

Gene Section

Mini Review

PDCD6 (programmed cell death 6)

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Identity

Hugo: PDCD6

Other names: ALG-2; MGC111017; MGC119050; MGC9123; PEF1B

Location: 5p15.33

DNA/RNA

Description

The PDCD6 gene contains 43351 bp. The coding sequence extends from 324738 nt to 368089 nt and contains 6 exons. The initiation codon is located at position 101 in exon 1. Exon 3 sequence is identical

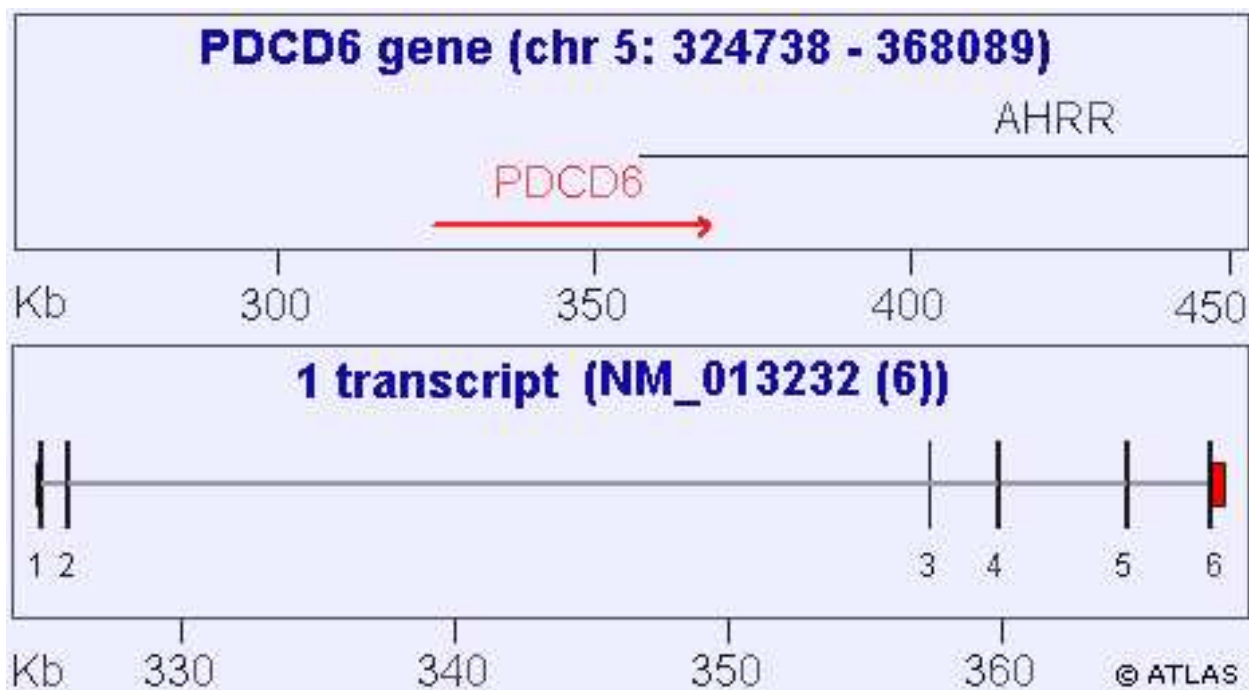
with AHRR (HGNC symbol synonyms: AHH, AHHR, KIAA1234) position 357291-357336 at the same locus.

Transcription

Is in a telomere to centromere direction. There is one alternative splice site (validated by ESTs and RNase protection analysis) at the 5' of exon 4 creating a 6 bp shorter exon corresponding of a protein lacking GF121/122.

Pseudogene

Q7Z6L2_HUMAN, IOC728613, p15.33, NC-000005.8, 1650672 - 1705673 in a centromere to telomere direction.



Map of the PDCD gene at 5pt-15.2, black boxes indicate exons, red boxes indicate untranslated exons.

Protein

Description

191 amino acids, 21.7 kDa, member of the penta EF hand protein family.

Expression

Ubiquitously expressed, higher abundance in some tumor tissues.

