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Gene Section
Mini Review

TP53INP1 (tumor protein p53 inducible nuclear protein 1)

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Identity

Other names: SIP; TEAP; p53DINP1; TP53INP1A; TP53INP1B; TP53DINP1

HGNC (Hugo): TP53INP1

Location: 8q22.1

DNA/RNA

Description

Gene is ~24 kb, with 5 exons.

Transcription

Alternative splicing: 2 transcripts: TP53INP1alpha (exons 1, 2, 3, 4 and 5 with a stop codon in the fourth exon) and TP53INP1beta (exons 1, 2, 3 and 5 with a stop codon in the fifth exon).

Protein

Description

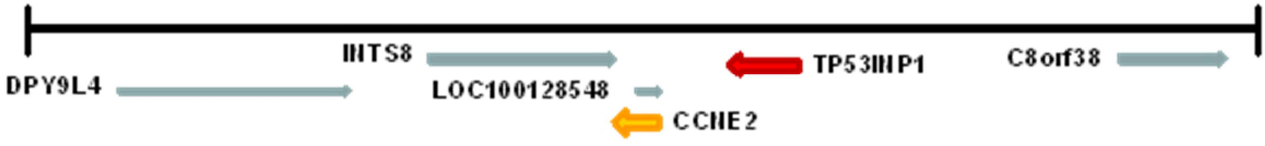
2 isoforms: TP53INP1alpha, 18 kDa (164 amino acids) and TP53INP1beta, 27 kDa (240 amino acids). Both isoforms contain a PEST domain (sequence rich in proline, glutamic acid, serine and threonine between amino acids 26 and 62 found in proteins with half-lives of less than 2 h).

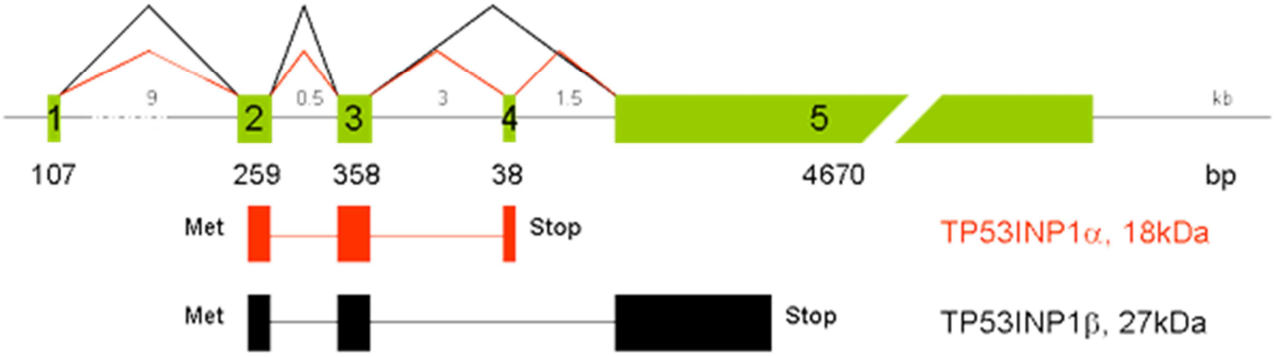
Expression

In mouse: TP53INP1 is expressed in thymus, spleen and bone marrow. It is also expressed at low levels in heart, stomach, liver, intestine, testis, kidney and pancreas. TP53INP1 expression is highly induced during the acute phase of mouse experimental pancreatitis (caerulein induced).
In cells lines: TP53INP1 is transcriptionally induced in response to stress in a p53-dependent and independent manner. Examples: in mouse fibroblast, it is induced upon adriamycin, methyl-methane sulfonate, ethanol, H2O2, UV exposure and heat shock treatment; in neuronal cells by copper treatment; in pancreatic cancer cell lines by gemcitabine; in pro-B cells by IL-3 deprivation or treatement with staurosporine, cisplatin, campto-thecin, methotrexate and paclitaxel; in mouse embryonic fibroblast (MEF), human fibroblasts and MCF7 by gamma irradiation; in melanoma cells by UV mimetic compound (4NQ).
TP53INP1 expression is regulated by different transcriptional regulators: p53, E2F1, p73 (in p53-/- cells), myc (in neuroblastoma cell lines) and PLZF (in hematopoietic cell lines).

Localisation

Nuclear when over-expressed and in PML-bodies (Promyelocytic leukemia protein) upon PML-IV over-expression.





Green boxes: exons, black lines: introns, alternative splicing for TP53INP1beta in black and TP53INP1alpha in red.

Function

TP53INP1 is a tumor suppressor gene induced with different stress conditions. TP53INP1 overexpres-sion leads to cell cycle arrest (G1 phase) and p53-dependent or independent apoptosis. TP53INP1 interacts with p53 and two kinases (HIPK2, and PKCd). These kinases phosphorylate p53 on serine 46 modifying the p53 activity. TP53INP1 can modulate the p53 and p73 transcriptional activity to potentiate pro-apoptotic pathways. Colitis and colitis-associated cancer are exacerbated in mice deficient for TP53INP1.

Homology

TP53INP1 is conserved between species (from fly to human). In vertebrates, one paralog has been identified, TP53INP2 localized on chromosome 20q11.2. TP53INP2 is involved in autophagy.

Mutations

Note

No mutation identified.

Implicated in

Pancreatic Adenocarcinoma

Note

TP53INP1 is lost early during pancreatic cancer progression (from the neoplasia stages PanIN2). This downregulation seems to be important for tumour development. TP53INP1 expression is down regulated by the oncogenic micro-RNA miR-155 during pancreatic cancer progression.

Disease

Sporadic cancer, very aggressive, epigenetic disease with known mutations/deletions of p53, K-Ras, SMAD4, p16, BRCA2, EGFR and HER2.

Prognosis

Very bad, with only 20% of patients reaching two years of survival, and 3% after 5 years.

Breast cancer

Note

TP53INP1 expression is lost during breast cancer development.

Disease

Mainly in female (only 1% in male). Genetic disorders known: loss of HER2 and ER expression, mutations in p53 and BRCA1.

Prognosis

Mortality rate: 25%.

Gastric cancer

Note

TP53INP1 expression is lost during cancer development. The decreased expression of TP53INP1 protein may reflect the malignant grade of gastric cancer.

Disease

10% are familial. Mutations in APC, p53, Bcl-2.

Prognosis

The 5-year survival after surgical resection is 30-50% for patients with stage II and 10-25% for patients with stage III.

Anaplastic carcinoma of the thyroid (ATC)

Note

TP53INP1 is overexpressed in anaplastic thyroid carcinoma.

Disease

ATC is less than 2% of total thyroid cancer but represents 40% of death by thyroid cancer. It is a very aggressive cancer with early dissemination.

Prognosis

5-year survival rate is less than 10%.

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