Letters to the Editor

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Localization of a Gene for Bitter-Taste Perception to Human Chromosome 5p15

To the Editor:

Some people perceive the taste of phenylthiocarbamide and its chemical relative propylthiouracil (PROP) as intensely bitter at low concentrations, whereas others are unable to detect them, even at high concentrations. This taste blindness is an inherited trait (Snyder 1931). Although inheritance is thought to be recessive, other possibilities have been suggested, such as multiple genes (Boyd 1950; Olson et al. 1989), incomplete dominance (Johnson et al. 1966; Bartoshuk et al. 1994; Reed et al. 1995), or multiple alleles of a single gene (Rychkov and Borodina 1973). This trait is among the most-studied in human genetics, but the relevant gene has not been characterized. Therefore, we conducted a genomewide scan by using 98 nuclear families and 356 markers spaced at ~10-cM intervals.

Three hundred ninety-three adults and their parents participated as research subjects. The 98 families were originally recruited as part of an ongoing study of the genetics of body weight at the University of Pennsylvania's Behavioral Genetics Laboratory, and the details of family collection have been published elsewhere (Price et al. 1998). The protocol was approved by the Committee of Studies Involving Human Beings at the University of Pennsylvania.

To phenotype the subjects, filter paper was soaked in a saturated PROP solution, dried, and cut into strips. Subjects were asked to place the paper in their mouths and to rate the bitterness of taste. The scale used by the subjects to rate the taste intensity utilized descriptive words and is referred to as a "labeled-magnitude scale" (LMS; Green et al. 1993). Because the LMS is continuous, it prevents the loss of information associated with categoric scales and therefore provides the type of data essential for quantitative linkage analysis. In addition, the LMS minimizes ceiling effects and is better at discriminating sensitive tasters from nontasters than the classic nine-point scale (Lucchina et al. 1998*b*). The scale is labeled as follows (with numeric values assigned to each level of taste intensity): barely detectable (0), weak (6), moderate (17), strong (35), very strong (54), and strongest imaginable (100). The scores from the LMS were used as phenotypes for the quantitative linkage analysis.

The LMS is also a valid instrument to classify individuals as "nontasters" or "tasters." Studies scaling the suprathreshold bitterness of PROP with magnitude estimation demonstrate that psychophysical functions for nontasters and tasters diverge (Bartoshuk et al. 1994). The LMS produces suprathreshold functions equivalent to magnitude estimation (Green et al. 1996). Because the LMS is easier for naïve subjects to use, it is replacing magnitude estimation in studies of PROP (Snyder et al. 1996; Intranuova and Powers 1998; Lucchina et al. 1998*a,* 1998*b*; Schwartz et al. 1998; Prutkin et al., in press). Thus, the LMS provides a convenient, reliable, and reasonable choice for a large-scale gene-mapping study.

The mean rating of suprathreshold taste intensity was 31.2 ± 29.3 units, near the label "strong." As expected, the distribution of scores was kurtotic (-0.454) and skewed (.73). There was no relationship between subjects' ratings of PROP and height, weight, or body-mass index ($P > .05$).

We genotyped microsatellite markers spaced ~10.1 cM apart by using methods described by Lee et al. (1999). All half-siblings were eliminated prior to analysis. Computation of descriptive statistics and correlation coefficients were conducted with SPSS (6.1.1.). Quantitative trait loci analysis was conducted with the computer program MAPMAKER/SIBS version 2.0 (Kruglyak and Lander 1995). For analysis of transmission disequilibrium, the quantitative data were dichotomized into taster and nontaster categories, with all tasters reporting that suprathreshold concentrations of PROP tasted "strong," "extremely strong," or "strongest imaginable" ($n = 180$; 45.8%). Nontasters rated PROP as "barely detectable" or "weak" ($n = 115$; 29.3%). Subjects giving intermediate responses were excluded from analysis ($n = 98$; 25%). These cut-off values are conservative. Transmission of alleles from heterozygous parents to nontaster offspring was computed with TDTLIKE version 2.1 (Terwilliger 1995), which corrects for multiple-allele testing.

The telomeric portion of 5p gave the strongest evidence for linkage (t-score = 3.28, P = .0005; fig. 1), with the peak score near D5S2505. The linkage peak spanned ~10 cM, from D5S406 to D5S2081, and was the only region of the genome that had a t score $\geq$ 3.0. No candidate genes are apparent in 5p15. Markers from the telomeric portion of chromosome 5 were then examined for transmission disequilibrium. There was significant distortion in transmission of alleles from heterozygous parents to nontaster children for markers from the linked region, with D5S2505 being the most significant (D5S406, P = .031; D5S2505, P = .007, D5S635, P = .017; D5S807, P = .034; D5S2081, P = .012). These results are consistent with the hypothesis that a gene that confers the ability to taste PROP lies on the telomeric region of human chromosome 5p.

In addition to chromosome 5, there was a suggestion of linkage on chromosome 7, ~35–40 cM centromeric to the KELL locus, with a maximum t-score of 2.34 (P = .008) near D7S1789 and D7S796. Initial linkage studies suggested a locus was near KELL on chromosome 7 (Chautard-Freire-Maia 1974; Conneally et al. 1976), but later reports were unable to replicate this finding (Spence et al. 1984). The results of the current study suggest that a region on chromosome 7 may also influence the taster phenotype.

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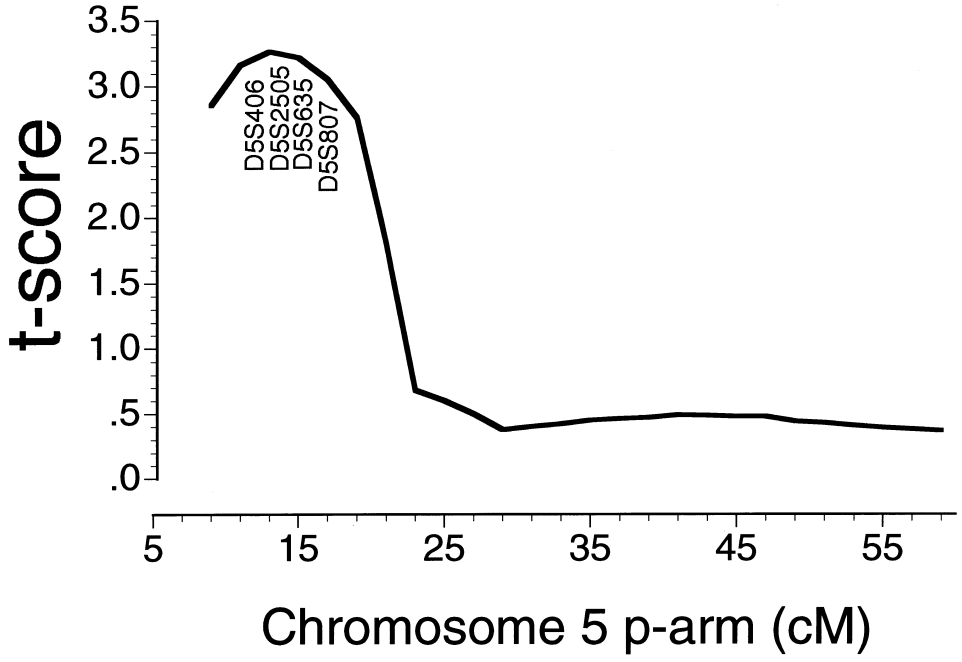

Figure 1 Multipoint results for chromosome 5

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