Reviewer's report

Title: Effect of the rs2259816 polymorphism in the HNF1A gene on circulating levels of C-reactive protein and coronary artery disease (The Ludwigshafen Risk and Cardiovascular Health Study)

Version: 1 Date: 18 June 2010

Reviewer: Vincent Diego

Reviewer's report:

Kleber et al. performed association analyses between the SNP rs2259816 with CRP levels and with CAD. They found evidence of association for the former, but not for the latter. The questions posed and investigated are important, their study is well designed, their methods are sound, the data are sufficient to be able to address the questions posed, the results are straightforward, and, finally, their conclusions are supported by the study results. Overall, this is a very good study. I have several minor essential revisions, and three discretionary revisions.

Minor essential revisions:

1) Perhaps the following consideration was addressed in their earlier study on CRP genotypes and CAD, but it is important here in this manuscript to establish the link between CRP and CAD in the study population. Are they even associated? If the two variables are associated, then this would be consistent with the literature (as they indeed cited). If not, then this lack of association would be consistent with their conclusions "... that CRP does not play a causal role in the development of CAD", but that it is more of an inflammatory mediator. Even if CRP levels and CAD are associated, however, this conclusion still stands on the strength of the evidence.

2) Triglycerides, HDL-C and LDL-C were included in the preliminary comparisons between CAD cases and controls, and were shown to be significant covariates, yet they were not included in the association analyses. Why not? This is all the more puzzling given their well known associations with both inflammation and CAD. Alternatively, perhaps a clinical definition for dyslipidemia could be used to construct a dichotomous variable simultaneously accounting for these factors?

3) At the second line from the bottom of page 8 in the Discussion section, you do mean the C allele, right? You currently have it as "the G allele".

Discretionary revisions:

1) The second sentence in the background subsection of the Abstract is awkwardly constructed.

2) In the Results section under the subsection on association between the SNP and CRP levels, change "... cardiovascular risk factors like ..." to "..."
cardiovascular risk factors, namely . . . ". The word "like" makes it sound as if the full list of risk factors were not included and you only gave several examples.

**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.