L

Luteinizing Hormone

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Synonyms

Interstitial cell-stimulating hormone; Lutrophin; Lutropin

Definition

Luteinizing hormone (LH) is secreted by the anterior pituitary and plays a role in reproductive functions such as ovulation in females and synthesis of androgens in males.

Introduction

The endocrine system plays an imperative role in the management of the human reproductive cycle. LH along with the two other gonadotropin hormones, follicle-stimulating hormone (FSH) and human chorionic gonadotropin (hCG), are essential for the regulation of sexual and reproductive functioning. LH has an important evolutionary function as it acts on both male and female gonads (testes or ovaries). It plays key roles in biological processes such as sex steroid synthesis (for both sexes) and the critical reproductive mechanism of ovulation in females.

Biochemical Profile of LH

LH along with FSH are both stored in the anterior segment of the pituitary gland – pea-sized endocrine gland sitting at the base of the brain. Their secretion is stimulated by gonadotropin-releasing hormone (GnRH) secreted by the hypothalamus into the pituitary via the hypophyseal portal system (Martini et al. 2012). LH is a member of a heterodimeric glycoprotein family along with thyroid-stimulating hormone (TSH) and the other gonadotropin hormones (Choi and Smitz 2014). Members from this hormone family all share the same 92-amino acid α subunit, yet they each have their own respective hormone-specific β subunit that garners receptor specificity and subsequent functional specificity (Choi and Smitz 2014). In humans, the gene sequence encoding for the LH β subunit is located among a cluster of gene sequences on chromosome 19q13.32. Transcription of the LH β subunit is particularly important as it also happens to be the

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step in which production rates of LH are modulated (Choi and Smitz 2014). The structure of the highly conserved β subunit amino acid sequence is what provides LH with its essential biochemical behavior and function (Choi and Smitz 2014). Additionally, hCG has a 145 amino acid sequence coded from other genes among the aforementioned gene cluster but in the case of LH, this polypeptide is cleaved, thus shortening it to the complete 121 amino acid polypeptide used to form LH. This cleavage of the polypeptide ultimately results in a shorter circulating half-life for LH compared to hCG. This shorter half-life is key in generating the release of LH in the form of pulses that work in direct accordance with GnRH pulses (Choi and Smitz 2014; Martini et al. 2012). The release of LH in a pulsatile fashion as opposed to a constant secretion is fundamental since GnRH pulses and corresponding LH pulses vary in frequency (amount released per minute) and amplitude (amount released per pulse), which ultimately drive cellular responses and the regulation of the reproductive cycle at its various stages, especially in females (Martini et al. 2012). LH exerts its action by binding the transmembrane LH/chorionic gonadotropin receptor (LHCGR) that is expressed in thecal cells, luteal cells, and differentiated granulosa cells of the ovaries as well as in interstitial cells of the testes, which is why LH is sometimes referred to as interstitial cell-stimulating hormone among males (Choi and Smitz 2014). This causes a conformational change in the receptor that activates a stimulatory G protein, which in turn activates enzymes such as adenylate cyclase and phospholipase C (Choi and Smitz 2014). Signal transduction pathways such as the phospholipase C/inositol phosphate pathway, the cyclic adenosine monophosphate/protein kinase A pathway, and the extracellular signal-regulated kinase 1/2 pathway result in proliferation and differentiation of the respective LHCGR expressing cells. These cellular developments consequently lead to maturation of the ovarian follicle and residing oocyte throughout the female menstrual cycle (Brown et al. 2010) as well as the regulation of sex steroid production in male testes.

LH Isoforms

Hormones such as LH exist within the human body as a conglomeration of isoforms (i.e., different forms of the same protein) that are created by natural gene sequence variation, metabolism of the hormone, or by posttranslational modification (Choi and Smitz 2014). Posttranslational modification has yielded in the upward range of 30 various LH isoforms and this is achieved mostly by the addition of carbohydrate side chains that are typically sialic and sulfonic acid compounds (Choi and Smitz 2014). These modify the hormones' biopotency (represented indirectly by bioactive-to-immunoreactive LH ratios [B/I]) and serum half-life. Sialylation extends longevity of the hormone in blood serum while sulfonation shortens it (Choi and Smitz 2014).

