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Gene Section

Review

PDCD5 (programmed cell death 5)

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Abstract

Programmed Cell Death 5 (PDCD5) was originally identified as an apoptosis-accelerating molecule that was widely expressed and well-conserved in the process of evolution.
It has significant homology to the corresponding proteins of species ranging from yeast to mice gene.
PDCD5 can accelerate apoptosis in different type of cells in response to different stimuli, and can also induce different types of cell death, including paraptosis-like cell death. In cells undergoing apoptosis, PDCD5 rapidly translocates from the cytoplasm to the nucleus before phosphatidylserine is externalized and genomic DNA undergoes fragmentation.
PDCD5 interacts with TIP60 and TP53 and plays an important positive role in TIP60-P53 signaling pathway.
PDCD5 also participates in immune regulation through regulating the level of FOXP3 protein and percentage of regulatory T cells.
Dysfunction of PDCD5 was associated in many diseases including different tumors, rheumatoid arthritis and presbycusis, etc.

Keywords
Programmed Cell Death 5 (PDCD5), Apoptosis, Tumor, Immnuoregulation.

Identity

Other names: TFAR19

HGNC (Hugo): PDCD5

Location: 19q13.11

Local order: Orientation: Plus Strand.

DNA/RNA

Description

The PDCD5 gene, with 6286 bases in length, consists of 6 exons and 5 intervening introns.

Transcription

The PDCD5 gene encodes a 604 bp mRNA transcript. Transcription site is located 75 bp upstream the first ATG of the PDCD5 ORF. The translation start site is located in exon 1.

Pseudogene

Pseudogenes have been identified on chromosomes 12p12.3 and 5q13.2.

Protein

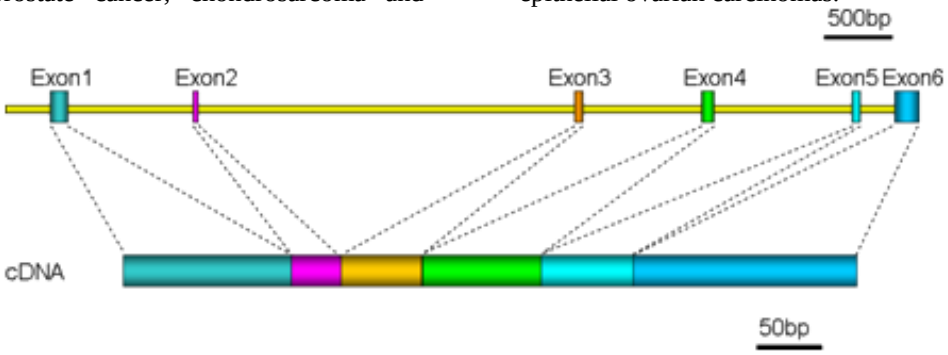
Description

PDCD5 protein is composed of 125 amino acids, with a calculated molecular mass of 14.285 kDa. In the protein sequence exist six phosphorylation sites, including a cAMP and cGMP depended protein kinase phosphorylation site (Ser100), 4 PKC phosphorylation sites (Ser51, Ser84, Thr103, Thr108), and a casein kinase 2 (CK2) phosphorylation site (Ser118) (Saivi et al., 2009). Five of the phosphorylation sites are located in the C-terminal region.

Expression

PDCD5 is widely expressed in different organs and different stages. Decreased expression of PDCD5 has been detected in various human tumors, such as lung cancer, gastric cancer, chronic myelogenous

leukemia, prostate cancer, chondrosarcoma and epithelial ovarian carcinomas.



The DNA sequence of PDCD5.

The abnormal expression of PDCD5 is also involved in some autoimmune diseases and inflammatory processes, such as lupus nephritis, osteoarthritis, rheumatoid arthritis, hepatitis, sepsis and bronchial asthma. In the patients with rheumatoid arthritis, the levels of PDCD5 in serum and synovial fluid are inversely associated with the expression of inflammatory cytokines IL-17 and TNF- α and disease activity.

Localisation

PDCD5 protein has been reported to be localized mainly in the cytoplasm and nucleus, and translocated to the nucleus during apoptosis (Chen et al., 2006).

Function

PDCD5 can promote apoptosis in different cell types in response to various stimuli. PDCD5 interacts with the histone acetyltransferase TIP60 and the transcription factor TP53 to promote apoptosis (Xu et al., 2009; Xu et al., 2012). PDCD5 can also interact with other molecules such as NF-kB p65 and CCT in which participate in the regulation of cell apoptosis. It also associates with TAJ/TROY-induced paraptosis-like cell death (Wang et al., 2004), focal cerebral ischemic reperfusion injury (Jiang et al., 2014), virus infections (Li et al., 2014) and cardiac remodeling (An et al., 2012). PDCD5 negatively regulates autoimmunity by enhancing the level of FOXP3 protein, upregulating FOXP3+ regulatory T cells and suppressing Th17 and Th1 responses (Xiao et al., 2013).

Homology

PDCD5 gene is highly-conserved among species (from yeast to human).

Mutations

Germinal

No data.

Somatic

The promoter with -27G/-11A is associated with reduced PDCD5 promoter activity and increased susceptibility to chronic myelogenous leukemia (Ma et al., 2005).
A C/G polymorphism (rs1862214) located 35 kb upstream of the PDCD5 gene was associated with lung cancer susceptibility (Spinola et al., 2006).

Implicated in

Various cancers

Note
Reduced PDCD5 expression has been found in a few types of human tumors and is also associated with the high progression and poor prognosis. Decreased expression of PDCD5 has been reported in various human tumors, such as gastric cancer (Gao et al., 2012), brain tumors (Li et al., 2008), bone tumor (Chen et al., 2010a), ovarian carcinomas (Zhang et al., 2011), leukemia (Ruan et al., 2006), renal tumor (Tan et al., 2006), lung cancer (Spinola et al., 2006), prostate cancer (Du et al., 2009), hepatocellular cancer (Fu et al., 2013), laryngeal cancer (Xu et al., 2013), oral squamous cell carcinoma (Zhao et al., 2013) and cervical cancer (Liu et al., 2013).
PDCD5 expression predicts a favorable outcome in patients with hepatocellular carcinoma, epithelial ovarian carcinomas, chondrosarcoma.
PDCD5 may make significance to inhibit tumor malignant transformation and progress. Recombinant human PDCD5 (rhPDCD5) has been shown to enter a variety of cells by clathrin-independent endocytosis and exert biological activities.
RhPDCD5 could enhance cell death of tumor cells and enhance the sensitivity to chemotherapeutic, such as cisplatin (Chen et al., 2010b; Shi et al., 2010; Wang et al., 2013c).

Rheumatoid arthritis

PDCD5 is associated with rheumatoid arthritis and osteoarthritis, which can regulate the apoptosis of synoviocytes and chondrocytes (Wang et al., 2007). The levels of PDCD5 in serum, synovial fluid and cartilage are higher in RA and OA than healthy control, which are negatively correlated with IL-17 or TNF-α levels (Wang et al., 2013a). The expression of PDCD5 may be down regulated by Insulin-like growth factor 1 (Yi et al., 2013). Recombinant human PDCD5 has an anti-inflammatory effect in collagen-induced arthritis (CIA) rats (Xiao et al., 2014).

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