Reviewer's report

Title: A role for CETP TaqIB polymorphism in determining susceptibility to atrial fibrillation: a nested case control study

Version: 1 Date: 21 February 2006

Reviewer: Jan Albert A Kuivenhoven

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General
Asselberg et al sought to find gene polymorphisms that may be associated with atrial fibrillation (AF) to better understand the complex etiology of this disease. Although interesting, the authors failed to provide a logical study.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1. The authors failed to sufficiently motivate the choice of their candidate genes to study their primary research question. This should be corrected.
2. It is striking that the authors do not provide any biological explanation for their primary finding that the CETP TaqIB gene polymorphism is associated with AF. How does this work? Does TaqIB exert its effect through e.g. the -629 C->A polymorphism, via effect on CETP protein concentration in plasma? It is apparent that HDL cholesterol levels is not different amongst cases and controls, so maybe, CETP is not involved at all? It is likely that the CETP TaqIB a mere marker for genetic variation elsewhere, i.e. outside of the CETP gene locus. Coming back to their primary research question, this paper does provide - at current - no better understanding of the genetic causes of AF.....
3. The MDR model used gives some interesting gene-environment interactions, but the reader is left at a loss when it comes to the biology that may truly relate TaqIB with the presence of micro- or macroalbuminuria, moderate renal dysfunction, and the presence of elevated levels of CRP. The authors should properly discuss their results.
4. In their analyses the authors should include factors such as alcohol intake, medication, and history of CHD.
5. The focus of the current paper is the description of the statistical methods used while the resulting data set is hardly discussed. This should be changed.
6. The definition of atrial fibrillation needs clarification. Did the cases with AF have paroxysmal AF? Specify the type of AF and frequency of recording. This should be clear from the methods section/results.

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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. Please specify odds ratio’s (odds for what?) in the section on statistical analysis and in the table legends.
2. Provide description of technology used to measure lipids.
3. Provide LDL-c values of subjects.
4. page 7 second paragraph, change table 3 into table 2
5. page 9 second paragraph, provide references.
6. table 2, give for the controls number of cases (n=)
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:** Acceptable

**Statistical review:** Yes