Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section
Mini Review

KLK10 (kallikrein-related peptidase 10)

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Published in Atlas Database: August 2007

Online updated version: http://AtlasGeneticsOncology.org/Genes/KLK10ID41076ch19q13.html
DOI: 10.4267/2042/38493

Identity

Hugo: KLK10
Other names: NES1; PRSSL1
Location: 19q13.41
Local order: Telomere to centromere.

DNA/RNA

Description

Spanning 5.7 kb of genomic DNA, the KLK10 gene consists of 5 introns and six exons.

Transcription

The KLK10 gene has several splice variants with different lengths of the first exon. The predominant form is 1443 bp. Since the first exon is untranslated, all splice variants encode the same protein.

Pseudogene

Not identified so far.

Protein

Description

KLK10 is a 30 kDa serine protease containing 276 amino acids. It consists of a signal peptide (aa 1-33), an activation peptide (aa 34-42), and a mature chain (aa 43-276).

Expression

High levels of KLK10 expression are typically found in glandular epithelia in a wide variety of organs, such as salivary gland, gastrointestinal tract, prostate, lung, breast, and ovary.

Localisation

KLK10 is synthesized as a precursor protein of 276 amino acids. Within the secretary pathway, its signal peptide is cleaved and it is secreted into the extracellular milieu as an inactive zymogen.
KLK10 has been identified in many biological fluids, such as blood, amniotic fluid, cerebrospinal fluid, milk, and nipple aspirate.

Function

How KLK10 is activated remains undetermined. It is expected that upon activation, the peptide bond between arginine42 and lysine43 is proteolysed to release the mature chain. Mature KLK10 exhibits some typical characteristics of a trypsin-like serine protease, such as the catalytic triad (Histidine86, serine229, and aspartic acid137) and an aspartic acid in its substrate-binding pocket. However, its enzymatic activity has not been experimentally confirmed so far. Consequently, its potential physiologic substrates have not been identified.

Homology

Human KLK10 shares 98.2% and 69% identity with chimpanzee and mouse/rat klk10, respectively.

Mutations

Note: No germinal or somatic mutations are identified to be associated with cancer so far.

Implicated in

Various cancers with upregulated KLK10

Disease

Epithelial ovarian carcinoma, uterine serous papillary carcinoma, head and neck squamous cell carcinoma, lung squamous cell carcinoma, and gastrointestinal tract cancer.

Prognosis

In these malignancies, KLK10 has been reported to be upregulated. Among them, epithelial ovarian carcinoma is by far studied the most. KLK10 is overexpressed in ovarian tumor tissue than in normal epithelium and stromal tissues both at the mRNA and protein levels. Due to increased leakage of KLK10 into the circulation, serum concentrations of KLK10 in ovarian cancer patients are elevated. High levels of KLK10 in tumor tissue or in serum are associated with more advanced disease stages and poor survival. In particular, preoperative serum KLK10 levels can serve as a complimentary biomarker for CA125, a well-established tumor marker routinely used in ovarian cancer. It has been demonstrated that nearly all CA125-negative tumors show KLK10 immunostaining positivity and that about 35% of CA125-negative patients have increased serum levels of KLK10. In combination with CA125, KLK10 can improve the diagnostic sensitivity by about 20% compared to that of CA125 alone.

Cytogenetics

No cytogenetic abnormalities are identified so far.

Hybrid/Mutated Gene

Not identified so far.

Various cancers with down regulated KLK10

Disease

Breast cancer, testicular cancer, leukemia, and prostate cancer.

Prognosis

In contrast to ovarian cancer, KLK10 is down regulated in these malignancies, with breast cancer as a prototype. Several lines of evidence have demonstrated that KLK10 is progressively down regulated during breast cancer development. In a clinical study, it is observed that essentially all normal breast specimens had KLK10 expression, whereas about 46% of ductal carcinoma in situ (DCIS) and the majority of infiltrating ductal carcinoma (IDC) had no detectable KLK10 expression. More importantly, the KLK10 negative-DCIS was found to subsequently develop to IDC. In in vitro studies, it has been shown that KLK10 is expressed in normal breast epithelial cells but dramatically reduced in breast cancer cell lines. Moreover, reintroduction of KLK10 expression into these cancer cells can suppress their tumorigenecity in nude mice. KLK10 was thus considered to function as a tumor suppressor in breast cancer. The mechanisms governing the down regulation of KLK10 in breast cancer is not clear. One explanation is CpG island hypermethylation of exon 3, as demonstrated in a number of cancer cell lines. Noteworthy, expression of KLK10 is modulated by some steroid hormones and retinoid acid. They may, under certain conditions, also contribute to the aberrant expression of KLK10 in tumor tissues. However, the paradoxical expression of KLK10 in different types of tumors remains obscure.

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This article should be referenced as such:

Luo LY, Diamandis EP. KLK10 (kallikrein-related peptidase 10). Atlas Genet Cytogenet Oncol Haematol.2008;12(2):108-110.