

Short Report

Regional Assignment of Ptpre Encoding Protein Tyrosine Phosphatase to Mouse Chromosome 7F3

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ABSTRACT

Protein tyrosine phosphatases (PTPases) regulate the tyrosine phosphorylation of target proteins involved in several biological activities including cell proliferation and transformation. Protein tyrosine phosphatase (PTP) contains duplicated PTPase-like domains and a short extracellular region. Using the fluorescence *in situ* hybridization method, the gene encoding PTP (locus symbol Ptpre) was mapped to mouse chromosome 7F3. These results indicate that there is a conserved syntenic group between human chromosome 10q26 and mouse chromosome 7F3. Iran. Biomed. J. 2: 133-135, 1998

Keywords: PTP, Mouse, Gene mapping, Chromosome 7.

INTRODUCTION

Changes in the level(s) and pattern(s) of protein tyrosine phosphorylation are involved in a vast array of biological events including cell activation, growth, differentiation, and neoplastic transformation [1]. Since the number of cloned members of the PTPase family has increased, this family has been divided into three classes based on their overall structures [2]. Class I contains the cytoplasmic molecules with one phosphatase domain, class II contains the transmembrane molecules with one cytoplasmic phosphatase domain, and class III contains the transmembrane molecules with two cytoplasmic phosphatase domains [2].

Protein tyrosine phosphatase (PTP), which belongs to class III of PTPases, contains duplicated PTPase-like domains and a short extracellular region with 27 amino acids [2-4]. The PTP has been cloned in human [2], rat [4], and mouse [3]. Comparisons of the deduced amino acid and nucleotide sequences of PTP between human, rat, and mouse revealed its high level of conservation during the course of evolution of these three species [2-4].

Given the potential role(s) of PTPases in cell growth control [1, 3, 5] and high level of their evolutionary conservation [2-4], it is of particular in

terest to determine the chromosomal localization of the gene encoding PTP in order to investigate the correlation between the location of PTP gene and recurrent cytogenetic abnormalities in neoplasms, as well as its usefulness in comparative analysis of genomic organization during mammalian evolutionary history. Although the gene encoding PTP (locus symbol Ptpre) was mapped on mouse chromosome 7 [6], its regional localization is unknown. The present report deals with a more precise localization of the Ptpre gene in mouse chromosome 7 by fluorescence *in situ* hybridization (FISH) method.

MATERIALS AND METHODS

Chromosome preparations were made from primary culture of skin of DRC mouse. Because the nucleotide sequences of PTP showed high level of conservation during the course of evolution [2, 4], the cDNA of human PTP was used as a probe for gene assignment on mouse chromosomes. A biotin-16-dUTP labeled cDNA of human PTP [2] was hybridized to mouse metaphase chromosomes and the fluorescence signals detected according to the FISH protocol as previously described [7]. Metaphase chromosomes were identified by Q-bands

after staining with quinacrine and Hoechst 33258 as previously described [8].

RESULTS AND DISCUSSION

Hybridization with the human cDNA probe yielded a clear specific hybridization signals on mouse chromosomes. Analysis of 71 mouse metaphases showed that 65% of metaphases had two symmetric fluorescence signals on both chromatids of chromosome 7 at band F3. It should be emphasized that such specific accumulation of signals as mentioned above could not be detected on any other regions of mouse chromosomes. Thus the present data demonstrates more precise localization of the Ptpre gene on 7F3, confirming the previous assignment [6]. Recently, the gene encoding PTP has been mapped to human chromosome 10q26.2-q26.3 [9]; therefore the present results revealed that the Ptpre is a member of conserved syntenic group between human chromosome 10q26 and mouse chromosome 7F3.

The localization of the gene encoding PTP at human chromosome 10q26 and mouse chromosome 7F3, is potentially of great interest, since the karyotypic analysis of human astrocytoma and glioblastoma [10-12] and mouse skin tumors [13-15] revealed that loss of genetic material on human chromosome 10 and mouse chromosome 7 plays a crucial role in these tumors. Using genetic linkage analysis, a genomic region important in determining quantitative variation in liver tumor susceptibility was identified on mouse chromosome 7 [16]. And finally, the Ptpre located near a fragile site on mouse chromosome 7 [17]. Taken together, it is possible that the PTP may be related to malignancy, but further studies are required to clarify the biological function(s) of PTP in carcinogenesis.

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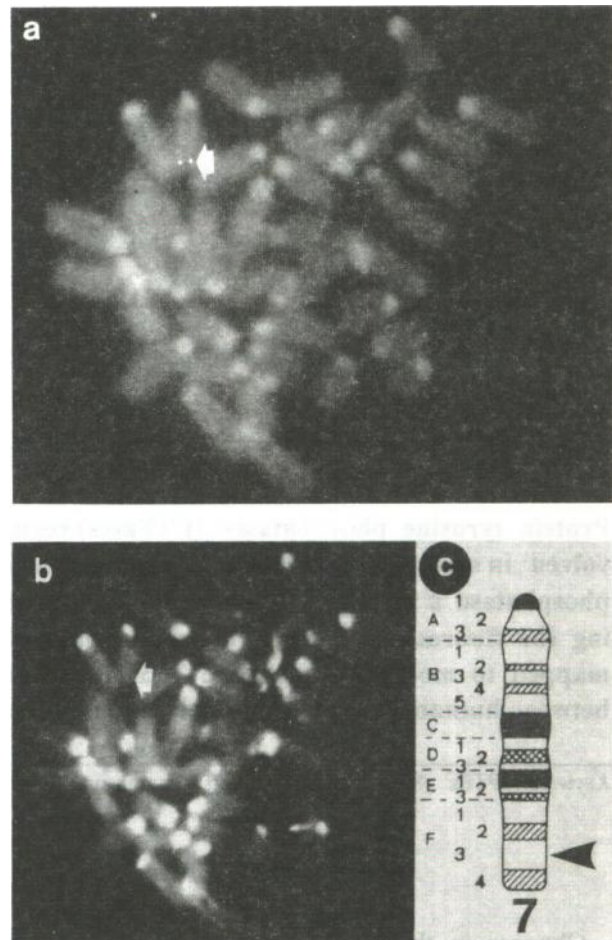


