

Gene Section

Mini Review

WFDC1 (WAP four-disulfide core domain 1)

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Identity

Other names: ps20

HGNC (Hugo): WFDC1

Location: 16q24.1

DNA/RNA

Description

The gene encompasses 35 kb of DNA; 7 exons.

Transcription

1366 nucleotides mRNA; 660 bp open reading frame.

Protein

Description

220 amino acids; 24 kDa protein. Like rat ps20, human ps20 protein contains a WAP signature domain.

Expression

Widely expressed, absent in thymus.

Function

The rat homologue of ps20 was originally identified as a secreted growth inhibitor. These growth regulatory effects and the cell phenotypic properties *in vitro*, suggest that ps20 may function as a mediator of stromal-epithelial interactions and contribute to the maintenance of tissue homeostasis. The ps20 protein is assumed to function as a protease inhibitor. *In vitro* studies indicate that exogenous addition of ps20 protein stimulates endothelial cell migration, and promotes angiogenesis and tumour growth in a xenograft model of prostate cancer.

Homology

The human WFDC1 protein shares approximately 86% and 88% identity with the rat and mouse proteins, respectively. WFDC1 is related to a family of human proteins that also have homology with WAP. The WFDC1 gene organization presents similarities with that of the KAL gene, which extends on 210 kb of DNA, includes 14 exons and is the largest gene in the WAP signature domain family.



Representation of the position of the conserved cysteines for the category of "four-disulfide core" domain and the location of the signature pattern for such a domain in the human WFDC1 amino acid sequence.

Mutations

Note

Although WFDC1 was mapped to human chromosome 16q24, an area of frequent loss of heterozygosity (LOH) in prostate and hepatocellular carcinomas, no tumour-associated mutations were identified in the coding region of WFDC1 in these cancer types. Mutations in WFDC1 gene resulting in Gly9Asp, Pro211Ser and Lys217Arg substitutions have been found at low frequency in the stroma of breast carcinomas. One mutation resulting in a Pro167Ser substitution has been identified in the epithelium of breast carcinoma.

Implicated in

Disease

Prostate cancer

Oncogenesis

WFDC1 is significantly down-regulated in prostate cancer making it a candidate tumour suppressor gene. However, WFDC1 seems predominantly expressed in the stroma of normal prostate. In tumors, decreased stromal WFDC1 expression has been associated with increased epithelial WFDC1 expression. This correlates with shorter recurrence-free survival times and may indicate progression to a more aggressive epithelial phenotype and an epithelial mesenchymal transition process.

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