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## The 5-HT2B Receptor Gene Maps to 2q36.3–2q37.1

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Multiple receptor subtypes of serotonin (5-hydroxytryptamine, 5HT) neurotransmitters with multiple physiological functions have been recognized. At least 16 different types are known, and the respective genes have been cloned, and some have been mapped (7). 5-HT2 receptors mediate many of the central and peripheral physiological functions of serotonin. Cardiovascular effects include contraction of blood vessels and shape changes in platelets; central nervous system effects include neuronal sensitization to tactile stimuli and mediation of hallucinogenic effects of lysergic acid diethylamide and related phenylisopropylamine hallucinogens. Many investigators have observed that the 5-HT2A and 5-HT2C receptors cannot mediate all these functions. For example, some 5-HT2-like effects of serotonin smooth muscles are classified as "atypical," leading to the hypothesis that other 5-HT2 receptor subtypes might exist and differ in different species (8).

We cloned a new 5-HT2 receptor cDNA, the mouse 5-HT2B receptor, with an original pharmacology and with expression in the mouse brain, heart and intestine (6). A similar receptor but with distinct expression and pharmacology has been described in the rat fundus (5). More recently, we isolated a human serotonin 5-HT2B receptor from a liver cDNA library (3). Its pharmacological profile shows divergence from that of the mouse and rat serotonin 5-HT2B receptors: although strong correlation is observed between human 5-HT2B and rat 5-HT2B receptor pharmacology, the correlation is almost as significant between human 5-HT2B and mouse 5-HT2B

or the human 5-HT1D receptor agonists. The major sites of expression of the 5-HT2B mRNA were found to be in the human liver and kidney, with detectable expression in lung and heart. Fainter signals were observed in the brain and placenta. Identical 5-HT2B cDNA sequence has also been detected in the human spinal cord, fetal brain, aorta, internal mammary artery, placenta, neuroblastoma cell line SHSY-5Y, and CSH carcinoid tumor libraries.

Although the physiological functions of this human serotonin 5-HT2B receptor remain to be investigated, we wished to localize this gene within the human genome and to compare its position with respect to the other serotonin receptor genes.

The first probe used for FISH was a 1.45-kb *Bam*HI–*Bam*HI cDNA fragment corresponding to the translated part of the 5HT2B human receptor cDNA. The FISH technique was performed with normal metaphase chromosomes according to our usual technique (2). Only double spots, one on each sister chromatid of a metaphase chromosome, were considered significant hybridization signals. Hybridization signals were seen at 2q36.3–q37.1 on 51 chromosomes 2 of 78 chromosomes examined (39 metaphase cells) (Fig. 1). Since the 5-HT2B receptor belongs to a multigene family and crosshybridization might occur, we also used two other probes for FISH experiments, namely a genomic 2.4-kb *Pst*I–*Eco*RI fragment, including the proximal promoter region and most of the 5'-untranslated region (5T1), and a genomic 4.0-kb *Eco*RI fragment, which includes 150 bp encoding the C-terminus region and the 3'-untranslated region (5T2). Double spots were observed with the two probes at the same 2q.36.3–q37.1 site as the 1.45-kb probe on, respectively, 27/42 chromosomes 2 (21 metaphase cells) with 5T1 and 42/60 chromosomes 2 (30 metaphase cells) with 5T2.

The location of the human HTR2B gene is thus on 2q36.3–q37.1. This gene has sequence homologies and a structural organization similar to those of the 2A and 2C receptor genes: the human HT2B receptor genomic structures include two introns that are present at positions identical to those of the HTR2A gene (1) and to the HTR2C genes, but lack the first introns of HTR2C (4). Despite these homologies and similarities, none of these receptor genes are localized on the same chromosome: HTR1A maps to 5cen–q11, HTR1B to 6q13, HTR1DA to 1p36.3–p34.3, HT1E to 6q14–q15, HTR1DP1 (pseudogene) to 12, HT2A, (formerly HTR2) to 13q14–q21, and HTR2C (formerly HTR1C) to Xq24.

