ACTA SCIENTIFIC NUTRITIONAL HEALTH

Volume 3 Issue 6 June 2019

Short Communication

Kiss Peptin: The Gatekeeper of Puberty

Divya R[1], Rajajeyakumar M[2]* and Ashok V[3]

[1]Assistant Professor, Department of Physiology, Karpagam Faculty of Medical Sciences and Research, Coimbatore, India. (Affiliated by Dr. MGR Medical University, Chennai)

[2]Assistant Professor, Department of Physiology, Trichy SRM Medical College Hospital and Research Centre, Trichy, India (Affiliated by Dr. MGR Medical University, Chennai)

[3]Assistant Professor, Biochemistry, Karpagam Faculty of Medical Sciences and Research, Coimbatore, India (Affiliated by Dr. MGR Medical University, Chennai)

***Corresponding Author:** Rajajeyakumar M, Assistant Professor, Department of Physiology, Trichy SRM Medical College Hospital and Research Centre, Trichy, India (Affiliated by Dr. MGR Medical University, Chennai).

Received: April 23, 2019; **Published:** May 09, 2019

Discovery of kisspeptin/Metastin

In 1996, Scientists identified Kisspeptin 54 as a tumor metastasis suppressor in melanoma cell lines without affecting tumorigenicity. It was termed as Metastin as it supressed tumor metastasis. It also regulates cell migration in physiological condition such as trophoblast invasion in pregnancy and pathological conditions such as tumors [1].

A neuropeptide hormone

Kisspeptin is a newly discovered reproductive neuropeptide hormone encoded by the KiSS-1 gene [2]. human and non-human genes for kisspeptins are KISS1 and Kiss1 respectively [3]. Human KISS1 gene maps to chromosome 1q32 [1]. The gene products of KISS1 and Kiss1 are together referred to as kisspeptins [3]. Kisspeptins are expressed in the hypothalamus, gonads, placenta, liver and pancreas [4].

Kisspeptin receptors and kisspeptin system

The Kisspeptins binds with the endogenous receptors, KISS1R/Kiss1r.The human kisspeptin receptors are KISS1R, non-human receptors are Kiss1r.[3] These receptors are located in the hypothalamus, pituitary gland, kidney, gonad, pancreas and placenta.[4]In 1999, GPR54 was cloned as an orphan receptor. Apart from KISS1 receptors, Kisspeptins also binds and activates the G protein-coupled receptor, GPR54. The KISS1/G protein-coupled receptor-54(GPR54) is called the kisspeptin system which has lately been denoted as an indispensable concierge of onset of puberty and secretion of gonadotropin [1].

Endogenous kisspeptin neurons

Kisspeptins and their receptors are expressed by neurons in the in the arcuate and anteroventral periventricular nuclei of the hypothalamus, basal ganglia and amygdala [3,4].

Physiological actions of Kisspeptin

Sexual dimorphism

The Hypothalamus Kisspeptins neuron are critical for brain gender differentiation which functions through the regulatory secretion of Testosterone during the postnatal period of development [1]. The variance in neuroanatomy of kisspeptin system amounts for HPG axis sexual dimorphism between genders [3].

Secretion of reproductive hormones

- Kisspeptin neurons synapses with and acts upstream of gonadotrophin-releasing hormone (GnRH) expressing neurons. This tempers the release of luteinising hormone (LH), follicle-stimulating hormone (FSH) thus playing a most important part in maturation and function of the reproductive axis [3].
- Periventricular hypothalamic neurons are synapsed with the SON and paraventricular nuclei, that modulates the peripheral release of Oxytocin and Vasopressin [5].

Puberty

Kisspeptins are involved in in uterosexual growth and development. Maturation of kisspeptin neurons and their interaction with leptin are essential for puberty onset [3].

Sexual and bonding stimuli

Due to the expression of kisspeptin receptors in limbic cortex, it acts as a neuroendocrine modulator of the limbic brain activity thereby regulating the human behavior and human brain sexual-processing network. It acts as an integrating grid between reproduction, sexual response and bonding [2].

