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Gene Section
Mini Review

WISP3 (WNT-1 inducible signaling pathway protein 3)

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Identity

Other names: PPD: CCN6; LIBC; PPAC; Wnt1 signaling pathway protein 3

HGNC (Hugo): WISP3

Location: 6q22-q23

DNA/RNA

Description

5 exons spanning 967kb of genomic.

Transcription

Alternative splicing generates at least three transcript variants, their sizes are 1212bp, 1307 bp and 1068 bp.

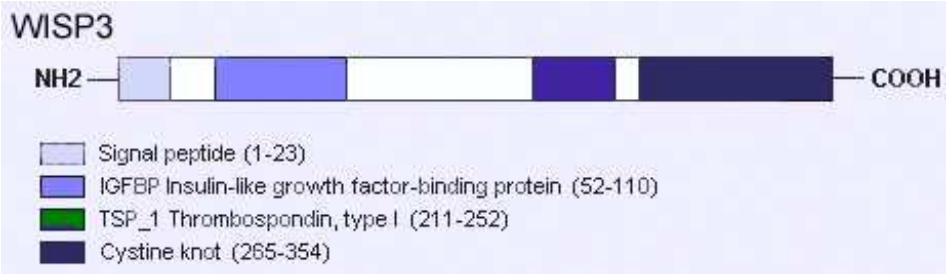
Protein

Description

WISP3 contains four conserved cysteine-rich domains: insulin-like growth factor-binding domain, von Willebrand factor type C module, thrombospondin domain and C-terminal cystine knot-like domain. It has three isoforms: 1) variant 1, 354 aa, 39292 Da; 2) variant 2, 331 aa, This variant differs from variant 1 in two regions. It has an alternate 5' end which results in a different N-terminus.
It also uses two alternative donor and acceptor sites in the middle coding region which result in a few internal aa differences between variant 1 and 2. 3) variant 3, 372 aa, This variant differs in the 5' UTR and CDS, compared to variant 1.
The resulting protein is longer and has a distinct N-terminus, compared to variant 1.

Expression

Predominant expression in adult kidney and testis and fetal kidney. Weaker expression found in placenta, ovary, prostate and small intestine. Also expressed in skeletally-derived cells such as synoviocytes and articular cartilage chondrocytes.



Localisation

Secreted (Probable).

Function

It is a member of the WNT1 inducible signaling pathway (WISP) protein subfamily, which belongs to the connective tissue growth factor (CTGF) family and may be downstream in the WNT1 signaling pathway that is relevant to malignant transformation. It is over-expressed in colon tumors. It is essential for normal postnatal skeletal growth and cartilage homeostasis. It acts as a putative growth regulator contributing to the inflammatory breast cancer by regulating tumor cell growth, invasion and angiogenesis.

Homology

Wnt1-inducible signaling proteins.

Mutations

Germinal

Various types of mutations have been described, dispersed throughout the gene, including nucleotide substitutions, small deletions and small insertions. There are patients who are compound heterozygous, heterozygous or homozygous. The mutations cause progressive pseudorheumatoid dysplasia.

Somatic

Somatic mutations that cause reading frameshifts at a polyadenosine tract within the WISP3 coding sequence have been observed at higher-than-expected rates in gastrointestinal tumors from patients with mutations in the mismatch repair pathway.

Implicated in

Arthropathy, progressive pseudorheumatoid, of childhood

Disease

Mutations in the WISP3 gene result in an arthropathy of childhood beginning at about age 3-8. Usually several joints were affected with pain and soft tissue swelling. The proximal interphalangeal joints of the hand were most commonly affected and the hips and elbows next most often involved.

Inflammatory breast cancer

Oncogenesis

Loss of WISP3 is one of the key genetic alterations in the development of IBC.

Rheumatoid arthritis

Colon cancer

Oncogenesis

Frameshifts, non-sense mutations and non-synonymous changes involving cysteines or affect a splice-donor site.

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