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Phosphorylation of cellular protein tyrosine residues is an important mechanism for the transduction of external signals to the intracellular compartment. Protein tyrosine phosphatases (PTPases) act in concert with protein tyrosine kinases (PTKs) to regulate the level of tyrosine phosphorylation in these proteins. PTKs have been studied in detail, and many have been shown to be proto-oncogenes (1). Because PTPases can be considered functional antagonists of PTKs it has been postulated that these PTPases might act as tumor suppressors. Over 30 different PTPase genes have been isolated so far, and the chromosomal localization has been determined for many of them (13). Comparison of such mapping data with temporal and spatial expression patterns of individual PTPase genes and losses of heterozygosity (LOH) in relevant tumor types could be indicative of their proposed tumor suppressive activity. Until now, chromosomal deletions have been reported only for the PTPRG gene in primary renal and lung carcinomas and cancer-derived cell lines (7, 12), but a tumor suppressor activity. Until now, chromosomal deletions have been reported only for the PTPRG gene in primary renal and lung carcinomas and cancer-derived cell lines (7, 12), but a causal role for a loss of PTPase activity in tumor formation remains to be determined.

We have isolated cosmids containing human PTPase epsilon (PTPRE) gene sequences and used them to determine the chromosomal localization of the gene by fluorescence in situ hybridization (FISH). PTPRE, first isolated by Krueger et al. (6), has a characteristic short extracellular domain (27 aa) and two tandemly repeated intracellular PTPase domains. No specific ligand nor a specific function has been reported for PTPRE yet. Partial cDNA clones for the murine homolog have also been isolated (5, 15) and were used to probe Northern blots. High expression levels of murine PTP epsilon (Ptpe) were observed in brain and testes and low levels in various tissues and hematopoietic cells (15).

To serve as an identification probe, we first generated a PTPRE cDNA fragment by reverse transcription PCR, essentially according to Hendriks et al. (4). Briefly, human keratinocyte total RNA was used as a template for random-primed cDNA synthesis. Subsequently, a 900-bp PTPRE cDNA fragment was specifically amplified (35 cycles of 45 s at 94°C, 30 s at 51°C, and 2 min at 72°C) with primers (primer FPTPE, 5'AGCCACAGCTCCCCGA-3', and RPTPE, 5'-CTGCTCCTCCTGGC-3') that correspond to nucleotides 889-904 and 1786-1799, respectively, of the PTPRE sequence (6). Use of this PCR product in the screening of a human cosmid library resulted in the identification of two independent but overlapping clones, E-1 and E-2. To rule out the possibility of having cloned close homologs of the PTPRE gene or pseudogenes, Sau3AI subclones of cosmid E-2 were screened with the PTPRE cDNA probe. Sequence analysis of one of the subclones revealed 100% identity with the published PTPRE sequence between nucleotides 1091 and 1192 and an exon/intron junction between codons 362 and 363. This splice junction is also found at the corresponding position between exons 14 and 15 of the closely related LRP (PTPRA) gene (14) and between exons 25 and 26 of the more distantly related CD45 (PTPRC) gene (3), but is absent in the gene coding for PTPase LAR (PTPRF) (9).

Both cosmids were used as probes for fluorescence in situ hybridization (FISH), essentially according to De Leeuw et al. (2). A single positive signal was identified with both cosmids on chromosome band 10q26 on both homologs in 31 of 32 total 40 metaphase spreads analyzed (Fig. 1). In addition, a panel of 24 monochromosomal somatic cell hybrids (Lorieu Repository, Camden, NJ) was analyzed by PCR using the previously mentioned primer FPTPE and R2PTPE primer (5'-GCGTGCATCATGGCCA-3'), corresponding to nucleo-
tides 1105-1120 of the PTPRE cDNA sequence (6)). A PTPRE fragment of 1.9 kb containing intronic sequences was specifically amplified (33 cycles of 45 s at 94°C, 30 s at 54°C, and 2 min and 30 s at 72°C) using this primer set on DNA of the chromosome 10-only cell hybrid as well as on human genomic control DNA and PTPRE E-1 and E-2 cosmid DNA (data not shown). All other somatic cell hybrids were negative in this PCR assay. Taken together, we conclude that the human PTPRE gene resides on chromosome 10q26. To our knowledge, this is the first tyrosine-specific PTPase to be localized to chromosome 10.

Distinct chromosomal aberrations involving the chromosomal 10q26 region have been reported to occur in, for instance, prostatic carcinomas, early stages of melanocytic neoplasia, hepatocellular carcinomas, glioblastomas, and other malignant astrocytomas (8, 10, 11). In most of these cases the loss of segments of chromosome 10q was not restricted to band q26. Chromosome band 10q26 is also involved in various translocations in hematopoietic disorders, including chronic lymphocytic leukemia and chronic myeloid leukemia (8). As mentioned above, Ptpre is expressed in brain and at low levels in hematopoietic cells. Whether PTPRE has a causal role in any of the aforementioned leukemias and/or solid carcinomas remains to be investigated.

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REFERENCES


Assignment of the Human GAS6 Gene to Chromosome 13q34 by Fluorescence in Situ Hybridization

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GAS6 was originally isolated as a set of growth-arrest-specific genes (gas) whose expression is increased at growth arrest and becomes negatively regulated after synchronous