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Gene Section
Short Communication

CADM4 (cell adhesion molecule 4)

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Abstract

Short communication on CADM4, with data on DNA/RNA, on the protein encoded and where the gene is implicated.

Identity

Other names: IGSF4C, NECL4, Necl-4, TSLL2, synCAM4

HGNC (Hugo): CADM4

Location: 19q13.31

DNA/RNA

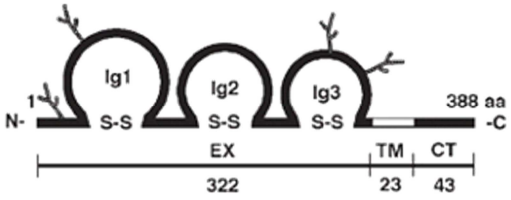
Description

DNA contains 17470 bases composed of 9 coding exons.

Transcription

2176 bp mRNA transcribed in telomeric to centromeric orientation; 1164 bp open reading frame.

Protein



Description

CADM4 encodes an immunoglobulin (Ig) superfamily cell adhesion molecule containing three Ig-like loops in their extracellular domain, a single transmembrane domain, and a short cytoplasmic domain with a protein 4.1-binding motif and a PDZ II-binding motif.

The cytoplasmic domain is bound to the actin cytoskeleton through protein 4.1 such as 4.1B/DAL-1. CADM4 protein is 388 amino acids long and its molecular weight ranges from approximately 50 to 55 kDa dependent on N-glycosylation in the extracellular domain (deglycosylated form: 45 kDa).

Expression

Brain, peripheral nerve, lung, large and small intestines, kidney, bladder, and prostate.

Loss of expression is frequently observed in various cancers.

Localisation

Cell membrane (type I transmembrane protein); Cell-cell contact site in epithelial tissues.

Function

CADM4 forms homophilic cis-dimers on the cell surface and mediates $Ca2^{+}$-independent cell-cell adhesion in a heterophilic manner with CADM2/Necl-3 or CADM3/Necl-1. CADM4 associates with 4.1B in the kidney.

Homology

Pan troglodytes - CADM4; Canis lupus familiaris - CADM4; Bos taurus - CADM4; Mus musculus - Cadm4; Rattus norvegicus - Cadm4; Danio rerio - cadm4.

Mutations

Note

No reports.

Implicated in

Prostate cancer

Oncogenesis

CADM4 protein is lost or markedly reduced in nine of nine primary prostate cancers and two of four prostate cancer cell lines, PPC-1 and Du145, in comparison with that in normal human prostate. The tumorigenicity of PPC-1 was strongly suppressed by restoration of CADM4 expression without inducing significant cell death or growth inhibition in vitro, suggesting that the inactivation of CADM4 would be involved not in the direct cell growth but in the aberrant cell-cell contact in the prostate carcinogenesis.

Renal clear cell carcinoma

Prognosis

The expression of CADM4 is lost or markedly reduced in 70% of primary renal clear cell carcinoma (RCCC), where loss of CADM4 in RCCC correlates with vascular infiltration.

Oncogenesis

CADM4 and its binding partner 4.1B are specifically expressed along the cell membrane in the proximal convoluted tubules, from which RCCC is derived.

Approximately 80% of primary RCCC showed loss or marked reduction of either CADM4 or 4.1B, indicating that disruption of the CADM4-4.1B cascade is one of the most frequent events in RCCC.

The CADM4 gene in human renal cell carcinoma cell 786-O was inactivated by promoter methylation, while restoration of CADM4 expression strongly suppressed subcutaneous tumor formation in nude mice by 786-O cells.

Colorectal adenocarcinoma

Prognosis

CADM4 expression is lost or reduced in 23% or 36% of colorectal adenocarcinoma, respectively. Loss or down-regulation of CADM4 is correlated with larger tumor size, mucinous tumor type, poorer differentiation, lymph node metastasis, and higher Dukes stage.

Oncogenesis

Loss or down-regulation of CADM4 expression was positively correlated with low E-cadherin expression and high Ki-67 expression in colorectal adenocarcinoma.

The restoration of CADM4 expression in LS174T human colon cancer cells suppressed cell growth, colony formation, motility, and tumorigenic capacity. These results suggest that CADM4 may be involved in the maintenance of epithelial structure and suppression of tumor growth.

Breast cancer (ductal carcinoma)

Prognosis

CADM4 expression was higher in ductal carcinoma in situ cases (82%) than invasive ductal adenocarcinoma cases (68%). Loss or reduced expression of CADM4 was significantly correlated with higher histological grade, overexpression of ErbB2 and absence of estrogen and/or progesterone receptors. CADM4 expression is associated with longer disease-free survival in stages I and II invasive ductal adenocarcinoma cases.

Oncogenesis

Loss or reduced expression of CADM4 may play an important role in breast cancer invasiveness.

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