TNS4 (tensin 4)

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Identity

Other names: CTEN
HGNC (Hugo): TNS4
Location: 17q21.2

Note
The TNS4 gene was identified by Lo and Lo. They found that it is composed of 12 exons encoding an mRNA of 4015 bp with an open reading frame encoding 715 amino acid residues. The amino acids 418-715 are very similar to the COOH termini of tensin 1, tensin 2 and tensin 3. There are six potential tyrosine phosphorylation sites found in TNS4 although the gene product is a shorter polypeptide and lacks the NH2-terminal homologous regions found in tensins. This gene was found to be distant member of the tensin family and given name cten for the COOH-terminal tensin-like molecule.

DNA/RNA

Note
It was found that the human cten gene is located on chromosome 17q12-21 and has 12 exons. The SH2 domains bind ligands containing pTyr residues within a specific sequence and high affinity binding is provided by the pTyr residue itself and by subsequent residues toward the COOH-terminal.

Protein

Note
TNS4, as the others tensins, contains a phosphotyrosine-binding domain (PTB), which plays the role of interacting with the cytoplasmic tail of the β-integrin. Also they all contain, at the C-terminal, Src homology domain 2 (SH2 domain).
Figure 1. Analysis of cten amino acid sequence. A. The cDNA-derived amino acid sequence of human cten. The potential tyrosine phosphorylation sites are in bold. B. Organization of human cten gene. Exon/intron boundaries were determined by comparison of sequences of genomic DNA and cDNA. In the splice site, exon sequences are indicated by uppercase letters, and intron sequences are indicated by lowercase letters. Codon phase refers to the codon split at the splice acceptor. Introns that do not split codon triplets are indicated by phase 0, interruption after the first nucleotide is indicated by codon phase I, and interruption after the second nucleotide is indicated by codon phase II. N indicates noncoding region. Numbers in the brackets indicate the sizes of the corresponding exons in human tensin 1 and tensin 2, respectively.

Figure 2. Schematic structure of tensins. The C-terminus of tensin contains SH2 and PTB domains, allowing TNS4 to interact with tyrosine-phosphorylated proteins and β integrin respectively. The FAB domain is present in the C-terminal region, and it involved in mediating binding of tensin 4 to other focal adhesion molecules.

While tensin 1, tensin 2 and tensin 3 interact with actin at multiple sites in the N-terminal, tensin 4 (Cten) lacks the n-terminal region actin binding domain (ABD). TNS4 has only one focal adhesion binding (FAB) domains in C-terminal while others have it in both N- and C-terminals.

Expression
The expression of Cten messenger RNA (mRNA) was evaluated in normal tissues by K. Sakashita et al. using the human total RNA master panel and found that Cten is expressed at high levels in prostate, oesophagus, breast and salivary glands. Moderate Cten expression was found in the thyroid and trachea. In contrast, very low expression was reported in colon, lung, small intestine, spleen, kidney, stomach and testis.

Localisation
It is localized to focal adhesions.

Function
The TNS4 is having a role in the cell motility by enhancing the migration as well as the invasion too. Also TNS4 is found to play a central role in HGF-
induced tubulogenesis. The role of TNS4 on cell proliferation is found to be minimal and not up to the level of the effect of migration. By enhancing the motility and having the effect on the tubulogenesis, TNS4 is believed to have a role in cancer cell metastasis.

**Mutations**

**Note**

No mutation has been reported.

**Implicated in**

**Various cancers**

**Note**

The role of cten in cancer is not well defined. In prostate cancer it is down-regulated, where in normal cells it is localized to focal adhesions recruiting the tumour suppressor, deleted in liver cancer (DLC-1), thus suppressing tumorigenesis. Ctn in prostate epithelial cells has also been found to regulate staurosporine-induced apoptosis where cten is cleaved by caspase 3 and results in reduction in cell growth rate. Therefore, loss of cten expression may lead to uncontrolled cell growth and result in cell transformation. Accordingly, in prostate cancer, cten may function as a tumour suppressor protein.

On the other hand, cten has been found to be up-regulated in a number of cancers. It is up-regulated in lung cancer and correlates with tumour progression. In breast cancer, the epidermal growth factor receptor (EGFR), which is involved in various cellular processes including proliferation and motility, up-regulates cten and down-regulates tensin 3. Tensin 3 is localized in cell matrix adhesions but it disappears upon EGF stimulation. These findings showed that EGF-induced up-regulation of cten and down-regulation of tensin 3 correlates with cten fibre remodelling. Cten disassembles actin stress fibres through its PTB domain and is required for tumor-suppressive function.

**References**


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