Letter to the Editor

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Revised 14.7-cM Locus for the Hyperparathyroidism–Jaw Tumor Syndrome Gene, *HRPT2*

To the Editor:

We reported previously that the locus for hyperparathyroidism–jaw tumor syndrome (MIM 145001), *HRPT2,* appeared to be within a 0.7-cM region on chromosome 1q, on the basis of shared haplotype data from two families (Hobbs et al. 1999). The map order of the markers was originally derived from the chromosome 1 maps from Généthon (Dib et al. 1996; Généthon Web site) and the Whitehead Institute for Genome Research (Whitehead Institute for Genome Research Web site). Recent work by Carpten et al. (2000) and the human genome sequencing project (Lander et al. 2001) have shed new light on the proposed locus. These detailed physical-map data change the order of two markers (underlined) that are important in defining the shared haplotype region (in parentheses), from (D1S466, D1S2701, CHLC.12F10, D1S240, D1S2848, D1S254), D1S191, D1S444 to (D1S466, D1S2701, CHLC.12F10, D1S240, D1S254), D1S444, D1S191, D1S2848 (centromeric to telomeric). This removes D1S2848 from the reported shared haplotype region. Telomeric to D1S240, a new marker also became available: 277P67-2A8 (GenBank accession number AF181675). This marker was not shared between the two families in question, further reducing the shared haplotype region to the area defined between D1S466 and D1S240 (~1.8 cM): (D1S466, D1S2701, CHLC.12F10, D1S240), 277P67-2A8, D1S254, D1S444, D1S191, D1S2848.

For the markers remaining in the shared haplotype region—D1S466, D1S2701, CHLC.12F10, and D1S240—the frequencies for the alleles found in the affected haplotype are 0.06, 0.74, 0.18, and 0.50, respectively. This gives a calculated frequency in the general population of 0.004, or 1/250. This haplotype is much more common than that calculated for the original proposed shared haplotype region (population frequency of 1/38,000) and indicates that the newly reduced shared haplotype region is not indicative of an *HRPT2* haplotype.

Furthermore, the reduced shared haplotype region (D1S466 to D1S240) now no longer overlaps with the nonrecombinant region for our families (277P67-2A8 to D1S306, or D1S477 in current databases [Human Genome Working Draft Web site]). We conclude that the *HRPT2* gene must lie within this 14.7-cM nonrecombinant region. Although our initial shared haplotype data provided misleading results, the examination of shared haplotype data in different families has proven valuable in refining the map location for other disease gene loci (i.e., the loci for autosomal dominant Stargardt-like macular dystrophy [Donoso et al. 2001] and primary erythermalgia [Drenth et al. 2001]) and should continue to be explored in uncommon genetic diseases.

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Electronic-Database Information

Accession numbers and URLs for data in this article are as follows:

GenBank, http://www.ncbi.nlm.nih.gov/Genbank/ (for marker 277P6-2A8 [accession number AF181675])
Généthon, http://www.genethon.fr/

Human Genome Working Draft, http://genome.ucsc.edu/ (for the sequence from D1S240 to D1S477, estimated at 17.5 Mb)

Online Mendelian Inheritance in Man (OMIM), http://www.ncbi.nlm.nih.gov/Omim/ (for hyperparathyroidism–jaw tumor syndrome [MIM 145001])

Whitehead Institute for Genome Research, http://www-genome.wi.mit.edu/

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