Olfaction

Odour informantion is transmitted to the GnRH neurons by the projections between the kisspeptin neurons in amygdalaand GnRH neurons in the preoptic area. This synchronises the apt response to odour cues [4].

Energy homeostasis

Reproductive system and the Energy homeostasis are interlinked. Research proves that Hypogonadotropic hypogonadism (HH) occurs more commonly in energy-deprived states. Animal studies shows that in energy-deprived sheeps and rats, levels of hypothalamic Kiss1 mRNA were markedly reduced which led to fall in levels of LH that caused arrest of puberty. After administration of kisspeptin, gonadotrophin levels normalised puberty was resumed, Interactions between kisspeptins and leptin may account for these observations [3].

Ovulation

The Pulsatile GnRH stimulates secretion of LH and FSH. Slow GnRH pulsatility (< 1 pulse per 2 to 3 hours) favors secretion of FSH, fast GnRH pulsatility (> 1 pulse per hour) stimulates LH secretion. Frequency of GnRH pulses varies throughout the menstrual cycle, which controls the differential secretion of pituitary gonadotropins [1].

Lactation

Rather than acting as a neuropeptide, Kisspeptin10 acts as a hormone on peripheral target cells, this activates oxytocin neurons indirectly. Recent studies shows that Kisspeptin-induced secretion of oxytocin is essential for parturition and lactation. it is also found out that Kisspeptin expression plays a major role in lactational anovulation [1].

Aging

Research advocates that age-related deterioration in reproductive competence may result, due to modifications in circadian signaling by the Kisspeptin system [1].

Role of Kisspeptin in Reproductive disorders

- **Idiopathic Hypogonadotropic hypogonadism (IHH):** mutations of kisspeptin receptor gene (KISS1R) is related to pubertal failure.
- **Polycystic Ovarian Syndrome (PCOS):** Slterations in Kisspeptin signalling pathway results in PCOS. Ovarian Kisspeptin alterations may lead to development of ovarian PCOS phenotype.
- **Central Precocious Puberty (CPP):** KISS1 mutations that leads to premature reactivation of the hypothalamic-pituitary-gonadal axis results in development of precocious puberty phenotype [1].

Therapeutic role of kisspeptin

Kisspeptin has been implicated in the regulation of puberty onset, ovarian function, trophoblast invasion, fertility regulation, parturition, and lactation. The Kisspeptin and its agonists/antagonists may be used in treatment for reproductive disorders that are categorized by increased or decreased GnRH pulsatility. kisspeptins can also be used to treat precocious puberty, contraception, sex steroid-dependent tumours, infertility and suppression of metastatic cancers [3]. Further scientific studies are warranted to determine if Kisspeptin can be used in unification with already existing gold-standard therapeutic approaches for treatment of reproductive disorders [1].

Bibliography

1. Zeydabadi Nejad S., *et al*. "The Role of Kisspeptin in Female Reproduction". *International Journal of Endocrinology and Metabolism* 15.3 (2017): e44337.
2. Comninos AN., *et al*. "Kisspeptin modulates sexual and emotional brain processing in humans". *Journal of Clinical Investigation* 127.2 (2017): 709-719.
3. Tng EL. "Kisspeptin signalling and its roles in humans". *Singapore Medical Journal* 56.12 (2015): 649-56.
4. Pineda R., *et al*. "Amygdala Kisspeptin Neurons: Putative Mediators of Olfactory Control of the Gonadotropic Axis". *Neuroendocrinology* 104 (2017): 223-238.
5. Armstrong WE. "Kisspeptin: a new peptidergic system regulating oxytocin neurons and their reproductive plasticity in the hypothalamo-neurohypophysial system". *Journal of Physiology* 595.3 (2017): 611-612.

Volume 3 Issue 6 June 2019