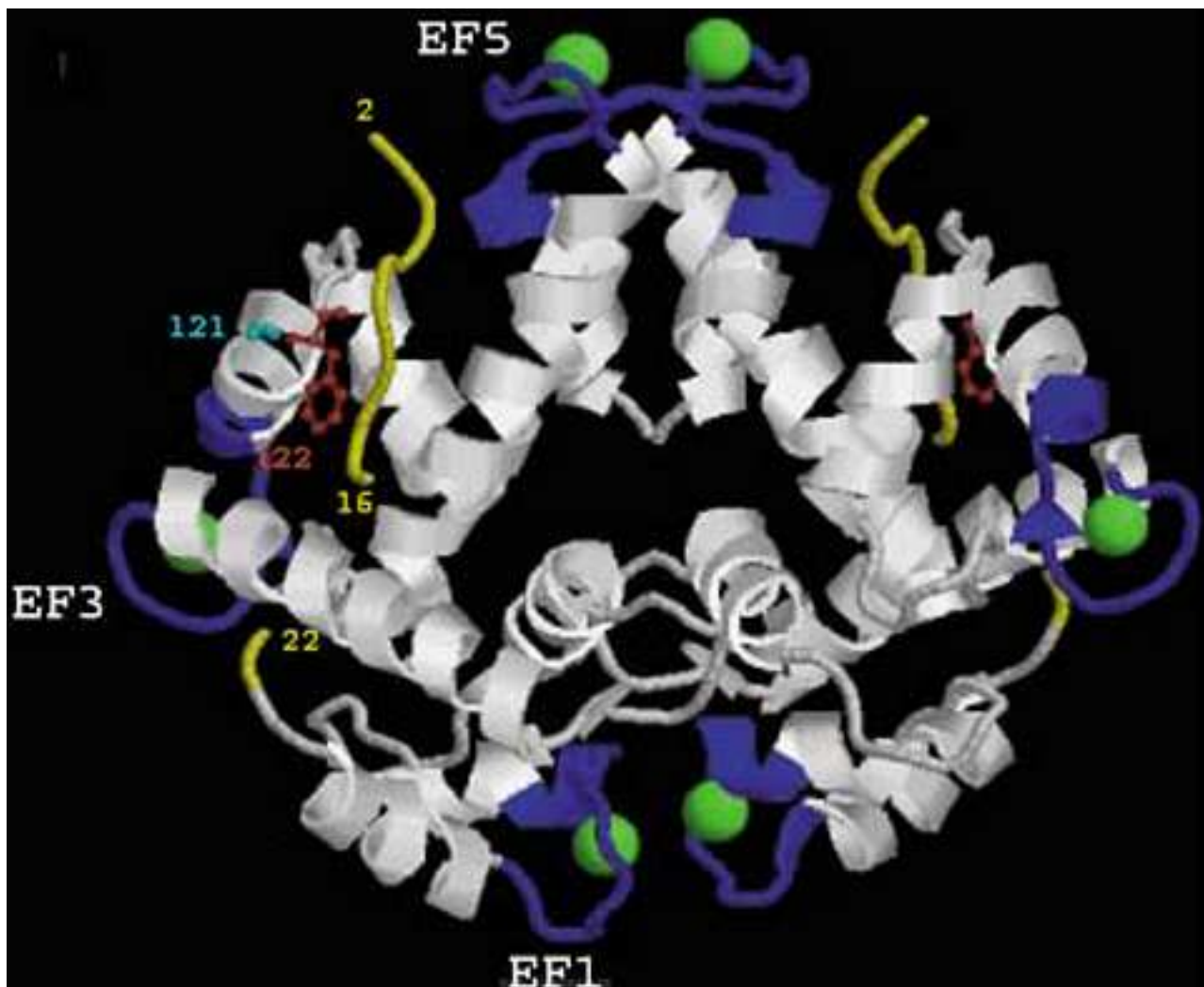
Localisation

Cytoplasmic, nuclear and unidentified structures in the cytoplasm.

Function

PDCD6 (product of the apoptosis-linked gene 2) is a calcium binding protein with 5 EF hand motifs originally identified as a proapoptotic protein in a genetic screen. A knock out mouse with deleted PDCD6 gene showed no obvious phenotype. Newer

results indicate that inhibition of PDCD6 expression reduces cellular viability. Several target proteins, which interact with PDCD6 in a calcium dependent fashion have been found. Most prominent are AIP1/Alix, an adaptor protein involved in apoptosis, endocytosis, adhesion and cytokinesis as well as TSG101, a tumor suppressor gene product, which is a component of the ESRT-1 (endosomal sorting complex required for transport I) and Sec31A, a component of the COPII, ER to Golgi transport vesicles. As all these proteins are linked to intracellular trafficking PDCD6 may connect calcium signaling to trafficking processes through these target proteins or yet to be identified novel PDCD6 targets and thereby regulates cell viability. As a commercial anti PDCD6 antibody, which turned out to be directed against the cochaperone protein p23 and not against PDCD6 was used to confirm interaction of PDCD6 with target proteins some of the early reports on PDCD6 have to be treated with caution.



Protein structure: 3-dimensional structure of the PDCD6 dimer: EF1, EF3, EF5 are the functional calcium binding domains (blue). In green are the calcium ions, in yellow is the N-terminal peptide modeled on the protein, in cyan and red are G121 and F122 missing in the known splice form.

Homology

PEF (Penta EF-hand) family proteins sorcin, grancalcin, calpain light and heavy chain, peflin.

Mutations

Note: Not known.

Implicated in

Various cancers

Note: PDCD6 has been reported to be downregulated in atherosclerotic plaques as shown by Western array analysis. However, it was found later that the cochaperone p23 and not PDCD6 was downregulated due to the use of a nonspecific antibody.

Oncogenesis

PDCD6 downregulation has been implicated in ocular melanoma, possibly giving cancer cells a growth advantage.

PDCD6 has been shown to be significantly upregulated in rat hepatomas and human small lung cancer as well as in non small lung cancer cells analyzed in specimens of 263 patients. In a tissue microarray analysis with ca 8000 samples of normal and tumor tissues strong PDCD6 signals were detected in urothelium (benign), adeno dysplasia, thymoma and neuroendocrine tumors with over 35 % of the samples to give a moderate or strong staining. Brenner, carcinoid and cribriform tumors gave the strongest signals. In normal tissues cells of the urothelium of the kidney and urinary bladder, islet cells of the pancreas, columnar ductal cells of the seminal vesicle, tall columnar cells of the epididymus and ciliated as well as secretory cells of the fallopian tube were stained for PDCD6 with strongest intensity but below the one found in strongly staining tumor cells. PDCD6 downregulation with siRNA inhibited growth of HeLa cells. PDCD6 might therefore play a role as a cellular viability factor. However, no correlation between PDCD6 staining intensity and survival of patients with lung cancer, colon cancer or breast cancer was found.

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