Reviewer's report

Title: Association of CETP TaqI and APOE polymorphisms with Type II Diabetes mellitus in North Indians: a case control study

Version: 1 Date: 25 February 2005

Reviewer: MM Sale

Reviewer's report:

General

The authors have investigated polymorphisms in two genes for associations with diabetes, lipid profiles, and diabetic complications. This is the first investigation of these genes in a North Indian diabetic population, thus providing novel data in this population. Although there are no strong associations and the authors conclude that these genes do not play a significant role in diabetes in this population, it is important that negative findings are published to counteract publication bias, allowing association results to be seen in the full context of all studies of these polymorphisms. Patient ascertainment, diabetes and lipid testing, and genotyping methods are appropriate for a study of this type.

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

1) Considerably more detail of the criteria used to define the patients’ complication status is required. Also, the numbers in each category do not appear to be presented. Were any patients on lipid-lowering medications? What forms of diabetes therapy were being used by patients?

2) Were all variables normally distributed? Were any covariates included when comparing mean values of the lipid traits between groups? Were lipid profile analyses also stratified by gender?

3) Since the 442G allele was not detected in this population, it would be informative to compare this result with the allele frequencies observed in other populations, rather than review positive associations reported by others. Is this result unexpected?

4) Although the negative diabetes association results are reported in detail (Tables 4 and 5), the positive findings in subsets of patients with complications or stratified by age are only mentioned briefly in the text so the reader is unable to evaluate the importance of these results. The analyses on complications and age strata need to be presented in full, at least for the significant results (hypertension and age), including the number of individuals in each group. Given the relatively small overall sample size, the number of individuals in each stratum would be anticipated to be small and may be appropriate to pool genotypes for some analyses.

5) The influence of the APOE alleles on lipid profiles in diabetes would be the analysis of greatest interest for this gene (even if the overall results were negative, trends may be informative), yet only the diabetes APOE association results are presented.

6) Discussion, p10, para 2: The Discussion of the CETP results is somewhat confusing. Since cardiovascular phenotypes weren't studied, it would more helpful if the body of literature supporting the association between B2 and high HDL were referenced. In the study of Tai et al., even though
Asian Indians from Singapore had the highest frequency of the B2 allele and the lowest HDL-cholesterol level of the three populations studied, the B2 allele was still associated with higher HDL in a dose-dependent manner across all groups, consistent with other reports and in contrast to the results of this study.

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

7) Introduction, p4: The authors describe D442G as a “silent” mutation, yet this substitution results in an amino acid change.

8) Male/female proportions appear to have been left out of the Methods. Methods, p8, Statistical evaluation: Significant p-values should be changed to those <0.05 (rather than >0.05). Results, p8, para 1: p-values shown as (p=0.000) should be reinterpreted as p<0.001.

9) It would be helpful to have the statistically significant differences between groups highlighted in Tables 1 and 2.

10) Fewer significant figures for ORs and CIs in Tables 3 and 4 would be sufficient. Table 3, row 1, the final parenthesis is shown as a zero.

11) The Conclusion needs to be modified to state that these polymorphisms show no evidence of association with diabetes or complications *in this population*.

12) The manuscript needs editing to conform to accepted English grammar, primarily the inclusion of articles (“a” and “the”) in several sentences (for example, see the final sentence of the Introduction).

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.