PTEN (phosphatase and tensin homolog deleted on chromosome ten)

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Published in Atlas Database: July 1999

Online updated version: http://AtlasGeneticsOncology.org/Genes/PTENID158.html
DOI: 10.4267/2042/37528

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Identity

Other names: MMAC1 (Mutated in Multiple Advanced Cancer 1); TEP 1 (TGFb regulated and Epithelial cell enriched Phosphatase 1)
HGNC (Hugo): PTEN
Location: 10q23.3
Local order: between D10S1765 and D10S541.

DNA/RNA

Description
9 exons, all coding; exon 1 has an unusually long 5’ untranslated GC-rich region; exon 5 codes for the phosphatase core motif.

Transcription
2 major detected transcripts; respectively 2 and 5 kb; open reading frame: 1209 bp.

Protein

Description
403 amino acids, 47 kDa; N-terminal phosphatase domain (from a.a. 1 to 185) with the catalytic core motif between; a.a. 123-131 encoded by exon 5; C-terminal PDZ binding domain.

Localisation
Cytoplasmic localization (immunohistochemistry).

Function
Phosphatase activity; substrate: phosphatidylinositol 3,4,5-tri phosphate (PIP3); PTEN appears as a negative regulator of the PI3K/AKT signaling pathway; It is unclear if PTEN is able to dephosphorylate a protein substrate in vivo; tumor suppressive function: biallelic inactivation is observed in several tumor-types and inactivating germline mutations are responsible for a cancer prone syndrome, the Cowden disease; anti-invasive and anti-proliferative effects were documented in several cell lines.

Mutations

Germlinal
Germine mutations have been documented in Cowden disease and in Bannayan, Riley, Ruvalcaba phenotype (see below); they are observed along the various exons of the gene except the 9th (never described) and the 1st (very few reports); a mutational hot spot is observed in exon 5 in relation with the catalytic core motif; in the great majority of the cases, inactivating mutations are observed, either by protein truncation, or by misense mutation within the phosphatase domain.

Somatic
Mutations are observed in several tumor type; they lead to a biallelic inactivation of the gene either by homozygous deletion, or by a combination of point mutation and a large deletion of the second allele.

Implicated in

Cowden disease and Bannayan, Riley, Ruvalcaba phenotype

Disease
Cowden disease is also known as multiple hamartoma syndrome, a cancer prone condition with autosomal dominant pattern of inheritance and high susceptibility to breast carcinoma and in a less extent to thyroid carcinoma; Bannayan, Ryley, Ruvalcaba syndrome correspond to the pediatric counterpart of Cowden disease with phenotypic overlap between the 2
PTEN (Phosphatase and Tensin homolog deleted on chromosome Ten) Longy M

syndromes (macrocephaly, intestinal polyps, lipomas, genital pigmented macules).

**Sporadic malignant tumors**

**Disease**

Somatic mutations were observed mainly in glioblastoma and in endometrial carcinoma, about 30% of these two kinds of tumors showing point mutations; only a few mutations were reported in prostate carcinoma, malignant melanoma, non Hodgkin lymphomas, breast carcinoma.

**References**


Myers MP, Tonks NK. PTEN: sometimes taking it off can be better than putting it on. Am J Hum Genet. 1997 Dec;61(6):1234-8


**This article should be referenced as such:**