Differences and variations between isoforms do exist between the sexes and within the female sexes' own reproductive cycle. During the luteal phase, B/I is low but begins to rise as the follicular phase progresses until it peaks at mid-cycle, which corresponds appropriately with the marked decrease in sulfonation and subsequent high concentration of circulating LH that is associated with ovulatory induction and the LH surge (Choi and Smitz 2014). Men, on the other hand, tend to have greater B/I and LH sialylation than premenopausal women but age progression is yet another factor that influences the LH parameters between the sexes (Choi and Smitz 2014). Women undergo an actual rise in LH B/I after menopause and an increase in LH sialylation and sulfonation, thus they carry a more acidic LH profile (Bergendah and Veldhuis 2001). Men, on the other hand, actually experience a decrease or unchanged B/I as they age (Bergendah and Veldhuis 2001). Furthermore, LH variants yielded from genetic sequence variations/mutations also have implications to both male and female reproductive function and success as these variants are

frequently associated with fertility problems and dysfunctional LH properties. A common LH variant derived from a mutation in the β subunit gene sequence has been associated with female subfertility and menstrual irregularity (Bergendah and Veldhuis 2001). In men, this same variant has been associated with the development of generally less favorable traits such as smaller testis, shorter stature, decreased serum insulin-like growth factor binding protein-3, and slowed linear growth rates (Bergendah and Veldhuis 2001).

Basic Reproductive Function

Evolution hinges upon reproductive fitness – the capacity of an individual to successfully pass on their genes to offspring. LH plays a crucial role in this process by acting as a precursor to important sex hormones involved in this process. The fundamental purposes of LH for the reproductive functions of adult women and men differ with respect to the obvious distinctions between male and female reproduction. In women, LH works to assist FSH in follicle stimulation and it also has the imperative role of stimulating ovulation and release of the ovum (Martini et al. 2012). This is accomplished by a large LH surge garnered by the positive feedback activity of rising estrogen on the pituitary, which triggers completion of meiosis I in the primary oocyte, rupture of the follicular wall, and subsequent ovulation 9 h proceeding peak LH levels (Martini et al. 2012). In the postovulatory phase, LH subsequently forms/maintains the corpus luteum by promoting progesterone secretion (Martini et al. 2012). The corpus luteum is a small yellowish hormone secreting structure that is formed from the remainder of the sac/follicle that once held the developing ovum. It functions in releasing large amounts of progesterone and small amounts of estrogen, which are critical to implantation and preparation for pregnancy (Martini et al. 2012). In men, LH is needed for androgenization during puberty, sexual differentiation, and sexual functioning. Male fertility is closely tied to adequate LH functioning since it is the precursor to testosterone, which in turn is crucial for sperm production, sperm motility, and energy acquisition by the way of augmenting sperm fructolysis and adenyl cyclase activity (Ramanujam et al. 2000).

Indirect-Reproductive Adaptive Functions

LH appears to serve an important role in fertility-contingent shifts in women's reproductive physiology and psychology across the phases of the menstrual cycle. For instance, women in the periovulatory phase (i.e., around ovulation) of the menstrual cycle when there is a surge in LH, experience changes in body odor (Miller and Maner 2010), adorn more promiscuous clothing (Durante et al. 2008), and are more flirtatious (Cantú et al. 2014). This research tends to be guided by the ovulatory shift hypothesis (Gangestad et al. 2005), from which it is argued that as the likelihood of conception increases toward ovulation pair-bonded women are predicted to be more attracted to men possessing characteristics putatively associated with good genes (Gildersleeve et al. 2014). This effect is argued to be most pronounced when evaluating a man's desirability as a short-term partner and absent, or heavily attenuated, when assessing his desirability as a long-term mate. This is because women may only obtain genetic benefits from a mate when fertile. For example, men found women's body odors to be more attractive during the periovulatory phase (higher LH) relative to women in a low fertile phase (lower LH) of the menstrual cycle (e.g., luteal phase; Gildersleeve et al. 2012). During the periovulatory phase, relative to the luteal phase, women have also been shown to experience greater interpersonal closeness and satisfaction with their current relationships when pair-bonded to a sexually attractive mate (Larson et al. 2013).

