SHORT COMMUNICATION

Neural Retina-Specific Leucine Zipper Gene NRL (D14S46E) Maps to Human Chromosome 14q11.1–q11.2

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The product of a neural retina-specific gene, NRL, belongs to the "leucine zipper" family of DNA-binding proteins and has a strong similarity to the v-*maf* oncogene product. The NRL gene maps to human chromosome 14 by Southern blot analysis of genomic DNA from a human–rodent somatic cell hybrid panel. *In situ* hybridization to metaphase chromosomes has further sublocalized the gene to the region 14q11.1–q11.2. D14S46E has now been assigned to the NRL gene. Because of its specific pattern of expression, NRL is a candidate gene for retinal diseases.

Visual information is collected, encoded, and transmitted to brain by specialized and functionally distinct neuronal cells in retina. Recent molecular and biochemical studies have elucidated the initial steps of the phototransduction cascade; however, the molecular events underlying differentiation of retinal neurons and development of their function remain unclear. It is now believed that the complex neuronal systems are the result of a differential and coordinated expression of various transcription factors (4, 7). The morphological and functional diversity of neural phenotypes is achieved by the combinatorial interaction and regulation of DNA-binding proteins, including those expressed in a cell-, tissue-, or developmental stage-specific manner. A number of distinct families of DNA-binding proteins have been defined based on the conservation of specific functional domains. Using subtraction cloning (8), we have identified a gene, NRL, that is expressed specifically in neuronal cells of retina (9). The NRL gene encodes a putative DNA-binding protein of the "leucine zipper" family with strong similarity to the DNA-binding domain of the v-*maf* oncogene product. It is, therefore, suggested that the NRL gene product might play a role in the regulation of retinal development and/or differentiation. We report here the localization of the NRL gene to human chromosome 14q11.1–q11.2.

The genomic DNAs from a human–rodent somatic cell hybrid panel (No. 1) were obtained from NIGMS repository (Camden, NJ). The human chromosome content and a description of the hybrids are provided in the repository's catalog. The Southern blot of hybrid panel DNA, digested with *Eco*RI, was hybridized with a ^{32}P-labeled fragment of human NRL cDNA (clone name AS321, base pairs 24–989, Fig. 3 of Ref. (9)). The human probe identifies a 3-kb human genomic fragment and cross-hybridizes to 5- and 3.5-kb bands in the hamster

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TABLE 1

Segregation of Human AS321 Sequence with Human Chromosomes in Human × Rodent Somatic Cell Hybrids

Hybridization chromosome	Human chromosomes																							
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	X	Y
Concordant hybrids																								
+/+	4	5	8	8	7	10	9	7	0	4	3	8	5	12	7	1	12	7	6	9	6	7	0	3
−/−	6	5	5	5	4	4	4	3	5	5	4	4	6	5	4	5	3	5	5	5	4	5	5	6
Discordant hybrids																								
+/−	8	7	3	2	4	2	2	2	12	4	7	3	4	0	2	10	0	5	4	2	5	4	9	7
−/+	0	1	1	1	2	2	1	2	1	0	2	2	0	0	2	1	3	1	0	1	2	0	1	0
Total discordant hybrids	8	8	4	3	6	4	3	4	13	4	9	5	4	0	4	11	3	6	4	3	7	4	10	7
Informative hybrids*	18	18	17	16	17	18	16	15	18	13	16	17	15	17	15	17	18	18	15	17	17	16	15	16

* Hybrids in which a particular chromosome was present in 10% or less of the cells were excluded from this.

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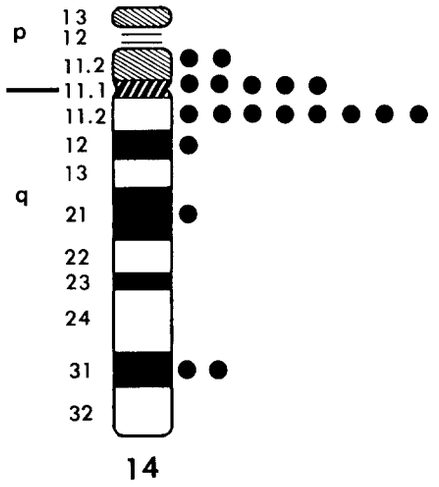

FIG. 1. Idiogram of human chromosome 14 showing silver grain distribution after *in situ* hybridization with NRL cDNA (clone AS321) probe.

and mouse genomic DNA lanes, respectively. The human-specific 3-kb fragment was scored in the human–rodent hybrid panel. The results of discordancy analysis are shown in Table 1. The human NRL fragment showed perfect segregation with chromosome 14.

Regional assignment of the NRL gene was accomplished by *in situ* hybridization. The AS321 cDNA clone (9) was nick-translated with [^{3}H]dCTP and [^{3}H]TTP to a specific activity of 2.5×10^7 cpm/μg and hybridized to human chromosome spreads at a concentration of 25 ng/ml (10). Of the 50 cells analyzed, 14 exhibited specific labeling at chromosome 14q11.1–q11.2 (Fig. 1). Silver grains over this region represent 16% (14/86) of the total label. No other site was labeled above the background. The NRL gene has been assigned the human gene number D14S46E.

The search for mutations in retinal genes (1) has led to the identification of rhodopsin and peripherin-RDS as the genetic loci for two forms of autosomal dominant retinitis pigmentosa (2, 3, 5). The specific pattern of expression in retinal neuronal cells suggests that NRL may be a candidate gene for as yet unmapped retinal diseases or for those mapping to chromosome 14 (e.g., rod monochromacy) (6).

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