# Mapping of the Gene Encoding the β-Subunit of $H^+,K^+$-ATPase to Human Chromosome 13q34 by Fluorescence *in Situ* Hybridization[1]

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The hydrogen–potassium adenosine triphosphatase ($H^+,K^+$-ATPase; EC 3.6.1.36) belongs to a family of P-type cation-transporting ATPases that also includes $Ca^{2+}$-ATPase and $Na^+,K^+$-ATPase (EC 3.6.1.3). The membrane-bound enzyme couples the hydrolysis of ATP with the electroneutral exchange of $H^+$ and $K^+$ ions through the formation of an acid-stable phosphorylated intermediate (12). In gastric parietal cells, $H^+,K^+$-ATPase plays an essential role in the formation of hydrochloric acid, and $H^+,K^+$-ATPases associated with epithelial cells of the kidney and colon may function in luminal acidification and $K^+$ reabsorption (12). Like the $Na^+,K^+$-ATPase, $H^+,K^+$-ATPase is a heterodimer consisting of a high (≥100 kDa) molecular weight catalytic α-subunit and a smaller (≥30 kDa) but heavily glycosylated β-subunit (12). The β-subunit of $Na^+,K^+$-ATPase forms functional complexes with its corresponding α-subunit and appears to regulate the intracellular processing and translocation of $Na^+$ pumps to the plasma membrane (8). Although its role remains undefined, the $H^+,K^+$-ATPase β-subunit similarly increases membrane $Na^+$ pump density when it is coexpressed in yeast cells or frog oocytes with the α-subunit of $Na^+,K^+$-ATPase (2, 3). In the stomach, the $H^+,K^+$-ATPase β-subunit may act as a target antigen in autoimmune gastritis (16).

The genes encoding the α- and β-subunits of gastric $H^+,K^+$-ATPase from several mammalian species have been cloned and sequenced. In contrast to the 22-exon gene encoding the α-subunit (7, 10), the β-subunit is encoded on a gene comprising 7 exons (1, 7, 11). The human $H^+,K^+$-ATPase β-subunit is encoded on a 1.4-kb-long cDNA (5). Its deduced amino acid sequence bears >80% identity to that of rabbits, rodents, cattle, and swine (13, 14, 16). Using fluorescence *in situ* hybridization (FISH), we have recently mapped the gene encoding the α-subunit of $H^+,K^+$-ATPase to human chromosome 19q13.1 (15). In the present study, we examined the chromosomal location of the gene encoding the human $H^+,K^+$-ATPase β-subunit.

To identify the chromosomal loci encoding this gene, 1 μg of a clone of the human $H^+,K^+$-ATPase subunit β (designated HKB3-1-1a), which contains the coding region including exons 1 to 4 (approximately 17 kb), was labeled with biotin and hybridized to human metaphase chromosomes as previously described (9). A total of 32 metaphase cells were examined, and all cells examined had "double" fluorescent signals (i.e., one on each chromatid) on the terminal long arm of chromosome 13. In 17 cells double signals were observed on both homologs, and 15 cells had one homolog with a double signal on chromosome 13. Only chromosomes in which both chromatids displayed a signal were included for analyses, making the background hybridization essentially zero. The same cells hybridized for FISH had been previously G-banded (using trypsin–Giemsa) and photographed to allow direct comparisons of the results. The results demonstrated that the sequences hybridizing to a DNA fragment that contains the coding region for the β-subunit of $H^+,K^+$-ATPase can be localized to 13q34 (Fig. 1).

The genes encoding $H^+,K^+$-ATPase α- and β-subunits are present on different human chromosomes. This is in contrast to the convergence of genes encoding some $Na^+,K^+$-ATPase subunits. Within the human genome, the ubiquitous type 1 and the neuromuscular type 2 isoforms of the $Na^+,K^+$-ATPase

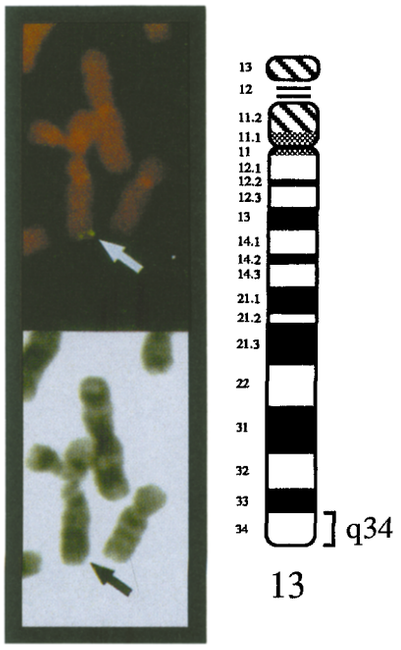


**FIG. 1.** Localization by FISH of the gene encoding the $H^+,K^+$-ATPase β-subunit to human chromosome 13q34. **Left, top:** G-banded partial metaphase chromosomes (arrow indicates chromosome 13). **Left, bottom:** Identical partial metaphase chromosomes after FISH with the biotin-labeled $H^+,K^+$-ATPase β-subunit probe documenting the localization of fluorescent signal to 13q34. **Right:** Idiogram of chromosome 13.

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$\alpha$-subunit are encoded in separate genes located on different arms of chromosome 1. The neuronal $\alpha_3$-isoform, in contrast, is encoded on the long arm of chromosome 19 in a region adjacent to that encoding the $H^+,K^+$-ATPase $\alpha$-subunit (4, 15). Human genomic sequences hybridizing to a DNA fragment containing the coding region for the $Na^+,K^+$-ATPase $\beta$-subunit have been identified on the long arm of chromosome 1 in a region distal to that encoding the $\alpha_2$-subunit (4). Nucleotide sequences related to the $\alpha_2$- and $\beta$-subunits of $Na^+,K^+$-ATPase have been similarly localized to the same chromosome (MMU1) in the mouse, although sequences encoding $\alpha_1$- and $\alpha_3$-subunits are localized to different chromosomes (4). As the cDNA coding for the human $H^+,K^+$-ATPase $\beta$ subunit possesses only 53% identity with the amino acid sequence deduced for cDNA encoding the human $Na^+,K^+$-ATPase $\beta$-subunit, it is perhaps not surprising that the DNA fragment encoding the human $H^+,K^+$-ATPase $\beta$-subunit did not hybridize to sequences in human chromosome 1 (5).

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# Localization of the Human Gene for $\mu$-Crystallin to Chromosome 16p

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$\mu$-Crystallin is a novel mammalian protein first identified as a major lens structural protein in many Austrialian marsupials (5). The complete sequence of Western Grey Kangaroo (*Macropus fuliginosus*) $\mu$-crystallin has been obtained by cDNA cloning from lens (3), revealing significant similarity with bacterial ornithine cyclodeaminases. Outside the lens, kangaroo $\mu$-crystallin is preferentially expressed in retina and brain, presumably in an enzymatic role (3). This is apparently another example of taxon-specific gene recruitment in which an enzyme acquires an additional role as a structural protein. A cDNA for human $\mu$-crystallin has been cloned and sequenced from a human retina cDNA library. In humans $\mu$-crystallin is expressed in neural tissue, muscle, and kidney (3). Although $\mu$-crystallin has not been recruited as a lens structural protein

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