

Gene Section

Mini Review

TAGLN (transgelin)

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Identity

Other names: DKFZp686B01212, DKFZp686P11128, SM22, SMCC, TAGLN1, WS3-10

HGNC (Hugo): TAGLN

Location: 11q23.3

DNA/RNA

Description

5.4 kb gene located on 11q23.2 consisting of 5 exons, a large intron 1 and 3 short introns. Several putative promoters present in 800 bp upstream region.

Transcription

A 1566 bp transcript is generated from TAGLN. All exon 1 and first 12 bp of exon 2 are untranslated. As are the last 432 bp of exon 5.

Protein

Note

Translated protein sequence is:

MANKGPSYGMSREVQSKIEKKYDEELEERLVEV
IIVQCGPDVGRPDRGRLGFQVWLKNGVILSKLVN
SLYPDGSKPVKVPENPPSMVFKQMEQVAQFLKA
AEDYGVIKTDMFQTVDLFEQKDMAAVQRTLMA
LGSLAVTKNDGHYRGDPNWFMKKAQEHKREFT
ESQLQEGKHVIGLQMGSNRGASQAGMTGYGRPR
QIIS

Description

A 201 aa peptide member of the calponin family of actin binding proteins by virtue of a N-terminal calponin homologue domain and a single C-terminal calponin-like module. This C-terminal CLIK is required for actin binding.

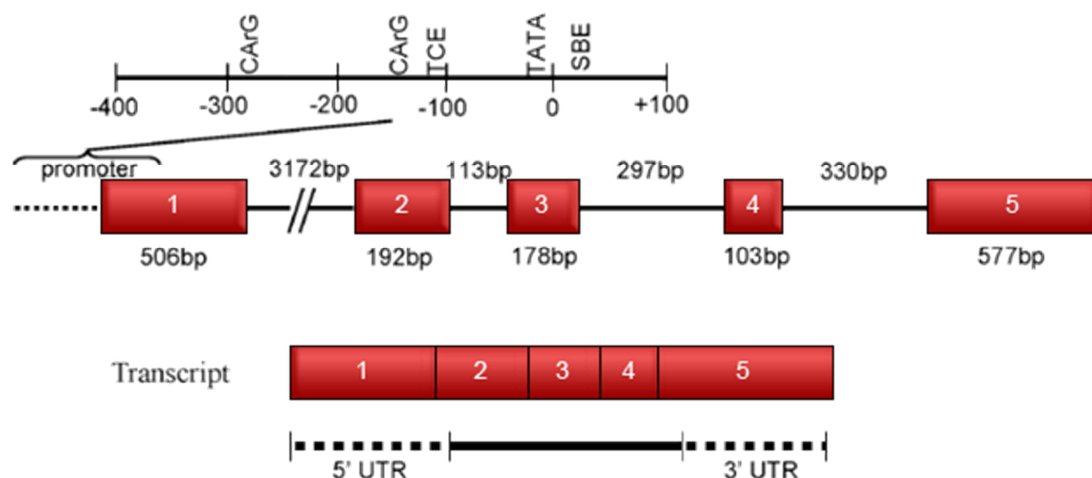


Figure 1. Gene structure showing 5 exonic regions (boxes) and 4 intronic regions (lines). Expanded promoter provides relative positions of promoters upstream (-) and downstream (+) of start site. CarG = serum response binding box; TCE = TGF-beta control element; SBE = Smad binding element. Resulting transcript is given, with 5' and 3' UTRs (broken line) and translated region (solid line).

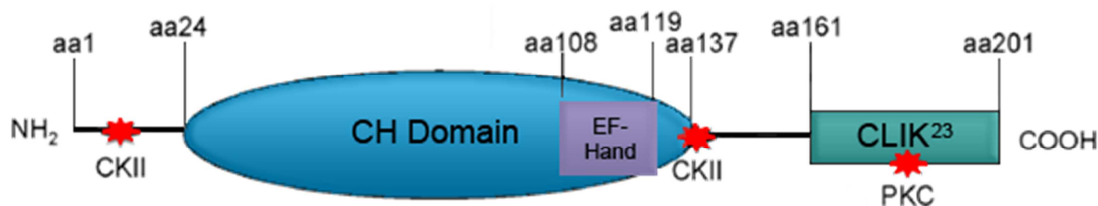


Figure 2. Primary protein structure with amino acid (aa) positions of the calponin homologue (CH) region with calcium binding site (EF-hand) and actin binding calponin-like (CLIK) region. CKII and PKC refer to putative casein kinase II and protein kinase C phosphorylation sites respectively.

Expression

Expression profiles are a point of debate. It is found throughout normal smooth muscle of adult vertebrates. It is also found outside of smooth muscle in the spinal chord, adrenal gland and heart, mesenchymal cells and fibroblasts, epithelium of the intestine, glomerular, breast and prostate.

Localisation

It is localised to the cytosol where it binds to F-actin.

Function

Transgelin is an actin stress fibre binding protein. It gels and stabilises actin gels. In the embryo it is involved in podosome formation and myocyte migration, vascular and visceral smooth muscle cell differentiation, and in the suppression of matrix metallo protease 9 (MMP9) where it is thought to be involved in the suppression of tissue re-modelling following muscle cell differentiation. Similarly in the adult, it is thought to suppress tumour cell invasion through MMP-9 suppression. Furthermore, it has been reported to suppress translocation of androgen receptor to the nucleus. Its expression is down-regulated in many cell lines, and this may be an early marker of the onset of transformation. Indeed it is becoming increasingly evident that transgelin may act as a tumour suppressor.

Implicated in

Various cancers

Note

Disorganisation of the actin cytoskeleton is a fundamental event of the developing cancer cell phenotype. Transgelin is one of several proteins that bind actin and subsequently cross-link and bundle filaments into stress fibres. Expression is decreased in prostate, breast and colon cancers.

Prostate cancer

Note

Transgelin is one of the 2% most significant of all down regulated genes in prostate cancer. Its expression has been shown to decrease with disease progression with lowest expression in metastasised lesions. Loss of transgelin may be significant to suppression of androgen induced proliferation of androgen dependant prostate cancer as it prevents

binding of a co-activator to androgen receptor, thereby blocking nuclear translocation and resulting in suppression of androgen mediated cell growth. Recent studies suggest that transgelin promotes p53 mediated mitochondrial dependent apoptosis. Indeed coimmunoprecipitation and two hybrid studies have shown p53 and transgelin to be binding partners, with re-expression of transgelin promoting cytoplasmic p53 translocation in the prostate cancer cell line LNCaP. The value of transgelin as a target for selenium treatment has very recently been highlighted in a mouse model of prostate cancer (TRAMP mouse) where transgelin is increased with an associated decrease in tumour development.

Prognosis

Unknown.

Colorectal cancer

Note

Loss of transgelin is closely associated with progression, differentiation and metastasis of colon cancer. Restoration of transgelin expression both in vitro and in vivo inhibits carcinogenesis. Decreased expression of transgelin in patients with colorectal cancer is associated with elevated levels of anti-transgelin antibodies, particularly during later stages, and subsequently with lower survival.

Prognosis

Decreased transgelin is associated with poor prognosis.

Breast cancer

Note

Expression of transgelin occurs early in the disease process, possibly through constitutive ras activation.

Prognosis

Unknown.

Ischaemic heart disease and vascular inflammation

Note

Coronary arteries of the ischemic heart display increased abundance of transgelin. In TAGLN null mice inflammatory response is increased following carotid artery injury. It is suggested that transgelin suppresses pro-inflammatory NF kappa B and oxidative stress (via suppression of superoxide dismutase and p47 phox).

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