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Gene Section
Short Communication

CARD10 (caspase recruitment domain family, member 10)

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Abstract

Caspase recruitment domain family, member 10, CARD10 (also known as CARMA3 or Bimp1), is a member of the membrane-associated guanylate kinase (MAGUK) superfamily proteins that act to organize signaling at the plasma membrane. This family of proteins contains Src-homology 3 (SH3), PDZ, GuK domains and caspase recruitment domain (CARD). The amino-terminally located CARD of CARD10 functions as an activator of BCL10 and NF-kappaB (NF-kB) signaling critical for the regulation of cellular survival and proliferation. CARD10 (CARMA3) is reported to be over-expressed in various cancer types that include breast, glioma, colon and non-small-cell lung cancers. It appears that the over-expression of CARD10 correlates with tumor status positioning CARD10 as a novel therapeutic target for the treatment of various cancers.

Keywords
CARD10 (CARMA3), NF-kB signaling, Apoptosis, Bcl-10, MALT1.

Identity

Other names: BIMP1, CARMA3

HGNC (Hugo): CARD10

Location: 22q13.1

DNA/RNA

Description

The human CARD10 gene (NM_014550) contains 20 exons and the encoding sequence is 3099 bases.

Pseudogene

No reported pseudogene.

Protein

Description

CARD10 (NP_055365) is a 1032 amino-acid long protein with a molecular mass of 116 kDa.
This protein consists of antiparallel alpha helices. CARD10 contains an N-terminal CARD domain, followed by a central coiled-coil (CC) domain and a C-terminal region encompassing a PDZ domain, a SH3 domain and a GUK domain (Wang et al., 2001). The CARD domain has a hydrophobic core and a hydrophilic outer surface, which mediate the interaction with the CARD domain of other proteins (Hayes-Bouchier et al., 2002; Sun, 2010). Coiled-coil domain is responsible for dimerization (Tanner et al., 2007).

Expression

CARD10 is expressed in a variety of epithelial and mesenchymal tissues including heart, kidney and liver (Wang et al., 2001; McAllister-Lucas et al., 2007).
It was reported that CARD10 is over-expressed in several cancers including breast, ovarian, colon, lung and glioma cancer.
It was also shown that CARD10 deficiency affects cancer cell proliferation, survival, migration and invasion (Jiang et al., 2011).

Localisation

CARD10 is localized in the cytoplasm (Li et al., 2012).

The structural domains of CARD10 protein are shown in different color boxes. CARD, caspase-recruitment domain; PDZ, PSD95, DLGA and ZO1 homology domain; SH3 domain, SRC-homology 3; and GUK domain, guanylate kinase. The numbers correspond to the amino-acid sequence.

Function

CARD10 participates in the organization of membrane signaling involved in cellular proliferation and death through highly specific CARD-CARD homophilic interactions. It appears that CARD10 acting as a scaffold is involved in NF-kB activation through interactions with Bcl10 and MALT1 (Grabiner et al., 2007; McAllister-Lucas et al., 2007).

Homology

CARD10 (CARMA3/Bimp1) shares a high degree of amino-acid sequence, structure and functional homology with CARD11 (CARMA1/Bimp2) and CARD14 (CARMA2/Bimp3).

Mutations

Note

Gene mutations have not been described yet.

Implicated in

Breast cancer

Disease

The levels of CARD10 protein are reported to be significantly higher in breast cancer than in normal breast tissue.

It appears that CARD10 over-expression correlates with tumor, node and metastasis (TNM) stage, tumor size and ErbB2, also known as HER2 (from human epidermal growth factor receptor 2) or HER2/neu, over-expression. The observations that CARD10 leads to the up-regulation of cyclin D1, which is involved in proliferation, and of Bcl-2, a critical component in apoptosis, gene expressions in cell models derived from breast carcinoma (Zhao et al., 2013) is consistent with suggestion that CARD10 is involved in cell survival and proliferation.

Glioma

Disease

CARD10 is over-expressed in glioma and correlates with tumor grades (Grade I, II, III and IV) but not with age or gender. Knocking down of CARD10 expression is shown to inhibit the proliferation and invasion of glioma cell lines (Feng et al., 2014).

Colon cancer

Disease

CARD10 is also over-expressed in colon cancer samples compared to the normal tissue. The expression levels appear to associate with TNM and the proliferation index.

Experimental studies suggest that CARD10 is a positive regulator of colon cancer proliferation (Miao et al., 2012).

Renal cell carcinoma

Disease

CARD10 mRNA expression was found to be significantly higher in renal cell carcinoma tissues compared with noncancerous renal tissues. Furthermore, it was shown that the high level of the CARD10 gene expression is associated with tumor size, histological differentiation, tumor stage and the presence of metastasis (Wu et al., 2013).

Ovarian cancer

Disease

CARD10 over-expression was observed to be positively correlated with tumor histology in ovarian cancer. It was shown that CARD10 depletion in various ovarian cancer cell lines inhibited cell proliferation and prevented cell cycle progression (Xie et al., 2014). It was also reported that protein kinase C alpha-CARD10 signaling axis plays an essential role in the lysophosphatidic acid (LPA)-induced in vitro invasion of ovarian cancer cells (Mahanivong et al., 2008).

Pancreatic carcinoma

Note

CARD10 was reported to be over-expressed in human pancreatic cancer (Du et al., 2014). Moreover, CARD10 appears to regulate malignant cell growth, invasion and NF-kB signaling (Du et al., 2014).

Non-small-cell lung cancer

Disease

As in other tissue cancers, the level of CARD10 protein is higher in non-small-cell lung cancer (NSCLC) than in normal lung tissues. There is a significant correlation between CARD10 levels and TNM stage (Li et al., 2012).

To be noted

Note

miRNA: It was reported that microRNA-146a which is a modulator of inflammatory signals, directly targets CARD10 and COPS8 (COP9 signalosome complex subunit 8) inhibiting the G-protein coupled receptor (GPRC)-mediated activation of NF-kB. It was also found that miR-146a represses the secretion of chemokines and growth factors controlled by NF-kB. It was therefore suggested that miR-146a may act as a tumor suppressor by inhibiting NF-kB activity (Crone et al., 2012).

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