Among the genes located in the 2q36–q37 region, the cholinergic receptor, the nicotinic delta polypeptide (CHRND), and PAX3 (paired box homeotic gene 3), implicated in the t(2;13)(q36;q14) specific for rhabdomyosarcoma (9), can be cited.

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## Localization of the Human Kinesin Light Chain Gene (KNS2) to Chromosome 14q32.3 by Fluorescence *in Situ* Hybridization

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The microtubule-associated protein kinesin is a plus-end-directed microtubule-based motor (1, 9). It consists of heterotetramers made up of two identical heavy chains (110–130 kDa) and two identical light chains (55–70 kDa). The kinesin ATPase activity resides in a pair of globular

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heads at the amino-terminal end of the heavy chain that also constitute microtubule-binding domains. They are followed by a long rod domain and a globular carboxy-terminal tail domain. The kinesin light chains bind to the carboxy-terminal end of the heavy chains, where they may play a role in specifying the cargo to be transported by particular kinesin molecules. Light chain sequences have been obtained from a number of invertebrate and vertebrate species, including humans. This has shown that multiple kinesin light chain isoforms are produced from a single gene by alternative mRNA splicing (4). A previous study has made use of somatic cell hybrid panels to assign provisionally the human kinesin light chain gene (KNS2) to the long arm of chromosome 14 (3). We report here that by fluorescence *in situ* hybridization it maps to 14q32.3.

A 493-bp piece of KNS2 cDNA was obtained by RT-PCR using adult human cerebral cortex cDNA and sequenced. It was used as a probe to screen a human genomic library in  $\lambda$  EMBL3. One positive clone of approximately 11 kb was obtained, and 1  $\mu$ g of this was labeled by nick-translation with biotin-16-dUTP. Metaphase spreads were prepared from lymphoblastoid cell lines treated for 5 h with 10  $\mu$ g/ml 5-bromodeoxyuridine, for 2 h with 10  $\mu$ g/ml ethidium bromide, and for 45 min with 0.05  $\mu$ g/ml Colcemid. *In situ* hybridization was performed essentially as described by Pinkel *et al.* (8) using 80 ng of labeled DNA and 1  $\mu$ g of human Cot1 DNA. The hybridization mixture was preannealed at 37°C for 30 min, and the slides were hybridized overnight at 37°C. The hybridization was detected using avidin-FITC (4  $\mu$ g/ml), biotinylated anti-avidin (4  $\mu$ g/ml), and avidin-FITC (4  $\mu$ g/ml) in three separate layers. Slides were stained in 4,6-diamidino-2-phenylindole (DAPI) and mounted with Vectashield. Images were acquired using a Zeiss Axioskop microscope, a photometrics KAF 1400 cooled CCD camera, and SmartCapture software (Digital Scientific). Chromosomes were identified using computer-enhanced DAPI banding and recolored in the Fig. 1 for the purpose of reproduction.

Twenty-five metaphase spreads were scored. Of the 50 chromosomes 14, 74% showed hybridization to both chromatids at 14q32.3 (see figure), 16% showed signal on one chromatid at 14q32.3, and in 10% no signal was found. Signals on chromosomes other than 14 were restricted to one homologue in three different spreads (chromosomes 4, 11, and 16).

The ubiquitous and neuron-specific kinesin heavy chain genes have been assigned to chromosomes 18 and 2, respectively (7); the gene for the heavy chain of cytoplasmic dynein, another molecular motor, has also been mapped to 14q32.3 (6). Two disease genes with a possible involvement of molecular motors have been linked with 14q32. A mouse gene that controls left-right asymmetry of heart and viscera has been mapped to a region of chromosome 12 that is syntenic with human chromosome 14q32 (2). Usher syndrome type 1B has been shown to be associated with mutations in the human gene for unconventional myosin VIIa (10). Interestingly, Usher syndrome type 1A maps to 14q32 (5). It remains to be seen whether mutations in the KNS2 gene are associated with these conditions.