To detect ovulation, researchers use different counting methods to approximate women's menstrual cycle phase position; however, investigators have tended not to verify these estimates using LH test strips to verify whether a surge in LH and ovulation have actually occurred or not (Jones et al. 2019). Recent tests of the ovulatory shifts

hypothesis using larger samples, within-subject designs, and LH test strips are casting some doubt on the robustness of earlier evidence. Another challenge with this research is that fertility-contingent shifts in women's mating is influenced by several interrelated complex hormonal mechanisms and not just LH, such as estradiol, progesterone, and oxytocin (Jones et al. 2019).

The impact of LH on men's mating physiology and behavior is also somewhat unclear. Earlier researchers found that increases in men's LH corresponded to viewing sexually explicit material and heightened ratings of sexual arousal (LaFerla et al. 1978). Increases in men's luteinizing hormone-releasing hormone (LHRH) were also found in anticipation of viewing erotic stimuli (Evans and Distiller 1979). It is difficult to gauge the validity of these earlier studies because they are hampered by small sample sizes and low statistical power. In contrast, LHRH agonists (increasing the binding potential of LHRH) have been shown to lower sexual thoughts and behavior among male sexual offenders (Turner and Briken 2018). Elevated LH levels may also be a reliable biomarker of hypogonadism (impaired sexual function) in older men (see Giannetta et al. 2012). These latter results suggest an inverse relation between heightened LH and decreased sexual arousal and mating effort. It is evident that more work is needed to examine the relations between men's LH levels and their reproductive physiology and psychology, which are complicated by the pulsatile release of this hormone.

Indirect Immune Function

Immune function has been linked to the reproductive hormones of males and females, with LH playing a contributory and noncausal role, as a precursor hormone. Estrogen acts as an immunoenhancing hormone by regulating B cell function, preventing selection of autoreactive B cells, and inducing a Th2 immune response, which includes various Interleukins (IL) that play an important role in immune/B cell function (Taneja 2018). Furthermore, estrogen stimulates T-lymphocyte homing via expression of the CCR5 gene (Taneja 2018). In contrast, testosterone, which is known widely for its immunosuppressive effects in human males and does so by evoking a Th1 immune response, reduces the action of natural killer cells and tumor necrosis factor-alpha (Taneja 2018). Testosterone also enhances the production of the anti-inflammatory IL-10, which inhibits many important immune cells (Taneja 2018). The obvious immunomodulating differences of the reproductive hormones imply an evolutionary link between LH and immune function, due to the principal actions of its downstream hormones.

Areas of Future Inquiry

Scientific evidence of LH's direct immune functions in humans is sparse and limited, but over the past decades animal researchers have suggested potential links between LH as a causal agent of immune function. For example, LH supplementation was found to promote fetal tolerance in abortion-prone female mice (Schumacher et al. 2014). It did so by increasing the number of regulatory T cells, and by reducing the effects of the tolerogenic dendritic cells – antigen-presenting cells (Schumacher et al. 2014). Lastly, areas of future inquiry may prove beneficial by investigating the direct immunological effects of endogenous LH in humans.

Cross-References

- ▶ Fertility
- ▶ Menstrual Cycle
- ▶ Ovulation
- ▶ Sexual Signaling During Ovulation

References

Bergendah, M., & Veldhuis, J. D. (2001). Is there a physiological role for gonadotrophin oligosaccharide heterogeneity in humans?: III. Luteinizing hormone heterogeneity: A medical physiologist's perspective. *Human Reproduction, 16*(6), 1058–1064.

Brown, C., LaRocca, J., Pietruska, J., Ota, M., Anderson, L., Smith, S. D., Weston, P., Rasoulpour, T., & Hixon, M. L. (2010). Subfertility caused by altered follicular development and oocyte growth in female mice lacking PKBalpha/Akt1. *Biology of Reproduction, 82*(2), 246–256.

