Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section
Mini Review

PTPN13 (Protein tyrosine phosphatase, non-receptor type 13)

Alessandro Beghini

University of Milan, Medical Faculty, Department of Biology and Genetics for Medical Sciences, via Viotti 5, 20133-Milan, Italy (AB)

Published in Atlas Database: September 2008

Online updated version : http://AtlasGeneticsOncology.org/Genes/PTPN13ID41912ch4q21.html
DOI: 10.4267/2042/44537

Identity

Other names: DKFZp686J1497; FAP-1; PNP1; PTP-BAS; PTP-BL; PTP-E1; PTP1E; PTPL1; PTPLE

HGNC (Hugo): PTPN13

Location: 4q21.3

Note: Genomic context: PTPN13 lies in a head-to-head conformation with MAPK10/JNK3 and they share a 633 bp bi-directional promoter which is a typical CpG island.

DNA/RNA

Description

The gene covers 220.87 kb (from 87734485 to 87955350-NCBI) and contains 48 exons and 51 different introns (49 gt-ag, 2 gc-ag), initiates transcription within exon 2 and terminates in exon 48.

Transcription

Transcription produces 13 different mRNAs, 9 alternatively spliced variants and 4 unspliced forms. RefSeq annotates 4 representative transcripts, but Homo sapiens cDNA sequences in GenBank support at least 9 spliced variants.

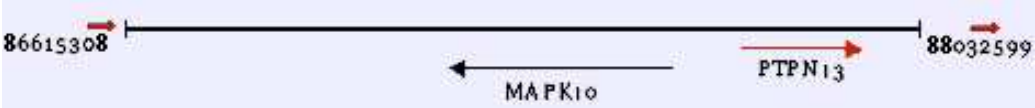
Protein

Description

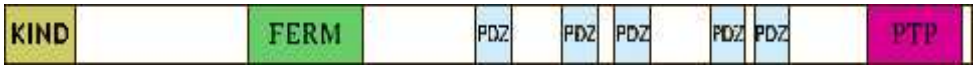
The protein encoded by this gene is a member of the protein tyrosine phosphatase (PTP) family. PTPs are known to be signaling molecules that regulate a variety of cellular processes including cell growth, differentiation, mitotic cycle, and oncogenic transformation. This PTP is a large protein that possesses a PTP domain at C-terminus, and multiple noncatalytic domains, which include a domain with similarity to band 4.1 superfamily of cytoskeletal-associated proteins, a region consisting of five PDZ domains, and a leucine zipper motif. This PTP was found to interact with, and dephosphorylate Fas receptor, as well as IkappaBalpha through the PDZ domains, which suggested its role in Fas mediated programmed cell death. This PTP was also shown to interact with GTPase-activating protein, and thus may function as a regulator of Rho signaling pathway. Eight spliced and the unspliced mRNAs putatively encode good proteins.

Expression

In all human normal tissues, including lymph node and peripheral blood mononuclear cells samples, PTPN13 is ubiquitously expressed.



Genomic view.



Schematic representation of PTPN13 structure and boxes represent functional domains. The KIND domain has been identified in silico by sequence homology.

Localisation

The FERM domain binds to phosphatidylinositol 4,5-biphosphate leading to the enrichment of PTPN13 at a juxtamembrane localization.However, the PTPN13 protein is also detected throughout the cytoplasm. In HeLa cells, PTPN13 localizes to the centrosomes during metaphase.

Function

Functionally, the gene has been tested for association to diseases (bone neoplasms; carcinoma; colorectal neoplasms; liver neoplasms; lymphoma; sarcoma, Ewing's), proposed to participate in a pathway (FAS signaling pathway (CD95)) and a process (protein amino acid dephosphorylation). Proteins are expected to have molecular functions (non-membrane spanning protein tyrosine phosphatase activity, hydrolase activity, protein binding, structural molecule activity) and to localize in various compartments (nucleus, cytoplasm, cytoskeleton).

Mutations

Note

Different somatic mutations was identified in colorectal tumors (19% of the colorectal cancer samples analyzed), predicted to result in missense or non-sense mutations. Some of these mutant proteins led to reduce phosphatase activity.

Implicated in

Colorectal cancers

Disease

A large-scale study that looked at the mutations in the tyrosine phosphatome from colorectal cancers identified PTPN13. The authors identified 19 mutations, non-sense and missense, seven of which were in the PTP domain.

Lymphomas (Hodgkin and non-Hodgkin), gastric and hepatocellular tumors

Disease

Hypermethylation of the PTPN13 promoter or allelic loss was observed leading to downregulation of PTPN13 mRNA.

