Assignment¹ of LHX1 to human chromosome bands 17q11.2→q12 by use of radiation hybrid mapping and somatic cell hybridization

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¹ This report is discordant with a previous assignment of this gene to 11p13→p12 by Dong et al. (1997).

Rationale and significance

The human LHX1 gene encodes a protein that is a member of the LIM family of homeodomain proteins. LHX1 was originally cloned as an apparent homologue of the mouse *Lhx1* gene and mapped to human chromosome 11p13→p12 (Dong et al., 1997). In the mouse, the *Lhx1* gene is expressed in the developing kidney, and portions of the CNS where it is believed to be an essential regulator of the vertebrate head organizer (Shawlot et al., 1995). Fujii et al. (1998) described the genomic organization of mouse *Lhx1* and mapped it to chromosome 11, in a region homologous to human chromosome 17. This finding is inconsistent with the published map location of human LHX1 to chromosome 11p13→p12 (Dong et al., 1997). To address this discrepancy, we carried out radiation hybrid mapping using the Stanford G3 human/hamster radiation hybrid-mapping panel and Southern hybridization using a panel of somatic cell hybrids containing individual human chromosomes.

Materials and methods

Radiation hybrid mapping

LHX1 was mapped to chromosome 17 by polymerase chain reaction (PCR) using the commercially available version of the Stanford G3 Human/hamster Radiation Hybrid (RH) Mapping Panel (Research Genetics, Inc., Huntsville, AL) in conjunction with the publicly available WWW servers (<http://shgc-www.stanford.edu> and <http://www.ncbi.nlm.nih.gov/genemap99>, respectively). The PCR primers (LHX1f/r) yield a 240-bp amplicon containing the exon 3-intron 3 boundary of the human LHX1 gene which was verified through sequencing. The data vector obtained for the RH mapping panel was: 00000 00000 00000 00000 00100 011R0 00000 10110 00000 00001 00000 00110 00010 01000 R0100 00000 0R0.

Southern blot hybridization

To confirm the results of radiation hybrid analysis we used Southern blot analysis of the Human NIGMS Mapping Panel #2 (National Institute of General Medical Sciences, Coriell Institute of Medical Research, Camden NJ). The hybridization probe (IMAGE ID#1041673, Research Genetics), comprised the first 650 nucleotides of the coding sequence of human LHX1, and was verified by sequencing.

Primer name:	Primer sequence:
1. LHX1f	5'-CGAGAATGACGACCAGAAC-3'
2. LHX1r	5'-GGCTCTCTGCTCGCCTGG-3'

Results and discussion

Radiation hybrid mapping

Analysis of the radiation hybrid data localized the human LHX1 gene to chromosome 17. The RH mapping results placed LHX1 29 centirays (cR) distal from unidentified marker SHGC-34858 on the G3 panel (LOD = 8.32). This marker is located between marker D17S822E and the AP2 (beta) gene (transcript IB756) on the SHGC Chromosome 17 RH Map (G3 v2). The proximal and distal flanking markers (D17S822E and AP2(beta), respectively) have also been physically mapped (NCBI GeneMap '99), positioning LHX1 to chromosome region 17q11.2→q12.

Supported by Institutional funding.

Received 19 February 2002; manuscript accepted 21 March 2002.

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Fig. 1. Southern blot analysis of NIGMS Mapping Panel #2, localizing a 10 kb human specific fragment to chromosome 17. Lane 1: mouse A9 genomic DNA. Lane 2: Chinese Hamster genomic DNA. Lane 3: mouse A9 + human chromosome 4. Lane 4: Chinese Hamster + human chromosome 11. Lane 5: mouse A9 + human chromosome 13. Lane 6: mouse A9 + human chromosome 17. Lanes 7 and 8: human genomic DNA.

Southern hybridization mapping results

The 0.65-kb LHX1 probe, comprising the two LIM domains and a portion of the homeobox domain, detected a human specific band of 10 kb hybridizing only to the chromosome 17 cell line. No human specific bands were detected in the chromosome 4, 11, or 13 cell lines.

Hybrid	Chromosome	Gene present (+) or absent (-)
GM11687	4	-
GM11782	11	-
GM11689	13	-
GM11339	17	+

Neither the RH mapping panel nor the Southern blot hybridization results give support for the 11p13→p12 localization of Dong et al. (1997). In that report the mapping was carried out using FISH with a biotinylated cosmid probe thought to contain the LHX1 gene. Our mapping used two independent methods to localize the LHX1 gene to chromosome 17. This localization of the LHX1 gene, places it in a region that is homologous to the distal region of mouse chromosome 11, where the mouse *Lhx1* gene has been mapped (Fujii et al., 1998), and provides further support for the chromosome 17q11.2→q12 location as being correct.

References

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