Fig. 1. Assignment of the mouse Ptpre gene to mouse chromosome 7F3 by FISH. FISH was performed using 600 ng denatured human cDNA probe per slide as described previously [7]. Mouse chromosomes were stained with propidium iodide (a) and Q-banding (b). Arrows are the positions of hybridization signals. Diagrammatic representation of mouse chromosome 7, illustrating the localization of the Ptpre gene in 7F3 (arrowhead) (c).

REFERENCES

1. Fischer, E. H., Charbonneau, H. and Tonks, N. K. (1991) Protein tyrosine phosphatases: A diverse family of intercellular and transmembrane enzymes. *Science* 253: 401-406.
2. Krueger, N. X., Streuli, M. and Saito, M. (1990) Structural diversity and evolution of human receptor-like protein tyrosine phosphatases. *EMBO J* 9: 3241-3252.
3. Schepens, J., Zeeuwen, P., Wieringia, B. and Hendriks, W. (1992) Identification and typing of members of the protein-tyrosine phosphatase gene family expressed in mouse brain. *Mol. Bio. Rep* 17: 241248.

4. Nakamura, K., Mizuno, Y. and Kikuchi, K. (1996) Molecular cloning of novel cytoplasmic protein tyrosine phosphatase PTP6. *Biochem. Biophys. Res. Commun.* 218:726-736.
5. Brutigan, D. L. (1992) Great expectations: Protein tyrosine phosphatases in cell regulation. *Biochim. Biophys. Acta.* 1114:63-77.
6. Elson, A., Kozak, C. A., Morton, C. C., Weremowick, S. and Leder, P. (1996) The protein tyrosine phosphatase ϵ gene maps to mouse chromosome 7 and human chromosome 10q26. *Genomics* 31: 373-375.
7. Saadat, M., Mizuno, Y., Kikuchi, K. and Yoshida, M. C. (1995) Comparative mapping of the gene encoding the catalytic subunit of protein phosphatase type Ia (PPP1CA) to human, rat, and mouse chromosomes. *Cytogenet. Cell Genet.* 70:55-57.
8. Yoshida, M. C., Ikeuchi, T. and Sasaki, M. (1975) Differential staining of parental chromosomes in inter-specific cell hybrids with a combined quinacrine and Hoechst 33258 technique. *Proc. Jpn. Acad.* 51:184-187.
9. Saadat, M., Nakamura, K., Mizuno, Y., Kikuchi, K. and Yoshida M. C. (1997) Assignment of PTPRE encoding protein tyrosine phosphatase ϵ to human chromosome 10q26.2-q26.3. *Chromosome Science* 1: 121-122.
10. Rey, J. A., Bello, M. J., de Campos, J. M., Kusak, M. E. and Moreno, S. (1987) Chromosomal composition of a series of 22 human low-grade gliomas. *Cancer Genet. Cytogenet.* 29:223-237.
11. Magnani, I., Gueneri, S., Pollo, B., Grenei, N., Colombo, B. H., Borggi, G., Galli, C., Bugiani, O., DiDonata, S., Finocchiaro, G. and Conti, A. M. F. (1994) Increasing complexity of the karyotype in 50 human gliomas, progressive evolution and de novo occurrence of cytogenetic alterations. *Cancer Genet. Cytogenet.* 75: 77-89.
12. Thiel, G., Losanowa, T., Kintzel, D., Nisch, G., Martin, H., Vorpahl, K. and Witkowski, R. (1992) Karyotypes in 90 human gliomas. *Cancer Genet. Cytogenet.* 58:109-120.
13. Bremner, R. and Balmain A. (1990) Genetic changes in skin tumor progression: Correlation between presence of a mutant *ras* gene and loss of heterozygosity on mouse chromosome 7. *Cell.* 61: 407-417.
14. Buchmann, A., Ruggeri, B., Klein-Szanto, A. J. P. and Balmain, A. (1991) Progression of squamous carcinoma cells to spindle carcinomas of mouse skin is associated with an imbalance of H-ras alleles on chromosome 7. *Cancer Res* 51:4097-4101.
15. Kemp, K. J., Fee, F. and Balmain, A. (1993) Allelo-type analysis of mouse skin tumors using polymorphic microsatellites: Sequential genetic alterations on chromosomes 6, 7, and 11. *Cancer Res.* 53:6022-6027.
16. Gariboldi, M., Manenti, G., Canzian, F., Falvella, F. S., Pierotti, M. A., Porta, G. D., Binelli, G. and Dragani, T. A. (1993) Chromosome mapping of murine susceptibility loci to liver carcinogenesis. *Cancer Res.* 53:209-211.
17. Djalali, M., Adolph, S., Steinbach, P., Winking, H. and Hameister, H. (1987) A comparative mapping study of fragile sites in the human and murine genomes. *Hum. Genet.* 77:157-162.