Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section

Mini Review

PTEN (phosphatase and tensin homolog deleted on chromosome ten)

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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 aminoacids, 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

Germinal

Germline 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 contrepart of Cowden disease with phenotypic overlap between the 2

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.

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