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BRIEF REPORT — GENE MAPPING

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Chromosomal assignment of a human apoptosis-associated tyrosine kinase gene on chromosome 17q25.3 by somatic hybrid analysis and fluorescence *in situ* hybridization

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Abstract Here, we report on the chromosomal location of the human apoptosis-associated tyrosine kinase gene. Based on polymerase chain reaction analysis with a human/rodent monochromosomal hybrid cell panel and fluorescence *in situ* hybridization, the gene was mapped on 25.3 region of chromosome 17.

Key words Apoptosis-associated tyrosine kinase · Chromosome 17q25.3 · FISH · Hybrid cell panel

A novel tyrosine kinase (apoptosis-associated tyrosine kinase, AATYK) gene was isolated from the 32Dcl3 cell line, which was derived from normal mouse bone marrow (Gaozza et al. 1997). The cells were strictly dependent on interleukin 3 (IL-3) for growth, and apoptosis occurred when they were deprived of IL-3 (Greenberger et al. 1983; Rovera et al. 1987; Valtieri et al. 1987). The expression of the AATYK gene was dramatically up-regulated during IL-3 deprivation as well as granulocyte colony-stimulating factor-induced terminal differentiation of the cells (Gaozza et al. 1997).

More recently, a human homolog of the AATYK gene has been reported (Ishikawa et al. 1998) and registered with the public database (accession number AB014541). This human gene and the mouse AATYK gene are 87% identical at the amino acid level, and both genes encode a protein with a tyrosine kinase domain in the N-terminal region and a proline-rich domain at the C-terminal end.

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Precise investigation of the chromosomal location of the human AATYK gene is important to investigate the role of AATYK in diseases such as tumorigenesis. First, chromosomal assignment of human AATYK was undertaken by polymerase chain reaction (PCR) analysis of a human/rodent somatic cell hybrid panel, as described previously (Saito et al. 1995, 1997; Seki et al. 1997). A set of specific PCR primers for human AATYK gene was designed in the 3′-untranslated region of the gene (5′-AGGCATGGCCCCGAGACACTG-3′; 5′-GATAAGGGCAGCGGAAACAGG-3′, PCR product 138 bp). The specific amplified product using the primer set was detected only from the hybrid containing human chromosome 17 (data not shown). This observation accords with a previous report (Ishikawa et al. 1998). To determine the precise location of the gene by an independent approach, we then performed fluorescence *in situ* hybridization (FISH) using P1 phage DNA containing the gene. The P1 clone was isolated by the method as described previously (Ohira et al. 1997), using the same primers described above. Clear doublet signals were consistently demonstrated for the q25.3 position of chromosome 17. A typical pattern from the FISH experiment is shown in Fig. 1. Thus, the gene was judged to map on 17q25.3.

Chromosome 17 is one of the major chromosomes showing frequent deletions in human malignancies (Seizinger et al. 1991). In the Loss of Heterozygosity (LOH) studies, interstitial losses in the chromosome 17q25 region were observed in both breast and ovarian neoplasms, suggesting that one or more novel tumor suppressor genes might exist in this region (Kalikin et al. 1997). Our precise chromosomal positioning data for such a gene should contribute toward LOH studies and genetic linkage analysis of this genomic locus.

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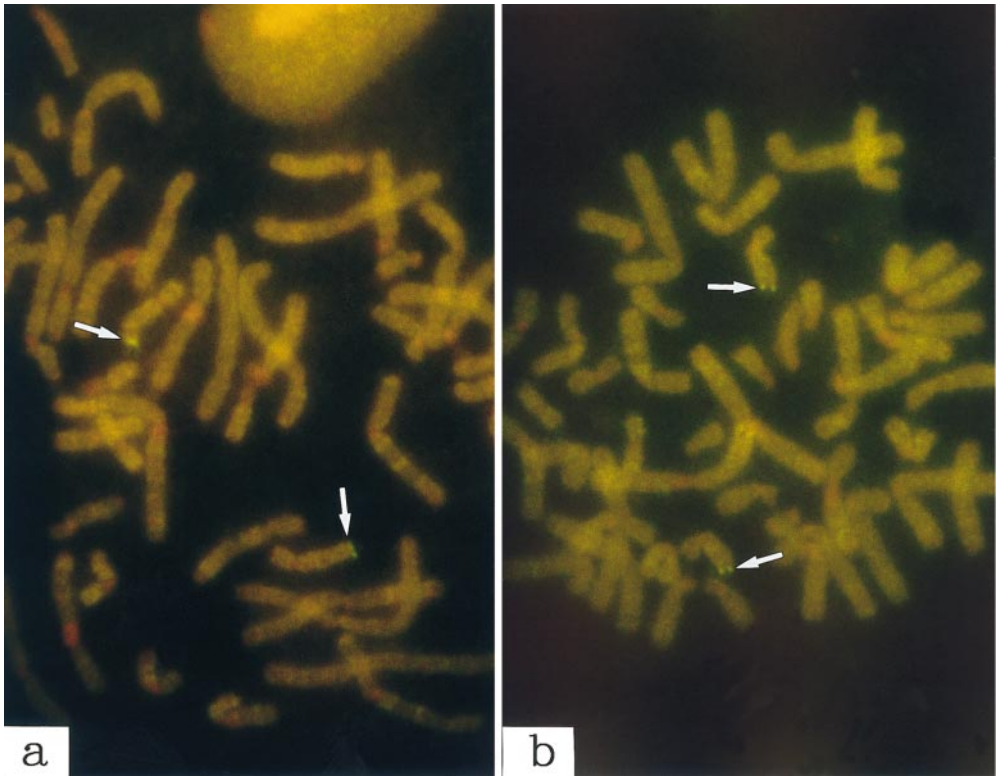

Fig. 1 Chromosome mapping of the human AATYK gene. FISH of the AATYK gene on human partial chromosomes. FISH was carried out using a biotinylated hybridization probe made from P1 phage clone harboring the AATYK gene. *Arrows* indicate the hybridization signals on human chromosome 17q25.3. The metaphase spreads were photographed with a Nikon B-2A filter (Nikon, Tokyo, Japan)

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