To be noted

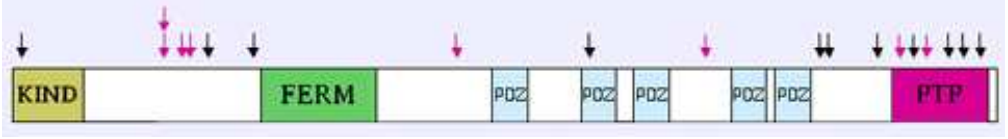
Note

Several evidences suggest that PTPN13 may act

Mutations of PTPN13 in colorectal cancers

(from Science 2004;Vol. 304. no. 5674, pp. 1164 - 1166)

Nucleotide	Amino Acid
C6G / G2854T	**H2Q** / E952X
855insA	frameshift
855del / G4426T	frameshift / G1476C
C1138T / G7329T	R380X / **M2443I**
C1204T	R402X
G1328A	**S443N**
C1586A	**A529D**
C5071T	Q1691X
A6393T	K2131N
G6460C	D2154H
C6613T / C7012T	R2205W / R2338X
C6837A	Y2279X
T6920C	**M2307T**
A7372G	I2458V
A7422C	**E2474D**



Distribution of mutations in PTPN13, black arrows indicate location of missense mutations, red arrows indicate location of nonsense mutations or frameshifts.

differently as a tumor promoting gene depending upon the disease context. The modulation of Fas-mediated cell death by PTPN13 could enhance tumor growth by blocking death signaling.

References

Banville D, Ahmad S, Stocco R, Shen SH. A novel protein-tyrosine phosphatase with homology to both the cytoskeletal proteins of the band 4.1 family and junction-associated guanylate kinases. J Biol Chem. 1994 Sep 2;269(35):22320-7

Maekawa K, Imagawa N, Nagamatsu M, Harada S. Molecular cloning of a novel protein-tyrosine phosphatase containing a membrane-binding domain and GLGF repeats. FEBS Lett. 1994 Jan 10;337(2):200-6

Saras J, Claesson-Welsh L, Heldin CH, Gonez LJ. Cloning and characterization of PTPL1, a protein tyrosine phosphatase with similarities to cytoskeletal-associated proteins. J Biol Chem. 1994 Sep 30;269(39):24082-9

Inazawa J, Ariyama T, Abe T, Druck T, Ohta M, Huebner K, Yanagisawa J, Reed JC, Sato T. PTPN13, a fas-associated protein tyrosine phosphatase, is located on the long arm of chromosome 4 at band q21.3. Genomics. 1996 Jan 15;31(2):240-2

van den Maagdenberg AM, Olde Weghuis D, Rijss J, Merkx GF, Wieringa B, Geurts van Kessel A, Hendriks WJ. The gene (PTPN13) encoding the protein tyrosine phosphatase PTP-BL/PTP-BAS is located in mouse chromosome region 5E/F and human chromosome region 4q21. Cytogenet Cell Genet. 1996;74(1-2):153-5

Yoshida S, Harada H, Nagai H, Fukino K, Teramoto A, Emi M. Head-to-head juxtaposition of Fas-associated phosphatase-1 (FAP-1) and c-Jun NH2-terminal kinase 3 (JNK3) genes: genomic structure and seven polymorphisms of the FAP-1 gene. J Hum Genet. 2002;47(11):614-9

Wang Z, Shen D, Parsons DW, Bardelli A, Sager J, Szabo S, Ptak J, Silliman N, Peters BA, van der Heijden MS, Parmigiani G, Yan H, Wang TL, Riggins G, Powell SM, Willson JK, Markowitz S, Kinzler KW, Vogelstein B, Velculescu VE. Mutational analysis of the tyrosine phosphatome in colorectal cancers. Science. 2004 May 21;304(5674):1164-6

Yeh SH, Wu DC, Tsai CY, Kuo TJ, Yu WC, Chang YS, Chen CL, Chang CF, Chen DS, Chen PJ. Genetic characterization of fas-associated phosphatase-1 as a putative tumor suppressor gene on chromosome 4q21.3 in hepatocellular carcinoma. Clin Cancer Res. 2006 Feb 15;12(4):1097-108

Ying J, Li H, Cui Y, Wong AH, Langford C, Tao Q. Epigenetic disruption of two proapoptotic genes MAPK10/JNK3 and PTPN13/FAP-1 in multiple lymphomas and carcinomas through hypermethylation of a common bidirectional promoter. Leukemia. 2006 Jun;20(6):1173-5

Abaan OD, Toretsky JA. PTPL1: a large phosphatase with a split personality. Cancer Metastasis Rev. 2008 Jun;27(2):205-14

This article should be referenced as such:

Beghini A. PTPN13 (Protein tyrosine phosphatase, non-receptor type 13). Atlas Genet Cytogenet Oncol Haematol. 2009; 13(8):573-575.