

# Mapping and verification of susceptibility loci for smoking quantity using permutation linkage analysis

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Following publication of the above paper, the authors identified errors in Table 2 and the text in the Results and Discussion sections. The marker intervals used were incorrect, and the authors apologize for any confusion this might have caused. Table 2 and the relevant sections of text are reproduced correctly below, with the corrected marker names given in bold.

## Linkage Regions for Smoking Quantity

Based on the empirical null distributions, an empirical *P*-value for each test position was found with the original data, which provides an overall picture of linkage signals on 22 autosomal chromosomes across the whole genome (see Figure 2). Analyses with the three forms of phenotypic transformations yielded very similar results, only with a minor trend of log-CPD > cat-CPD > CPD in terms of linkage signal. Under a genome-wide significance level of 0.05, 10 regions showed significant linkage (Table 2). These regions include three (ND1, ND3, and ND8) on chromosomes 1, 4, and 16 detected with all the phenotypic transformations, three (ND2, ND7, and ND9) on chromosomes 3, 11, and 17 detected with two transformations (cat-CPD and log-CPD), and four regions (ND4, ND5, ND6, and ND10) on chromosomes 7, 8, 9, and 20 detected with either log-CPD or cat-CPD. These detected regions varied in linkage strengths. Of them, two regions (ND1 and ND3) exhibited highly or near-highly significant linkage ( $P \leq 0.001$ ) for smoking quantity; the peak positions are flanked by markers GGAA22G10 and **GATA12A07** for ND1, and 165 × c11 and **GATA8A05** for ND3. Other regions, though all significant, have different extents of Significance from *P*-values of 0.0419 to 0.0171. Compared to the regions identified previously In the FHS cohort, we found that ND2 on chromosome 3 (between markers 059 × a9 and **GATA3H01**) and ND6 on chromosome 9 (between markers **GATA27A11** and GATA12C06) represent newly ulledcd loci for ND in our permutation test with the same dataset. On the other hand, while other regions were reported previously, they never reached the significance levels we obtained in this study for most of the positive regions.

## DISCUSSION

In this study, we conducted a genome-wide linkage analysis using the VC approach implemented in SOLAR for the FHS smoking data collected between 1970 and 1972. Unlike previous analyses with the same data set, we carried out

**Table 2** Linkage results for nicotine dependence using empirical thresholds

QTL	Chr.	Region (cM) <sup>a</sup>	Peak position <sup>b</sup>	Market Interval <sup>c</sup>	Min. P-value <sup>d</sup>	Transformed <sup>e</sup>
ND1	1	168–196	182	GGAA22G10-GATA12A07	0.0010	CPD, log-CPD, cat-CPD
ND2	3	190–208	206	059×a9-GATA3H01	0.0302	Log-CPD, cat-CPD
ND3	4	188–212	200	165×c11-GATA8A05	0.0020	CPD, log-CPD, cat-CPD
ND4	7	62–66	64	GATA31A10-GATA24D12	0.0370	Log-CPD
ND5	8	120–124	122	GATA26E03-GAAT1A4	0.0171	Log-CPD
N06	9	46–50	48	GATA27A11-GATA12C06	0.0419	Log-CPD
ND7	11	18–28	20	GATA23F06-GATA48E02	0.0281	Log-CPD, cat-CPD
ND8	16	24–64	46	ATA3A07-GGAA3G05	0.0185	CPD, log-CPD, cat-CPD
ND9	17	24–46	30	GATA8C04-GATA185H04	0.0251	Cat-CPD, log-CPD
ND10	20	78–86	84	GATA47F05-GATA45B10	0.0321	cat-CPD

<sup>a</sup>The entire region with empirical *P*-values  $\leq 0.05$  for one or more transformed smoking quantity (SQ).

<sup>b</sup>The peak position was identified with the minimum *P*-value among the three phenotype transformations.

<sup>c</sup>Flanking markers for the peak position.

<sup>d</sup>The minimum empirical *P*-value (strongest signal) for the position.

<sup>e</sup>Phenotype transformation(s) with which an empirical *P*-values  $\leq 0.05$  at the peak position was obtained.

linkage tests using empirical thresholds derived from permutations and obtained an appropriate estimate of genome-wide false-positive probability for each potential linkage. With the empirical thresholds, a total of 10 genomic regions were detected to have highly significant or significant linkages with nicotine dependence, which was assessed by number of cigarettes smoked per day. Two of the

regions (ND1 and ND3) on chromosomes 1 and 4 showed highly or near-highly significant linkages. Their peak positions are flanked by markers GGAA22G10 and **GATA12A07** for ND1, and 165 × c11 and **GATA8A05** for ND3. Additionally, we identified eight other regions that showed significant linkage of nicotine dependence to chromosomes 3, 7, 8, 9, 11, 16, 17, and 20.