

Recent progress in luteinizing hormone/human chorionic gonadotrophin hormone research

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ABSTRACT: The role of luteinizing hormone (LH) and human chorionic gonadotrophin hormone (hCG) in the regulation of normal reproductive functions in males and females is quite well established. Besides the use of hCG in the development of diagnostic immunoassays, it has been successfully used in the induction of final follicular maturation and ovulation in the assisted reproductive technologies. The basic and clinical research on the nongonadal actions of LH/hCG in the recent years has extended the potential of using these hormones in several clinical indications. Hereby we will analyze the advances in the LH/hCG research (briefly emphasizing the nongonadal research), which has the potential for multiple novel therapies in reproductive and the other areas of medicine.

Key words: luteinizing hormone / human chorionic gonadotrophin / luteinizing/human chorionic gonadotrophin receptor / gonadal and nongonadal effects

Introduction

Hypothalamic gonadotrophin-releasing hormone stimulated the secretion of luteinizing hormone (LH) by the anterior pituitary. Human chorionic gonadotrophin (hCG) is secreted by the placenta (Pierce and Parsons, 1981). Both LH and hCG are heterodimeric glycoprotein hormones belonging to cystine-knot growth factor families possessing the properties of cytokines and chemokines (Lapthorn et al., 1994). hCG is structurally related to LH and both hormones bind to the same LH/choriogonadotrophin receptor (LHCGR). LHCGR belongs to a family of seven-trans membrane spanning G-protein coupled receptors (McFarland et al., 1989; Ascoli et al., 2002). hCG is more potent than LH due to its higher receptor binding affinity and a longer circulatory half-life (Rao, 1979). Chorionic gonadotrophin is produced in primates, equines and in man, whereas LH is present in all species. hCG appears in the circulation around the time of implantation, increases to reach its peak about ninth week of pregnancy and then drops down to about one-tenth of the peak levels and remains there until the end of pregnancy. hCG is believed to be essential for the maintenance of the pregnancy by stimulating progesterone production by the corpus luteum gravidarum, although this concept was challenged by the discoveries of the multiple actions of hCG in nongonadal tissues throughout pregnancy and during labor (Lei and Rao, 2001a, b). hCG has been shown to

stimulate testosterone production of fetal Leydig cells (Huhtaniemi and Pelliniemi, 1992; Huhtaniemi et al., 1977; Apaja et al., 2005). This review will concentrate on the LH/hCG in reproductive biology and general medicine with particular emphasis on nongonadal research.

The majority of the studies on nongonadal LH/hCG receptors were done on human rather than on other species (Rao and Lei, 2007). Although the studies on nongonadal LH/hCG actions led to a greater potential for novel therapeutic uses of hCG/LH than from the studies on the gonadal actions of LH/hCG (for a review, see Rao and Lei, 2007), few studies have been done in transgenic murine models, where physiologic significances of nongonadal LHR expression in reproductive function is questioned (Ahtaiainen et al., 2007; Pakarainen et al., 2005, 2007). We will enclose a brief discussion on some recent studies based on transgenic murine models either overexpressing or showing disrupted genes, including analysis of the pros and cons of LH/hCG actions in nongonadal tissues.

The LH/hCG research on reproductive biology issues

Classical expression of the LHCGR has been well established in the testicular Leydig and ovarian theca, granulosa and luteal cells where

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