Gene Section

PRLR (prolactin receptor)

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Identity

Other names: PRL-R
HGNC (Hugo): PRLR
Location: 5p13.2

Note: The PRLR belongs to the class I cytokine receptor family.
This receptor binds the pituitary hormone prolactin with high affinity.
It contains an extracellular binding domain with 2 fibronectin-like type III domains, a single transmembrane domain, and an intracellular domain required for signal transduction (via JAK-2/STAT5 and other pathways) that lacks intrinsic kinase activity.

DNA/RNA

Description
No known pseudogenes.

Transcription
Transcription of human prolactin receptor gene is regulated by a multiple and tissue-specific promoter (hPIII for exons 1 species hE1 and hPN1,3 for exons 1 species hE1N1,3). The prolactin receptor promoters belong to the TATA-less/non-initiator class. The hPIII promoter contains Sp1 and C/EBP elements that bind Sp1/Sp3 and C/EBPβ [required for basal and regulated transcriptional activity, while hPN1 activity is conferred by domains containing an Ets element and an NR half-site. hPN1,3 have not been characterized.
Estrogen regulates PRLR transcription through the preferentially utilized PIII promoter via a non-classical ERE independent mechanism in target cells.
The protein association induced by estradiol of estrogen receptor α (ERα) with DNA-bound Sp1 (constitutive) and C/EBPβ (recruited by the ERα-SP1 complex) is essential for human prolaction receptor gene transcription (figure 1C).
Additional interaction between zinc fingers of Sp1 and leucine zipper of C/EBPβ stabilizes the ERα-Sp1-C/EBPβ complex.
The enhanced complex formation of ERα dimer (DNA binding domain) with Sp1 (zinc finger motifs) and C/EBPβ (basic region and leucine zipper) by E2 plays an essential role in the transcriptional activation of the hPRLR gene.

Pseudogene
No known pseudogenes.
Figure 1. A. Localization of multiple first exons and exons 2-11 of the human prolactin receptor gene in chromosome 5p 14-13. Alternative exons 1: hE1\textsubscript{1,3} (generic) and hE1N\textsubscript{1,6} (human specific); exon 2: non-coding exon; exon 3: non-coding/coding ATG translation initiation codon; exons 4-11: coding exons.

Figure 1. B. Schematic representation of multiple exons 1 and alternative splicing to common exon 2.
**Protein**

**Description**

Prolactin receptors have been identified in number of cells and tissues including the mammary gland, organs of the reproductive system, central nervous system, pituitary, adrenal cortex, skin, bone, lung, heart, liver, pancreas, GI tract, kidney, lymphoid tissue and spermatozoa. These are also present in breast cancer tissues and cells and in other tumoral tissues/cells.

**Expression**

Localized in the cell membrane, but also present intracellularly at various compartments.

**Localisation**

The prolactin receptor mediates prolactin signaling and triggers intracellular responses that participate in diverse biological functions including, mammary gland development (proliferation and differentiation), initiation and maintenance of lactation, regulation of water and salt balance, reproduction, gonadal steroidogenesis, preservation of sperm integrity, embryonic implantation, brain and behavior, and immune-regulation (see description).

**Function**

The prolactin receptor mediates prolactin signaling and triggers intracellular responses that participate in diverse biological functions including, mammary gland development (proliferation and differentiation), initiation and maintenance of lactation, regulation of water and salt balance, reproduction, gonadal steroidogenesis, preservation of sperm integrity, embryonic implantation, brain and behavior, and immune-regulation (see description).
Figure 2. A. Schematic representation of human PRLR variants. Forms generated by alternative splicing.

Figure 2. B. Structure of human prolactin receptor variants. Receptor structure of the various forms. LF: long form; IF: intermediate form; S: short forms; 10': partial exon 10; Δ#: deleted exon; #/#: exon/exon splice variant; D1, D2: N-terminal subdomain; WS: WSXWS motif; C: cysteine; Y: tyrosine; EC: extracellular domain; TM: transmembrane domain; IC: intracellular domain. Blue boxes (dark and light) in IC represent two unique sequences of short forms derived from exon 11. Amino acid number includes the signal peptide.
Changes in the expression of prolactin receptor variants were found in breast cancer tissues and cells lines when compared to adjacent normal tissues/cells. Polymorphism of prolactin receptor may be related to breast carcinoma, multiple sclerosis and systemic lupus erythematosus. Two missense variants found in patients with breast tumor, Valine for Isoleucine 76 (I76V) and Leucine for Isoleucine 146 (I146L) with gain of function were proposed to participate in breast tumorigenesis.

**References**


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