TPR (Translocated promoter region)

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Identity

Other names: Tumor potentiating region
HGNC (Hugo): TPR
Location: 1q25
Local order: The 3' coding end of Tpr overlaps with the 3' no-coding region of the PRG4 (Proteoglycan 4) gene (or MGCSF for megacaryocyte stimulating factor) which is involved in the Camptodactyly-arthropathy-coxa vara-pericarditis syndrom.

DNA/RNA

Description
51-52 exons spanning about 63 kb.

Transcription
In a telomeric to centromeric direction. 10kb mRNA.

Protein

Description
2349 amino acids, 267 kDa. The protein contains extensive coiled-coil domains and an acidic globular C-terminus, and is phosphorylated.

Expression
Widespread, if not ubiquitous; highest in testis, thymus, spleen and brain, lower levels in heart, liver and kidney.

Localisation
Nucleoplasmic side of the nucleopore and discrete foci in the nuclear interior, binds to the nucleoporin Nup98.

Function
Still controversial, part of a filamentous intranuclear network, role in nuclear protein and/or polyA+RNA export.

Homology
Yeast Mlp1 and Mlp2, drosophila Bx34, xenopus Tpr.

Mutations

Note
Tpr was first described as a fusion partner with the MET oncogene (7q) in a cell line rendered tumorigenic with the direct acting carcinogen N-methyl-N-prime-nitrosoguanidine (MNNG). Then, this Tpr-MET rearrangement was also described in gastric cancers and a TRK-Tpr fusion was found in thyroid cancers. Fusions with at least one other proto-oncogene have since been described.

Implicated in

Gastric cancers with TPR-MET hybrid gene

Disease
The TPR-MET oncogenic rearrangement is present and expressed in human gastric carcinoma and precursor lesions.

Hybrid/Mutated gene
5' TPR - 3' MET 5 kb mRNA.

Abnormal protein
65 kDa, the fusion protein contains the constitutive
promoter and first 424 coding nucleotides (142 amino acids) of Tpr, and the tyrosine kinase domain of the c-met protooncogene.

**Oncogenesis**
Transgenic expression of TPR-MET oncogene leads to development of mammary hyperplasia and tumors.

**Human papillary thyroid carcinomas with TPR-NTRK1 hybrid gene**

**Hybrid/Mutated gene**
TRK-T1 (TPR-NTRK1): 598 nucleotides of the TPR gene 5' end are fused to 1148 bp of the TRK protooncogene which contain the TRK tyrosine kinase domain. TRK-T2: 3073 nucleotides of Tpr 5' end fused to 1412 nucleotides of TRK. There is another hybrid gene between TPR and NTRK1 named TRK-T4. Arise by paracentric inversions on chromosome 1.

**Abnormal protein**
55 kDa for the TRK-T1 fusion protein.

**Oncogenesis**
TRK-T1 induces neoplastic transformation of thyroid epithelium in transgenic mice expressing the hybrid gene.

**Rat induced tumors (adenocarcinomas and fibroblastomas) with Tpr-raf**

**Note**
All TRK breakpoints fall within a 2.9 kb genomic region of NTRK1. In the Tpr locus, the TRK-T1 and TRK-T2 break points are at least 11 kb apart, indicating the absence of a region prone to rearrangements.

**References**


Frosst P, Guan T, Subauste C, Hahn K, Gerace L. Tpr is localized within the nuclear basket of the pore complex and has a role in nuclear protein export. J Cell Biol. 2002 Feb 18;156(4):617-30

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