Gene Section
Short Communication

PCSK5 (proprotein convertase subtilisin/kexin type 5)
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Abstract
Review on PCSK5, with data on DNA/RNA, on the protein encoded and where the gene is implicated.

Identity
Other names: PC5, PC6, PC6A, SPC6
HGNC (Hugo): PCSK5
Location: 9q21.13

DNA/RNA
Description
This gene can be found on chromosome 9 at location: 77695406-78164112.

Transcription
The DNA sequence contains 37 exons and the transcript length: 9538 bps translated to 1860 residues protein.

Protein
Description
PCSK5 is a member of the family of subtilisin-like proprotein convertase (PCs) that process proteins at basic residues. This protease undergoes an initial autocatalytic processing event in the ER to generate a heterodimer which exits the ER. It then sorts to the trans-Golgi network where a second autocatalytic event takes place and the catalytic activity is acquired.

Expression
PCSK5 is widely expressed and encoded by two alternatively spliced mRNAs: PC5A (which encodes a soluble 913-amino acid protein) and PC5B (which encodes a type I membrane-bound 1860-amino acid enzyme). PC5A is mostly found in the adrenal gland, uterus, ovary, aorta, brain and lung. PC5B is more limited with high expression in the intestine (jejunum, duodenum, ileum, colon), the kidney and the liver.

Localisation
Isoform PC6A: Secreted.
Isoform PC6B: Endomembrane system: Type I membrane protein localized.
Function

PCSK5 is capable of cleavage at the R-X-(K/R)-R consensus motif to release mature proteins from their proproteins. PCSK5 substrates include growth factors (GDF11, TGFβ, BMP2, CALD1, NGF, PDGF-A, PDGF-B, VEGF-C), receptors (IGF-1R), prohormones (prorenin), ECM proteins (N-cadherin, alpha-integrins), enzymes (phospholipase, pro-MT1-MMP, ADAM family), and viral protein (HIV-1 glycoprotein gp160). The activation/inactivation of these substrates implicated directly the latter to homeostatic balance, HDL metabolism, pregnancy establishment and development, and to cell adhesion, proliferation and migration.

Homology

The PCSK5 catalytic domain has a high percentage of homology with those of the other PCs: 65% between PCSK5 and Furin.

Implicated in

Gastric cancer

Note

Studies have shown that mice developing adenocarcinomas along the small intestine exhibited more tumours when they lack PCSK5 in enterocytes.

Currarino syndrome

Note

Exon sequencing of healthy individuals and patients with VACTERL malformations linked mutations in the human PCSK5 gene to this syndrome.

Viral infection

Note

The human immunodeficiency virus HIV envelope glycoprotein gp160 is synthesized as an inactive precursor, which is processed into its fusigenic form gp120/gp41 by host cell PCSK5 during its intracellular trafficking.

References

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