Reviewer's report

Title: Genomic Screen for Loci Associated with tobacco usage in Mission Indians

Version: 1 Date: 24 August 2005

Reviewer: Mary-Anne Enoch

Reviewer's report:

General
This study reports on a heritability analysis and whole genome linkage scan for both regular tobacco use and smoking persistence in 243 Mission Indians from 6 contiguous reservations in SW California. The authors found that the heritability for regular and persistent tobacco use were similar: 0.37 – 0.34. They identified several chromosomal loci associated with both phenotypes with LOD scores of up to 2.0.

This is the first genome scan for tobacco use in Native Americans. It is interesting that the several linkages identified in this study largely correspond to loci, either alcohol or smoking related, in earlier genome scans, mainly in Caucasians. It is impressive that they obtained a LOD score of 3.4 in a bivariate linkage analysis for both persistent tobacco use and drinking severity score and one wonders why this fact was not included in the abstract – perhaps because coincident linkage could not be ruled out?

In general, this manuscript is comprehensive and well written and I have only a few points that need to be addressed.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. The Discussion focuses on linkage findings that are common to both alcohol and alcohol dependence phenotypes and tobacco use phenotypes. Therefore mention should be made in the Introduction of the shared addiction vulnerability between alcohol and nicotine (True et al, 1999, Hettema et al, 1999, Swan et al, 1997). The linkage sample prevalence rates for alcohol dependence should be provided and the phenotype ‘drinking severity’ should be described in detail in Methods.

2. Please provide standard deviations for all means in the first paragraph of the results. What was the mean Native American ancestry of the linkage sample? On page 11 it is stated that this population has significant admixture. Please provide an analysis or at least a description of the admixture.

3. Did an IRB and the tribal councils review this study? This needs to be stated.

4. A paragraph detailing the 8 referenced earlier linkage studies, particularly with regard to phenotype, should be provided in the Introduction. Admittedly the authors do discuss these studies
in some depth in the Discussion but an earlier introduction would help put the current study into context. Also, LOD scores should be provided as a useful weighting of the studies, either in the text or Table 1.

5. Why were the 77 parent-child and 8 grandparent-grandchild pairs excluded? This is not clear.

Discretionary Revisions (which the author can choose to ignore)

**What next?:** Accept after minor essential revisions

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests.