TMPRSS2 (transmembrane protease, serine 2)

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Identity

Other names: FLJ41954, PP9284, PRSS10
HGNC (Hugo): TMPRSS2
Location: 21q22.3

DNA/RNA

Description
TMPRSS2 gene approximately extends 43.59 kb-long on chromosome 21 in the region q22.3, containing 14 exons.

Transcription
Two alternative splicing variants have been described, producing transcripts of 3.25 kb and 3.21 kb, respectively.

Protein

Description
TMPRSS2 is a 492 amino acid type II transmembrane serine proteases (TTSPs) which are expressed at the cell surface and are thus ideally located to regulate cell-cell and cell-matrix interactions.

Expression
TMPRSS2 is expressed in normal and diseased human tissues. Especially, TMPRSS2 is highly expressed in small intestine, but also in lower levels in several other tissues. Also expressed in prostate, colon, stomach and salivary gland.

Localisation
Subcellular location: Cell membrane; Single-pass type II membrane protein.
Activated by cleavage and secreted.

Function
This gene was demonstrated to be up-regulated by androgenic hormones in prostate cancer cells and down-regulated in androgen-independent prostate cancer tissue. To containing intra- and extracellular domains, TMPRSS2 could work as a receptor for specific ligand(s) mediating signals between the environment and the cell. TMPRSS2 has been proposed to regulate epithelial sodium currents in the lung through proteolytic cleavage of the epithelial sodium channel and inflammatory responses in the prostate via the proteolytic activation of PAR-2.

Homology
TTPs (type II transmembrane serine proteases) contain an integral transmembrane domain and remain cell-surface-associated, even after proteolytic activation of the protease zymogen. Human TTSPs, which consists of 17 members, were grouped into four subfamilies based on similarity in domain structure and phylogenetic analysis of the serine protease domains, namely the matriptase, corin, hepsin/TMPRSS and HAT/DESC subfamilies.
TMPRSS2 is a 492 amino acid single-pass type II membrane protein. It contains a Serine protease domain (aa 255-492) of the S1 family, followed by a Scavenger receptor cysteine-rich domain (SRDR, aa 149-242) of group A; an LDL receptor class A (LDLRA, aa 113-148) domain forms a binding site for calcium; a predicted transmembrane domain (aa 84-106). Letters H, D and S in the serine protease domain indicate the position of the three catalytic residues histidine, aspartate and serine, respectively.

**Multidomain structure of human TTSPs.** Human TTSPs were grouped into four subfamilies based on similarity in domain structure and phylogenetic analysis of the serine protease domains, namely the matriptase, corin, hepsin/TMPRSS and HAT/DESC subfamilies. Consensus domains are shown below. Each diagram was drawn using the web-based SMART software (http://smart.embl-heidelberg.de) with TTSP amino acid sequences obtained from GenBank. Abbreviations: CUB, C1r/C1s, urchin embryonic growth factor and bone morphogenic protein-1 domain; DESC1, differentially expressed squamous cell carcinoma gene 1; FRZ, frizzled domain; HAT, human airway trypsin-like protease; LDLA, low-density lipoprotein receptor domain class A; MAM, a meprin, A5 antigen and receptor protein phosphatase m domain; MSPL, mosaic serine protease long-form; Polyserase-1, polyserine protease-1; SEA, a single sea urchin sperm protein, enteropeptidase, agrin domain; SR, scavenger receptor cysteine-rich domain; TM, transmembrane domain. Letters H, D and S in the serine protease domain (active) indicate the position of the three catalytic residues histidine, aspartate and serine, respectively. Letter A in the serine protease domain (inactive) indicates a serine to alanine exchange.

**Implicated in**

**Prostate cancer**

**Prognosis**

TMPRSS2 was originally reported to be a smallintestine-associated serine protease. Later, however, its gene turned out to be expressed mainly in the prostate in an androgen dependent manner. In the prostate adenocarcinoma, TMPRSS2-EGR fusion mRNAs is highly expressed. Because of its location on the surface of prostatic cells, TMPRSS2 is a potential new diagnostic marker for prostate cancer.
Breakpoints

References


This article should be referenced as such: