PTPRD (protein tyrosine phosphatase, receptor type, D)

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Identity

Other names: EC 3.1.3.48; HPTP; HPTP-Delta; HPTPD; MGC119750; MGC119751; MGC119752; MGC119753; PTPD; R-PTP-Delta; R-PTP-delta

HGNC (Hugo): PTPRD

Location: 9p23

DNA/RNA

Description

The PTPRD gene is composed of 36 coding sequence exons and a 5’ UTR spliced together from 11 non-coding exons.

Transcription

There are five known transcript variants for PTPRD.

Transcript Variant 1: This variant encodes the longest isoform 1 and is 10078 bp in length (Figure A).

Transcript Variant 2: This variant lacks two separate internal segments within the coding region. It thus encodes a protein that lacks a 9 aa, and a 4 aa internal fragments, as compared to isoform 1 and is 10039 bp in length (Figure C).

Transcript Variant 3: This variant lacks an internal segment within the coding region. It thus encodes a protein that lacks a 9 aa internal fragment, as compared to isoform 1 and is 10051 bp in length (Figure D).

Transcript Variant 4: This variant lacks an internal segment within the coding region. It thus encodes a protein that lacks a 411 aa internal fragment, and has one amino acid change, as compared to isoform 1 and is 8845 bp in length (Figure B).

Transcript Variant 5: This variant omits several exons, and utilizes an alternate exon, in the coding region. The resulting protein (isoform 5) retains the same reading frame and has the same N- and C-terminus as isoform 1. This variant is 8848 bp in length (Figure E).

Pseudogene

No pseudogenes have been reported.

Protein

Description

Amino acids: 1912.

Molecular Weight: 214760 Da.

The PTPRD gene belongs to the receptor class 2A subfamily of the protein-tyrosine phosphatases. It contains an extracellular region composed of 8 fibronectin type-III domains and 3 Ig-like C2-type (immunoglobulin-like) domains, a single transmembrane segment and two tandem intracytoplasmic tyrosine-protein phosphatase domains.

Molecular Class: Receptor Tyrosine Phosphatase.

Molecular Function: Receptor Signalling Protein Tyrosine Phosphatase Activity.

Biological Process: Cell Communication; Signal Transduction.

Expression

Brain, Kidney.

Multiple isoforms are generated by either alternate splicing or by alternate transcriptional start sites in
a tissue specific manner. The predominant isoform in brain has an extended 711 base pair 5' UTR (L isoform), while the isoform (S) expressed in kidney lacks the extended 5' UTR. In addition, the brain isoform is characterized by the absence of exons 14 to 18 corresponding to amino acid residues 568 to 978 of the 4th through 7th fibronectin III-like domain and by the insertion of a 12 base pair mini-exon sequence between exons 23 and 24 (Nair et al., 2008). The full length PTPRD isoform has an extracellular region containing three Ig-like and eight FN-III like domains connected via a transmembrane peptide to an intracellular region with two PTPase domains (A), whereas another isoform lacks four of the eight FN-III like domains (B). Furthermore, other PTPRD isoforms exist that lack 9 AA within the second Ig-like domain and 4 AA at the junction of the 2nd and 3rd Ig-like domains (C) or 9 AAs within the 5th FN-III like domain (D). The fifth isoform lacks four of the eight FN-III like domains and has mutation in the second Ig-like domain (E). RT-PCR analysis demonstrated that PTPRD isoforms lacking these short peptides are expressed in kidney, whereas isoforms containing these peptides are expressed in the brain (Pulido et al., 1995).

**Localisation**
Membrane; Single-pass type I membrane protein.

**Function**
A cleavage occurs, separating the extracellular domain from the transmembrane segment. This process called 'ectodomain shedding' is thought to be involved in receptor desensitization, signal transduction and/or membrane localization. Plays key role in promoting neurite growth and regulating axon guidance.

**Homology**
PTPRD shares a PTP domain, involved in dephosphorylating phosphorylated tyrosine residues, with the other receptor-like protein tyrosine phosphatases. The human and mouse PTPRD sequences are 93% identical and 95% homologous.

**Implicated in**

**Lung adenocarcinoma**

**Disease**
Early evidence for the involvement of PTPRD in lung adenocarcinoma came from the detection of homozygous deletions in both primary tumours and cell lines representing both small cell lung carcinoma and non-small cell lung carcinoma (Cox et al., 2005; Zhao et al., 2005; Sato et al., 2005; Nagayama et al., 2007). In addition, somatically acquired PTPRD mutations were found in 11 out of 188 lung adenocarcinoma samples (Weir et al., 2007). Notably, three of the mutations encode predicted inactivating changes in the tyrosine phosphatase domain. Screening for somatic mutations in 623 candidate genes using 188 primary lung adenocarcinoma tissues also revealed sequence changes in PTPRD (Ding et al., 2008).
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Neuroblastoma

Disease
High resolution a CGH analysis of neuroblastoma (NBL) tumours and cell lines identified homozygous and hemizygous intragenic deletions of the PTPRD gene, implicating the gene as a candidate tumour suppressor gene in this type of cancer (Stallings et al., 2006). In addition, the 5’ UTR of PTPRD, consisting of 11 noncoding exons, was found to be aberrantly spliced in > 50% of NBL primary tumors and cell lines (Nair et al., 2008). mRNA levels were determined to be significantly reduced in unfavorable tumour subtypes relative to more favorable tumour subtypes.

Squamous cell carcinoma

Disease
Both homozygous and hemizygous deletions affecting the PTPRD gene have been reported in squamous cell carcinoma (Purdie et al., 2007).

Colorectal carcinoma

Disease
PTPRD was found to be somatically mutated in colorectal carcinoma with the sequence changes, R28Q, L276P, V901A (Sjoblom et al., 2006).

Glioblastoma multiforme and malignant melanoma

Disease
A high frequency of deletions in the PTPRD gene were detected in glioblastoma multiforme (GBM) tumours using Affymetrix 250K single nucleotide polymorphism arrays (Solomon et al., 2008). Missense and nonsense mutations of PTPRD were also identified in a subset of the samples lacking deletions, including an inherited mutation with somatic loss of the wild-type allele. The same group also identified 10 somatically acquired mutations in PTPRD among 7 of 57 melanoma tumors (12%). Ectopic reconstitution of wild-type PTPRD expression in GBM and melanoma cell lines harboring deletions or mutations of the endogenous PTPRD gene led to growth suppression and apoptosis, indicating that this gene functions as a tumour suppressor in multiple forms of cancer (Solomon et al., 2008).

Restless leg syndrome (RLS)

Disease
Genre-wide association study of RLS identified three SNPs within the PTPRD gene in the chromosome 9 linkage region (RLS3) as nominally significant (Winkelmann et al., 2007). PTPRD is identified as the fourth genome-wide significant locus for RLS from the genome wide association study in 2458 affected individuals and 4749 controls from Germany, Austria, Czech Republic and Canada (Schormair et al., 2008).

Pediatric asthma

Disease
A whole-genome linkage disequilibrium mapping study for asthma on 190 allergic and nonallergic asthma children in Taiwan revealed that polymorphisms of PTPRD are strongly associated with pediatric bronchial asthma in the Taiwanese population (Shyur et al., 2008).

References


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