Cantú, S. M., Simpson, J. A., Griskevicius, V., Weisberg, Y. J., Durante, K. M., & Beal, D. J. (2014). Fertile and selectively flirty: women's behavior toward men changes across the ovulatory cycle. *Psychological Science, 25*(2), 431–8. https://doi.org/10.1177/0956797613508413.

Choi, J., & Smitz, J. (2014). Luteinizing hormone and human chorionic gonadotropin: Origins of difference. *Molecular and Cellular Endocrinology, 383*(1–2), 203–213.

Durante, K. L., Li, N. P., & Haselton, M. G. (2008). Changes in women's choice of dress across the ovulatory cycle: naturalistic and laboratory task-based evidence. *Personality & Social Psychology Bulletin, 34*(11), 1451–60. https://doi.org/10.1177/0146167208323103

Evans, I. M., & Distiller, L. A. (1979). Effects of luteinizing hormone-releasing hormone on sexual arousal in normal men. *Archives of Sexual Behavior, 8*(5), 385–395.

Gangestad, S. W., Thornhill, R., & Garver-Apgar, C. (2005). Adaptations to Ovulation: Implications for Sexual and Social Behavior. *Current Directions in Psychological Science, 14*(6), 312–316. https://doi.org/10.1111/j.0963-7214.2005.00388.x.

Giannetta, E., Gianfrilli, D., Barbagallo, F., Isidori, A. M., & Lenzi, A. (2012). Subclinical male hypogonadism. *Best Practice & Research Clinical Endocrinology & Metabolism, 26*(4), 539–550.

Gildersleeve, K. A., Haselton, M. G., Larson, C. M., & Pillsworth, E. G. (2012). Body odor attractiveness as a cue of impending ovulation in women: Evidence from a study using hormone-confirmed ovulation. *Hormones and Behaviour, 61*(2), 157–166.

Gildersleeve, K., Haselton, M. G., & Fales, M. R. (2014). Do women's mate preferences change across the ovulatory cycle? A meta-analytic review. *Psychological Bulletin, 140*(5), 1205–1259.

Jones, B. C., Hahn, A. C., & DeBruine, L. M. (2019). Ovulation, sex hormones, and women's mating psychology. *Trends in Cognitive Sciences, 23*(1), 51–62. https://doi.org/10.1016/j.tics.2018.10.008.

LaFerla, J. J., Anderson, D. L., & Schalch, D. S. (1978). Psychoendocrine response to sexual arousal in human males. *Psychosomatic Medicine, 40*, 166–172.

Larson, C. M., Haselton, M. G., Gildersleeve, K. A., & Pillsworth, E. G. (2013). Changes in women's feelings about their romantic relationships across the ovulatory cycle. *Hormones and Behavior, 63*(1), 128–135.

Martini, F. H., Nath, J. L., & Bartholomew, M. S. (2012). *Fundamentals of anatomy and physiology.* San Francisco: Pearson.

Miller, S. L., & Maner, J. K. (2010). Scent of a woman: men's testosterone responses to olfactory ovulation cues. *Psychological Science, 21*(2), 276–83. https://doi.org/10.1177/0956797609357733.

Ramanujam, L. N., Liao, W.-X., Roy, A. C., & Ng, S. C. (2000). Association of molecular variants of luteinizing hormone with male infertility. *Human Reproduction, 15*(4), 925–928.

Schumacher, A., Poloski, E., Spörke, D., & Zenclussen, A. C. (2014). Luteinizing hormone contributes to fetal tolerance by regulating adaptive immune responses. *American Journal of Reproductive Immunology, 71*, 434–440.

Taneja, V. (2018). Sex hormones determine immunity. *Frontiers in Immunology, 9*(1931), 1–5.

Turner, D., & Briken, P. (2018). Treatment of paraphilic disorders in sexual offenders or men with a risk of sexual offending with luteinizing hormone-releasing hormone agonists: An updated systematic review. *The Journal of Sexual Medicine, 15*(1), 77–93.