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Gene Section
Mini Review

TNN (tenascin N)

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Identity

Hugo: TNN
Other names: TN-W; TN-N
Location: 1q25.1
Local order: tail to tail configuration next to the tenascin-R gene (TNR)

DNA/RNA

Description

The tenascin-W gene consists of 19 exons spanning 80.21 kb of genomic DNA.

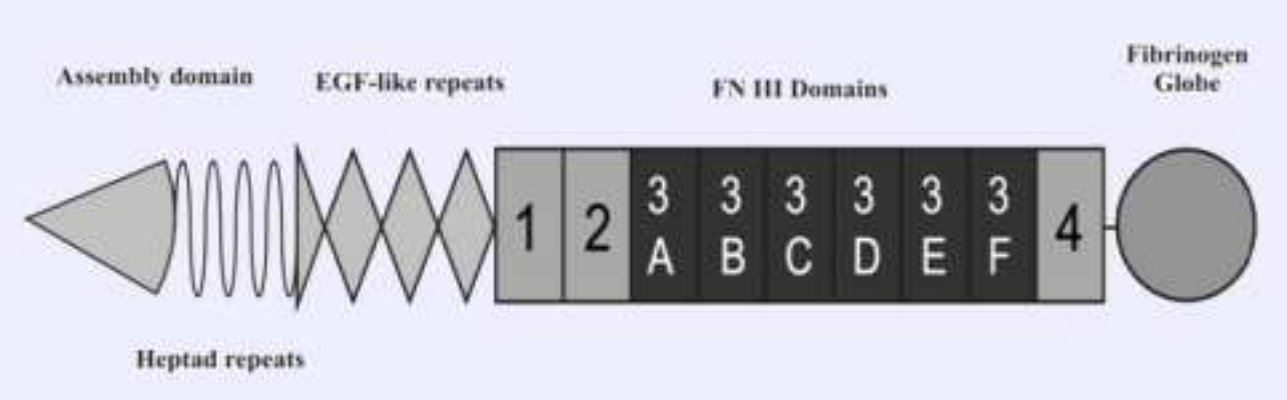
Transcription

5005 bp mRNA transcribed in centromeric to telomeric orientation on the forward strand; 3885 bp open reading frame.
The transcript starts with a non-coding exon followed by exon 2, which contains the start codon (ATG) for translation initiation. Exon 1 is located 9448 bp upstream of exon 2.

exon	1	2	3	4	5	6	7	8	9	10
exon length (bp)	75	444	375	264	186	90	264	267	264	267
intron length (bp)	9443	1505	455	3323	1469	8495	3163	648	18343	1355

exon	11	12	13	14	15	16	17	18	19
exon length (bp)	264	264	131	133	152	97	168	164	1136
intron length (bp)	4575	3291	946	430	7098	879	7398	2380	

The distribution of the 19 exons is shown in the upper part, whereas the lengths of exons and introns are indicated in the lower part.



Schematic representation of human tenascin-W is shown.

Protein

Description

Tenascin-W is built up of different structural motifs arranged in a linear order, namely amino-terminal heptad repeats, 3.5 EGF-like repeats, 9 FN III domains, and a carboxyl-terminal fibrinogen globe.

The primary sequence encodes a protein of 1294 amino acids. Amino acids 1-16 represent the secretion signal, amino acids 150-254 constitute the EGF-like repeats, and amino acids 255-1054 account for the FNIII domains. FN III domain number 3 was subject to duplication as indicated by the dark boxes in the schematic representation. Tenascin-W is known to form hexameric structures called hexabrachions.

SDS-Page analysis revealed a molecular weight of 160kDa per subunit under reducing conditions.

So far, there is no evidence for alternative splicing.

Expression

Initially, tenascin-W was identified in zebrafish where it was expressed in migrating cells of sclerotomal and neural crest origin. More recently, tenascin-W was characterized in mouse and chicken during embryogenesis as well as in the adult organism. These studies revealed that tenascin-W, similar to tenascin-C, shows tight regulation during development and in the adult. Immunohistochemistry showed prominent expression in the developing and adult metanephric kidney, developing and adult periosteum around ribs, and transient expression in smooth muscles of the developing gut, often but not always overlapping with tenascin-C expression. Furthermore, tenascin-W is highly expressed in the tumor stroma in different solid tumors.

Tenascin-W is most likely produced and secreted by mesenchymal cells such as fibroblasts and osteoblasts.

Known stimuli that induce tenascin-W expression include so far tumor necrosis factor alpha (TNFalpha) and bone morphogenetic protein 2 (BMP2).

Localisation

Extracellular matrix.

Function

Adhesion: Tenascin-W is an adhesive substratum for some cells (osteoblasts, fibroblasts), while others cannot attach and spread on tenascin-W.

Migration: Tenascin-W stimulates the migratory behavior of cells.

Homology

Tenascin-W belongs to the tenascin family, which is a highly conserved family of large oligomeric extracellular matrix proteins. Vertebrate genomes harbor four tenascin genes, which have been termed tenascin-C, tenascin-XB (TNXB), tenascin-R, and tenascin-W.

Human tenascin-W shows high sequence conservation with mouse tenascin-W.

Implicated in

Breast cancer

Oncogenesis

Tenascin-W is highly expressed in a large fraction of breast cancer patients whereas it is not detectable in normal human mammary tissue. Expression in tumors correlated with tumor grade. There is statistically significant higher mean expression of tenascin-W in low-grade tumors (Grade1/Grade2) compared to high-grade tumors (Grade3).

Tenascin-W is produced in the stromal compartment, most likely by cancer-associated fibroblasts, which are part of a tumor permissive microenvironment that facilitates tumor cell migration. In vitro, presence of tenascin-W stimulated breast cancer cell migration.

Benign tumors as well as carcinomas do express tenascin-W.

Furthermore, tenascin-W is elevated in sera of breast cancer patients compared to that of healthy volunteers.

Tenascin-W is postulated to be a marker for conversion of the normal physiological stroma to an activated stroma in breast cancer.

Colorectal cancer

Oncogenesis

Tenascin-W is highly expressed in colorectal cancer patients whereas it is not detectable in the normal colon mucosa. Furthermore, mean tenascin-W level in sera of colorectal cancer patients is statistically increased compared to that in sera of healthy volunteers. Follow-up studies of colorectal cancer patients revealed that 4 out of 5 patients who developed tumor recurrence after treatment showed high tenascin-W levels in their sera. Thus, tenascin-W might have prognostic value as a serum tumor marker.

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