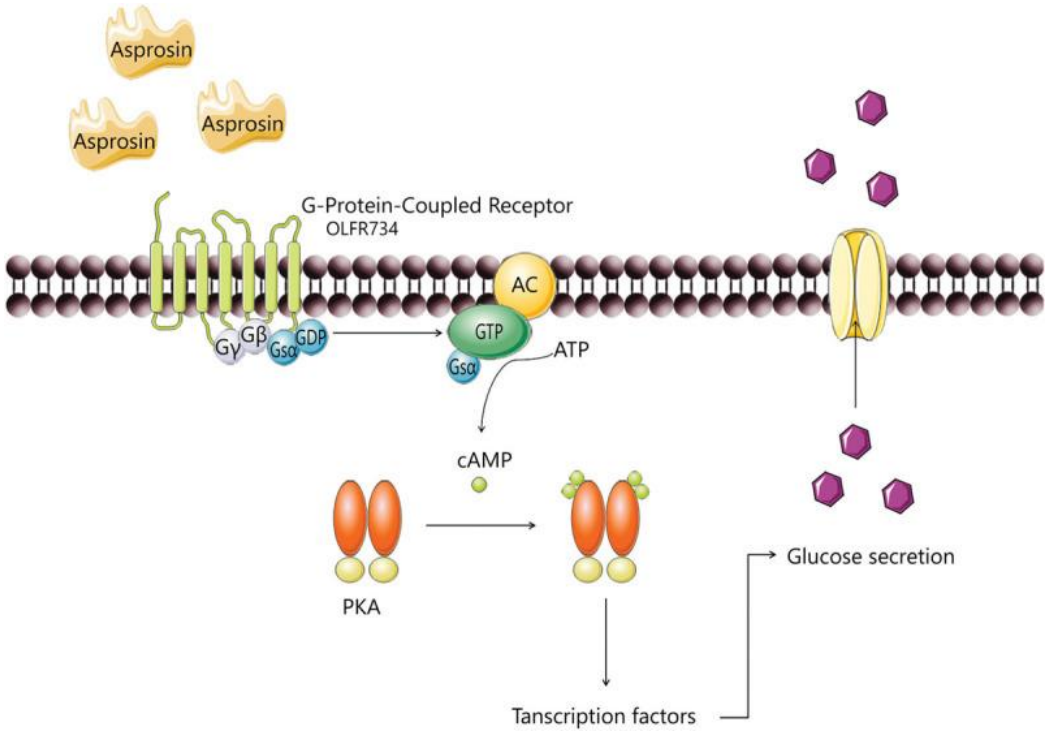

Figure 1

Asprosin pathway in the hepatocyte. G-protein-coupled receptors are activated and adenylyl cyclase (AC) synthesizes cAMP from ATP that binds to subunits of PKA, catalytic subunits will be released, will translocate to the nucleus, phosphorylating and subsequently activating the transcription factors. This downstream pathway will enhance the hepatic glucose release. Adapted from **(2).**

Asprosin and obesity

It has been reported that asprosin is also an orexigenic hormone and stimulates the increase in food consumption and body weight gain . Secreted asprosin reaches to the liver and triggers glucose release in response to low dietary glucose. In response to insulin, the liver stocks excess glucose in glycogen form following by the meal. In fasting, the liver is induced to break down the stored glycogen and secrete glucose, as well as synthesizing new glucose. The secreted . Research & Reviews in Health Sciences 55 glucose into the circulation so that the brain and other organs that utilize from the glucose can maintain their normal function **(3).** Glycogenolysis and gluconeogenesis are stimulated by hormones such as glucagon, which induce the cyclic AMP pathway in liver, and cAMP supports the activation of metabolic process that lead to glucose production and secretion; asprosin seems to use the same control system . One of the pathologies in which the hormone asprosin is most effective is obesity and metabolic syndrome. Metabolic syndrome affects 25% of the population in developed and underdeveloped countries and increases the risk of death due to cardiovascular diseases three times. The impaired glucose homeostasis seen in metabolic syndrome and obesity directs researchers to conduct new studies on this subject.

For example, **Wang et al. (4)** found in their study that there is a positive correlation between increased waist circumference, triglyceride level, HOMA-IR index and fasting plasma glucose, and increased asprosin level in those newly diagnosed with type 2 diabetes and people with impaired glucose regulation **(4).** Therefore, it is seen that there is a strong relationship between increased asprosin level, type 2 diabetes, and therefore metabolic syndrome and obesity **(3).**

Asprosin and obesity management

Obesity is one of the main features in MetS, and already considered a growing epidemic and a public health problem. One target organ in the management of adiposity is the central nervous system: the response of hypothalamus to neurotransmitters released by the gastrointestinal tract plays a key role in energy homeostasis and appetite control**(1).**

Appetite control is a complex neurometabolic network of physiology pathways in response to fasting hormones. Duerrschmid et al demonstrated that asprosin is able to cross the blood–brain barrier (BBB) and activate the hypothalamic feeding system and provoke appetite stimulation. The hypothalamus system responsible for appetite control consists on the regulation of NPY/AgRP$^+$ (orexigenic) and POMC/CART (Anorexigenc) neurons. The experiments carry by Duerrschmid et al in mice model observed that asprosin, not only activated AgRP+ neurons, (only ~50% were asprosin responsive by cells which contain the components necessary for transducing the asprosin-dependent signal) via a G-protein, adenylate cyclase, cAMP, and PKA pathway, but also inhibited ~85% of the POMC$^+$ neurons. The balance resulted in appetite stimulation (Fig.2).

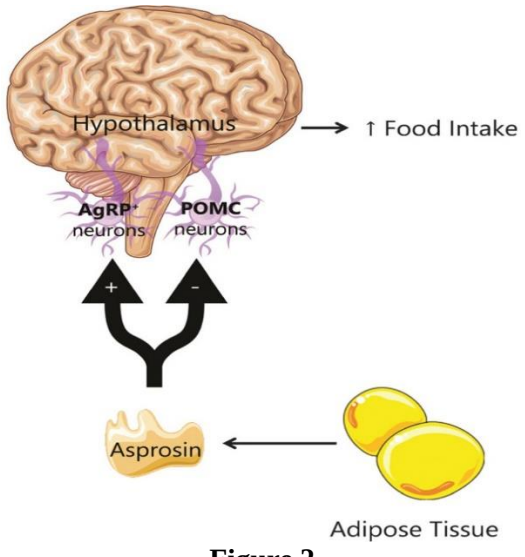

Figure 2

In the hypothalamus, asprosin released from the adipose tissue activates AgRP$^+$ neurons and inhibits the POMC neurons, leading to increased appetite. Adapted from **(5).**

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