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Gene Section
Short Communication

PCSK4 (proprotein convertase subtilisin/kexin type 4)

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Abstract

Review on PCSK4, with data on DNA/RNA, on the protein encoded and where the gene is implicated.

Identity

Other names: PC4, SPC5

HGNC (Hugo): PCSK4

Location: 19p13.3

DNA/RNA

Description

This gene can be found on chromosome 19 at location: at 1432427 and ends at 1441410.

Transcription

The DNA sequence contains 15 exons and the transcript length: 2661 bps translated to a 755 residues protein.

Protein

Description

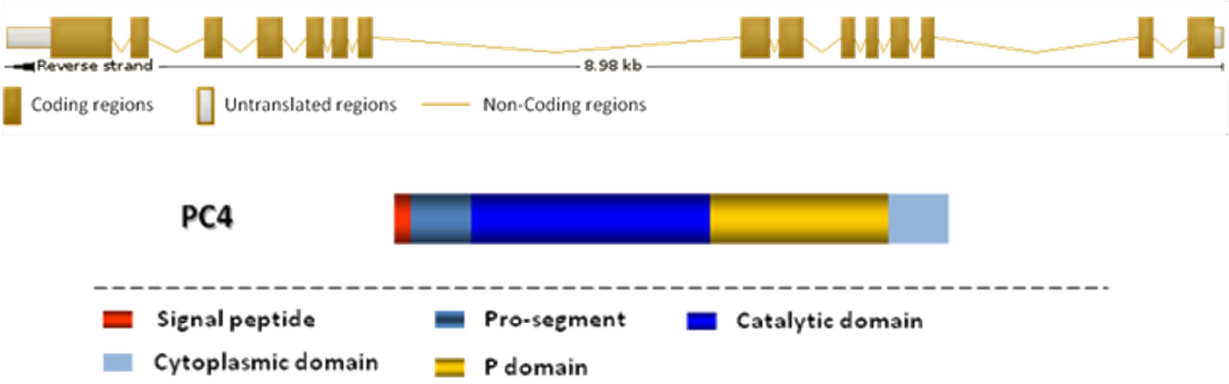
PCSK4 is a member of the family of subtilisin-like proprotein convertase (PCs) that process protein at basic residues.
This protein is produced in the inactive zymogen form and is activated by proteolytic removal of its prodomain in the N-terminal site.

Expression

PCSK4 is restricted to the reproductive tract and expressed primarily in testicular germ cells and sperm.
Low levels of PCSK4 mRNA have also been detected in ovaries and the placenta.

Localisation

PCSK4 exact intracellular location has not yet been determined.



Function

PCSK4 cleaves synthetic peptide substrates after an Arg in a basic sequence context; most often after paired basic residues (K/R-X-K/R), to release mature proteins from their proproteins. PCSK4 substrates include growth factors (DEAF-1, proIGF2, proenkephalin, proNGF, proPACAP, HGFR), receptors (IGF-1R, HGFR), and members of the ADAM (a-disintegrin-and-metalloproteinase) family (ADAM-1, ADAM-2, ADAM-3, ADAM-5). The activation/inactivation of these substrates implicated directly the latter to the regulation of gonadal functions, sperm motility, and species specific reproduction.

Homology

The PCSK4 catalytic domain has a high percentage of homology with those of the other PCs: 70% between PCSK4 and Furin.

Implicated in

Pregnancy difficulties

Note

An aberrant processing of IGF-II by PCSK4 plays a role in inadequate trophoblast migration and, thus, fetal growth restriction.

Infertility

Note

The fertilizing ability of PCSK4 null spermatozoa was also found to be significantly reduced. Moreover, PCSK4 cleavages lead to sperm acquisition of fertilization competence.

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