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Gene Section
Mini Review

TPR (Translocated promoter region)

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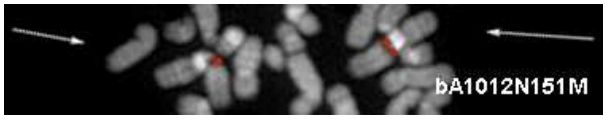
Identity

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.



Probe(s) - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

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 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 proto-oncogene 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

Breakpoints

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

Ishikawa F, Takaku F, Nagao M, Sugimura T. Rat c-raf oncogene activation by a rearrangement that produces a fused protein. Mol Cell Biol. 1987 Mar;7(3):1226-32

Gonzatti-Haces M, Seth A, Park M, Copeland T, Oroszlan S, Vande Woude GF. Characterization of the TPR-MET oncogene p65 and the MET protooncogene p140 protein-tyrosine kinases. Proc Natl Acad Sci U S A. 1988 Jan;85(1):21-5

Soman NR, Correa P, Ruiz BA, Wogan GN. The TPR-MET oncogenic rearrangement is present and expressed in human gastric carcinoma and precursor lesions. Proc Natl Acad Sci U S A. 1991 Jun 1;88(11):4892-6

Greco A, Miranda C, Pagliardini S, Fusetti L, Bongarzone I, Pierotti MA. Chromosome 1 rearrangements involving the genes TPR and NTRK1 produce structurally different thyroid-specific TRK oncogenes. Genes Chromosomes Cancer. 1997 Jun;19(2):112-23

Bangs P, Burke B, Powers C, Craig R, Purohit A, Doxsey S. Functional analysis of Tpr: identification of nuclear pore complex association and nuclear localization domains and a role in mRNA export. J Cell Biol. 1998 Dec 28;143(7):1801-12

Yu J, Miehlke S, Ebert MP, Hoffmann J, Breidert M, Alpen B, Starzynska T, Stolte Prof M, Malfertheiner P, Bayerdörffer E. Frequency of TPR-MET rearrangement in patients with gastric carcinoma and in first-degree relatives. Cancer. 2000 Apr 15;88(8):1801-6

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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