Reviewer's report

**Title:** Genetic variants of Complement factor H gene are not associated with premature coronary heart disease: a family-based study in the Irish population

**Version:** 2  **Date:** 30 July 2007

**Reviewer:** Pedro Moral

**Reviewer's report:**

**General**
Comments of the manuscript “Genetic variants of complement factor H gene are not associated with premature coronary heart disease: a family-based study in the Irish population”

The authors present the negative results from a gene-candidate association study of CHD. The manuscript is a brief and clear report of the negative results obtained for the association of six punctual mutations and related haplotypes determined in the CFH gene that are described in a very convenient way.

The study seems to be well-designed including a well-sized family sample, the choice of a gene with previous contradictory results, and adequate methodological –molecular and statistical- treatment. The discussion is hypothetical but logical as it is usual in this kind of studies.

-------------------------------------------------------------------------------

**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)**

The negative results found seem to be well established trough the considerable size of the sample used. However, it has been proved that many times the effect of gene-environmental interactions is more relevant that the gene effect alone in cardiovascular diseases.

Table 2 illustrates that the authors have control of some environmental variables. But I do not know if they have tested some gene-environmental interactions in spite of low sizes and failed to get positive associations. In any case, these additional TDT analyses in partial subgroups should be do and the results indicated, at least, in the text.

-------------------------------------------------------------------------------

**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, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.