Reviewer's report

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

Version: 1  Date: 15 September 2005

Reviewer: Laura Jean Bierut

Reviewer's report:

General - This manuscript reports on a genetic linkage study of two smoking phenotypes: daily smoking for at least one month or more and persistent smoking (defined by smoking at least 10 cigarettes daily for more than 1 year). This study demonstrates several areas of linkage, many of which overlap with other studies of smoking and alcohol phenotypes. This is a well written manuscript.

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

None

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

The multiple methods were used to calculate LOD scores (SOLAR, Genehunter, Merlin) and a consistency of results was required. However, when the results are shown in the table and figures 1 and 2, I am not sure which program has been used to produce these results. Please note the program.

The authors report that the demographic characteristics are "equivalent to U. S. census data". This statement is unclear and should be clarified. What characteristics is the sample equivalent to the U.S. census data? Age, gender? It cannot be ethnicity/race? Is the sample equivalent to the U. S. census data for Native Americans?

Discretionary Revisions (which the author can choose to ignore)

The second paragraph of the discussion focusing on the Chromosome 1 was a bit confusing to me. Bierut et al noted linkage to Chromosome 1 in a similar region that are seen in this study for a comorbid phenotype of habitual smoking (20 cigarettes per day for 6 months or more) and alcohol dependence. This region also demonstrated linkage with the alcohol dependence phenotype alone in COGA. The allele sharing for affected sibling pairs was similar for the comorbid smoking alcohol dependence phenotype and alcohol dependence alone. When the habitual smoking phenotype was examined, the affected sibling pair allele sharing was 50% with a LOD score of zero. The interpretation by Bierut et al, was that this region is likely an "alcohol dependence" susceptibility region, not a smoking region.

Yet, there is significant genetic overlap demonstrated by numerous twin studies with smoking and alcoholism. Though one study may identify an "alcoholism" region of interest, another study may demonstrate a "smoking" area of interest. So, these results may still be consistent.
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.