

Chromosomal localization¹ of tumor protein, translationally-controlled 1 (TPT1) encoding the human histamine releasing factor (HRF) to 13q12→q14

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¹ This is a confirmation of a gene previously mapped by Bonaldo et al. and reported by Bowcock (1993).

Rationale and significance

The human histamine releasing factor (HRF; <http://www.ncbi.nlm.nih.gov/htbin-post/Omin/dispim?600763>) also called tumor protein, translationally controlled 1 (TPT1; <http://www.gdb.org/>) causes histamine release from basophils of certain allergic donors (MacDonald et al., 1995). It has identity to the translationally controlled tumor protein (TCTP, an alias for TPT1) which was previously designated as p23 (Böhm et al., 1989), and is highly conserved from man to alfalfa plants. While originally described as a growth-related tumor protein, it has also been identified in healthy liver tissue (Hughes et al., 1993) and more recently in macrophages, platelets, keratinocytes, erythrocytes, hepatocytes as well as tumor cells (Sanchez et al., 1997).

The biologic function of TPT1 remained illusive until HRF was shown to cause histamine release from a subset of allergic donors' basophils (MacDonald et al., 1995). We proposed that HRF produced this secretion by interaction with a subpopulation of IgE molecules that we termed IgE+. By definition, baso-

phils expressing IgE- on their surface, did not support mediator release when stimulated with HRF. In a subsequent study, we were able to show that HRF enhanced IgE-dependent IL-4 and IL-13 secretion from all basophils (Schroeder et al., 1997). More recently, we have demonstrated that HRF promotes cytokine secretion and a calcium response in purified human eosinophils (Bheekha-Escura and MacDonald, manuscript submitted). Here we report the mapping of the gene encoding HRF (TPT1) to chromosome 13q12→q14.

Of interest is the report showing a linkage on chromosome 13 of loci D13S270 and D13S153 to atopy via sibpair analysis (Daniels et al., 1996). Due to the fact that HRF activates cells important in the allergic diathesis, it's gene could potentially be a candidate gene for allergies including allergic asthma. Therefore, it would be of considerable interest to determine if TPT1 maps close to those loci.

Materials and methods

Somatic cell hybrids and PCR amplification

For PCR mapping 100 ng of genomic DNA from the complete NIGMS panel 2 (Coriell Institute for Medical Research, Camden, New Jersey) consisting of 24 human-rodent somatic cell hybrids retaining one human chromosome was used. Although some of these hybrids have been found to contain portions of another human chromosome, the hybrid, NA 10898, contained human chromosome 13 alone. In addition to the DNAs from the hybrids, their cytogenetic characterization, and genomic DNAs of human, mouse, and Chinese hamster ovary were provided by the manufacturer. These DNAs were amplified with human HRF-specific primers, and the amplification products were visualized on a 1 % agarose and 1 % NuSieve gel stained with ethidium bromide. For further sublocalization, a panel of radiation hybrids specific for human chromosome 13 was utilized (Perlin and Chakravarti, 1993), and the same PCR amplification methodology was used.

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Primer Names	Primer Sequences
SM16	5'CAAATGTGGCAATTATTTGG3'
SM17	5'CTCTCAAATGAGTTTAAATGC3'

Amplicon: 217 bp

Conditions: 30 cycles; 60 s at 94 °C, 60 s at 59 °C and 60 s at 72 °C

Probe Type: cDNA

Reference: GeneBank/EMBL accession number: X16064

Chromosome 13 sublocalization using human yeast artificial chromosome (YAC) pools

To determine the chromosome 13 sublocation of the gene, human yeast artificial chromosome (YAC) library pools from the Génethon MegaYAC library were used (Research Genetics, Huntsville, AL) (Bellanne-Chantelot et al., 1992). Twenty-three PCR reactions were performed as above to screen for the appropriate subpool of YAC clones, and an additional 28 PCR reactions were done to select individual YAC clones which were positive by PCR amplification. YAC DNAs were isolated from these clones as previously described (Li, et al., 1994).

Results

The 217-bp human TPT1-specific product was amplified from hybrid cell line NA10898 which contains human chromosome 13 and not from the other 23 hybrids nor mouse and Chinese hamster ovary control DNAs. It was concluded that the gene maps to human chromosome 13 because there was 100% concordance between the presence of the PCR product and the presence of chromosome 13 and 8% (2/24 hybrids) discordance for all other chromosomes.

By PCR YAC clone 846A11 was found to contain not only the gene, but loci D13S291 (probe AFM330ya5a/AFM330ya5m+) which has been mapped to chromosome 13q14 (Genome Database: personal communication Jean Weissenbach of Centre d'Etude de Polymorphisme Humain and Ilya Chumakov of Génethon, Paris).

To confirm the location of the gene to chromosome 13q14, radiation hybrid mapping analysis was performed. Radiation hybrids specific for human chromosome 13 were utilized. In this panel, 1 cR (centiRay) is approximately 60–70 kb. The gene maps by PCR closest to loci D13S190 which is approximately 1.5 Mb away (Perlin and Chakravarti, 1993). D13S190 maps by somatic cell hybrid panel to 13q12→q14 (Washington et al., 1993). The best order is listed below: Centromere– (cR, odds) –D13S240– (6.7, 2.0) –D13S219– (6.8, 2.4) –D13S1– (40.2, 6.5) –D13S263– (45.2, 2.1) –D13S291– (70.0, 5.3) –TPT1 (human histamine releasing factor primers SM16/SM17)– (23.7, 1.9) –D13S190– (11.0, 4.7) –D13S126– (11.1, 2.6) –D13S118–Telomere.

These data confirm the mapping of TPT1 to chromosome 13q14 between loci D13S291 and D13S190. From the report of the first international workshop on human chromosome 13 mapping, we infer from the work of Bonaldo et al., that a phage clone for TPT1 was mapped by in situ hybridization to 13q14 (Bowcock, 1993). Loci D13S291 lies 43.7 cM on the genetic map of chromosome 13 and the loci linked to atopy, D13S270 and D13S153, are close to this loci. (An STS-Based Map of the Human Genome http://carbon.wi.mit.edu:8000/cgi-bin/contig/phys_map). Thus, examination of this gene in atopic patients is, indeed, warranted.



Fig. 1. Somatic cell hybrid mapping: each lane contains the electrophoresed product from PCR amplification of genomic DNA with primer pairs derived from the sequence of the 3' untranslated portion of the human histamine releasing factor. The lanes are numbered from 1–22, X, and Y to correspond to the single human chromosome which is contained in each hybrid. The PCR products amplified from human (H), mouse (M), and Chinese hamster ovary (C) genomic DNAs serve as controls. The PhiX174 RF DNA/HaeIII fragments are used as a size standard in the left lane.

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