

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; Pakarinen 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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Table of Contents Recent Progreb In Hormone Research

1. Understanding the eBook Recent Progreb In Hormone Research
 - The Rise of Digital Reading Recent Progreb In Hormone Research
 - Advantages of eBooks Over Traditional Books
2. Identifying Recent Progreb In Hormone Research
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an Recent Progreb In Hormone Research
 - User-Friendly Interface
4. Exploring eBook Recommendations from Recent Progreb In Hormone Research
 - Personalized Recommendations
 - Recent Progreb In Hormone Research User Reviews and Ratings
 - Recent Progreb In Hormone Research and Bestseller Lists
5. Accessing Recent Progreb In Hormone Research Free and Paid eBooks
 - Recent Progreb In Hormone Research Public Domain eBooks
 - Recent Progreb In Hormone Research eBook Subscription Services
 - Recent Progreb In Hormone Research Budget-Friendly Options

6. Navigating Recent Progreb In Hormone Research eBook Formats
 - ePub, PDF, MOBI, and More
 - Recent Progreb In Hormone Research Compatibility with Devices
 - Recent Progreb In Hormone Research Enhanced eBook Features
7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of Recent Progreb In Hormone Research
 - Highlighting and Note-Taking Recent Progreb In Hormone Research
 - Interactive Elements Recent Progreb In Hormone Research
8. Staying Engaged with Recent Progreb In Hormone Research
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers Recent Progreb In Hormone Research
9. Balancing eBooks and Physical Books Recent Progreb In Hormone Research
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection Recent Progreb In Hormone Research
10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
11. Cultivating a Reading Routine Recent Progreb In Hormone Research
 - Setting Reading Goals Recent Progreb In Hormone Research
 - Carving Out Dedicated Reading Time
12. Sourcing Reliable Information of Recent Progreb In Hormone Research
 - Fact-Checking eBook Content of Recent Progreb In Hormone Research
 - Distinguishing Credible Sources
13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
14. Embracing eBook Trends
 - Integration of Multimedia Elements

- Interactive and Gamified eBooks

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