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Gene Section

Mini Review

TGFBI (transforming growth factor, beta-induced, 68kDa)

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Identity

Other names: BIGH3; CDB1; CDG2; CDGG1; CSD; CSD1; CSD2; CSD3; EBMD; Kerato-epithelin; LCD1; RGD-CAP

HGNC (Hugo): TGFBI

Location: 5q31.1

DNA/RNA

Description

19 exons.

Transcription

2.8 Kb mRNA, 2049 bp open reading frame.

Protein

Description

TGFBI is a 683 amino acid extracellular matrix protein, 68 kDa. Contains an N-terminal secretory signal peptide, a cysteine-rich domain, four internal homologous repeats (fasciclin-like FAS domains), and a C-terminal RGD motif.

Expression

TGFBI is normally found in thymus, bone marrow, spleen, brain, heart, skeleton muscle, lung, kidney, liver, pancreas, and prostate.

Localisation

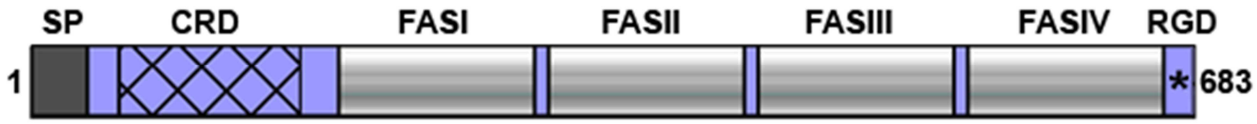
TGFBI is an extracellular matrix protein. It localizes in the extracellular matrix.

Function

Binds to type I, II, IV, VI collagens and fibronectin. The RGD motif may serve as a ligand recognition sequence for integrins. The protein may be involved in cell-matrix interactions, cell adhesion, migration and differentiation. The protein may be involved in endochondrial bone formation in cartilage. The roles of TGFBI in malignant progression are controversial. Some studies suggested that TGFBI suppresses the progression of ovarian, lung cancer and neuroblastomas, while other reports identify TGFBI as an overexpressed gene in colon, pancreatic, and liver cancer.

Homology

TGFBI contains four FAS1 domains. Proteins cantaining the FAS domain include Arabidopsis fasciclin-like arabinogalactan proteins, bacterial immunogenic protein MPT70, human extracellular matrix protein periostin, and mammalian stabilin proteins.



TGFBI contains a secretory signal peptide (SP) at the N-terminus, followed by a cysteine-rich domain (CRD), four internal homologous domains (FAS), and a C-terminal RGD motif.

Mutations

Germinal

Mutations in the human TGFBI gene have been linked to several inherited autosmal dominant corneal dystrophies. The abnormal protein deposits in the forms of amyloid fibrils and/or non-amyloid amorphous affregations in the corneal matrix. Progressive corneal cloudiness eventually leads to severe visual loss in later stage disease. Based on the clinial histopathological properties of the deposits, corneal dystrophy can be divided into two main types: lattice corneal dystrophy (LCD) and granular corneal dystrophy (GCD). These two types of corneal dystrophies are further divided into subtypes according to the differences in the clinical features of the disease. So far, 33 mutations have been identified in the TGFBI gene associated with all the GCDs and most of the LCDs, with two major mutational sites Arg124 and Arg555, accounting for more than half of all the patients with the disease.

Implicated in

Colon Cancer

Prognosis

Colon cancers associated with overexpression of TGFBI may have an increased metastatic potential, leading to poor prognosis in cancer patients.

Oncogenesis

Upregulation of TGFBI is associated with high-grade human colon cancers. We have found that TGFBI promotes extravasation, a critical step in the metastatic dissemination of cancer cells, by inducing the dissociation of VE-cadherin junctions between endothelial cells via activation of the integrin alphavbeta5-Src signaling pathway.

Pancreatic Cancer

Oncogenesis

TGFBI was found induced by TGFbeta1 in pancreatic cancer cell lines (CAPAN-1, PANC-1). In human pancreatic tissues, TGFBI was 32.4 fold upregulated in pancreatic cancers in comparison to normal control tissues at mRNA level.

Ovarian Cancer

Oncogenesis

Loss of TGFBI induces specific resistance to paclitaxel and mitotic spindle abnormalities in ovarian cancer cells. TGFBI expression restores the paclitaxel sensitivity via FAK- and RHO- dependent stabilization of microtubules.

Lung Cancer

Oncogenesis

TGFBI protein was absent or reduced in 45 of 130 primary lung carcinomas in comparison to normal lung tissues.

Neuroblastoma

Oncogenesis

Enhanced expression of TGFBI in human neuro-blastoma cells suppresses neuroblastoma cell cohesion and adhesion to various ECM proteins. TGFBI also inhibits neuroblastoma cell prolife-ration and invasion.

Liver Cancer

Oncogenesis

TGFBI expression promotes cell adhesion, invasion and MMP secretion of human hepatoma cell line SMMC-7721.

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