

Gene Section

Short Communication

PDCD10 (Programmed cell death 10)

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Abstract

PDCD10 is a novel apoptosis regulator which functions in the regulation of cellular proliferation and apoptosis.

Keywords: PDCD10, programmed cell death, apoptosis, cell survival, cellular proliferation

Identity

Other names: CCM3, TFAR15

HGNC (Hugo): PDCD10

Location: 3q26.1

Local order: From telomere to centromere: LINC01330, MEMO1P3, SERPINI1, PDCD10, HMGN1P8, WDR49, LOC105374197, SERPINI2

DNA/RNA

Description

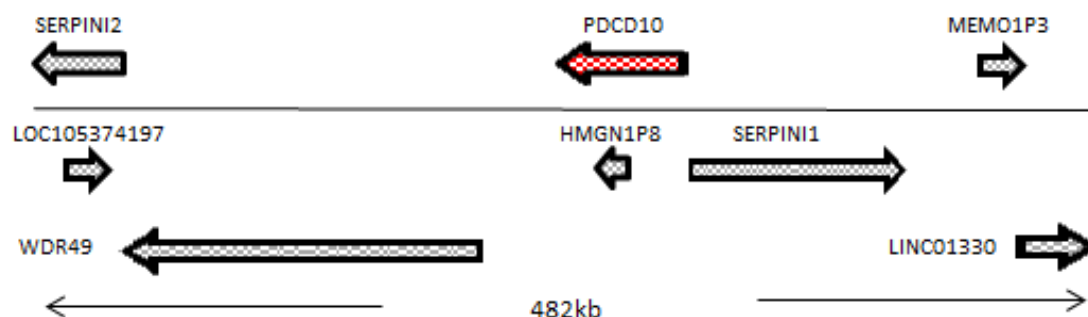
The PDCD10 gene is 51,688 bp in length, located on the minus strand and spans 9 exons (NCBI, 2016).

Transcription

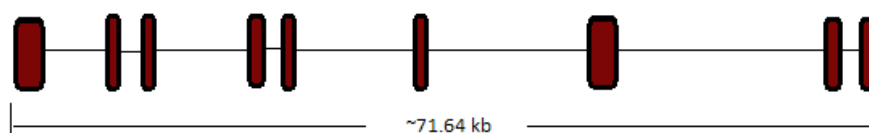
3 different alternatively spliced mRNAs (1454, 1313 and 1212 bp long, respectively) that differ only in 5'UTRs; 639 bp long open reading frame (NM_007217.3, NM_145859.1, NM_145860.1).

Pseudogene

LOC100128686 programmed cell death 10 pseudogene; located on 8q11.21 (NCBI, 2016).



Local order of PDCD10 is shown together with leading and subsequent genes on chromosome 3. The direction of arrows indicates transcriptional directions on the chromosome and arrow sizes approximate gene sizes.



Boxes are exons and the lines are introns.

Protein

Description

PDCD10 encodes an evolutionarily conserved 212 amino acid long protein (Wang et al, 1999). PDCD10 has an estimated molecular weight of 29 kDa.

Expression

PDCD10 is expressed in all tissues including brain, pancreas, breast, ovary, kidney, liver and lungs (The Human Protein Atlas, 2016).

Localisation

PDCD10 is localized in cytoplasm, near Golgi apparatus and nucleus (Fidalgo et al, 2010).

Function

The PDCD10 protein regulates cell proliferation and transformation by modulating the extracellular signal-regulated kinase (ERK) pathway through interaction with serine/threonine protein kinase STK26 (MST4) (Ma et al, 2007). It also interacts with another serine/threonine kinase, STK25, and triggers apoptosis under oxidative stress (Zhang et al, 2012). PDCD10 interacts with members of germinal center kinases III subfamily to promote normal Golgi assembly and cell orientation (Fidalgo, 2010). PDCD10 involves in the stabilization of KDR (VEGFR2) signaling and is vital for normal vascular development (He et al, 2010). PDCD10 acts downstream of gamma-protocadherins and regulate neuronal survival (Lin et al, 2010).

Mutations

Germinal

Cerebral cavernous malformations are associated with the mutations in 3 loci; one of which is CCM3/PDCD10. Bergametti et al reported a de novo deletion as well as six other deleterious mutations in PDCD10 gene. Three of these mutations were stated as nonsense mutations, two other mutations were reported to generate aberrant splicing in exon 9 with a frameshift and the last one caused an abnormal splicing in exon 5 without frameshift (Bergametti et al, 2005). In a study with 61 families with cerebral cavernous malformations, Guclu et al (2005) identified two identical mutations creating a premature stop codon in exon 7, two frameshift mutations in exon 6 and one additional frameshift mutation in exon 9 (Guclu et al, 2005). In patients

without KRIT1 (CCM1) and CCM2 mutations, Verlaan et al (2005) identified two mutations in CCM3 which lead to a truncated PDCD10 protein. One of the mutations was a nonsense mutation in exon 7 caused by a transversion of a C to a T that creates a stop codon and the other one was reported to be an invariant splice acceptor site mutation (Verlaan et al, 2005). Riant et al (2013) reported that, in 13 of 54 CCM3-mutated patients, there are deletions in one or several coding exons; 8 of which deletions are whole gene deletions. In 41 patients, several point mutations leading abnormal splicing, nonsense mutations and small insertions and deletions causing frameshifts and premature stop codons were identified. Additionally, they reported deletions in noncoding exons 1-3 in a 5-year old child with cerebral carcinomas (Riant et al, 2013).

Implicated in

Cerebral cavernous malformations

Cerebral cavernous malformations (CCM) is one of the frequently occurring cerebral vascular abnormalities characterized by abnormally enlarged blood vessels that cause brain hemorrhages and seizures which result in focal neurological deficits (Rigamonti et al, 1998; Bergametti et al, 2005). Bergametti et al identified PDCD10 as the CCM3 gene and reported several mutations in this locus (Bergametti et al, 2005). Several other studies also reported different mutations in PDCD10 gene in patients with cerebral cavernous malformations and cerebral carcinomas (see Mutations section above).

Prostate cancer

PDCD10 is expressed in both benign prostatic hyperplasia and prostate cancer with a stronger staining in prostate cancer cases. Germinal center kinases, MST4 and STK25, are also significantly overexpressed in prostate cancer and associated with the PDCD10 expression (Zhang et al, 2014). miR-103 is reported to regulate PDCD10 in prostate cancer and when overexpressed, it suppresses tumor cell proliferation by targeting PDCD10 (Fu et al, 2016).

T cell lymphoma

PDCD10 is constitutively expressed in malignant T cells and cell lines derived from peripheral blood of patients with Sezary syndrome (T cell lymphoma). PDCD10 is found to be constitutively associated with protein phosphatase-2A (PP2A) which is

essential in the regulation of cell proliferation and apoptosis in T cell lymphoma. Depletion of PDCD10 was reported to significantly increase apoptosis in various malignant T cells (Lauenborg et al, 2010).

Colorectal cancer

Zhang et al (2016) reported that PDCD10 expression was down-regulated in drug-resistant colorectal cancer cells. The expression of PDCD10 was regulated by MIR425 (mature sequence miR-425-5p) which directly targets 3'-UTR of PDCD10 (Zhang et al, 2016).

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