Reviewer's report

**Title:** Genetic Variation in Fc gamma Receptor IIa and Risk of Coronary Heart Disease: Negative Results From Two Large Independent Populations.

**Version:** 1  
**Date:** 11 November 2008

**Reviewer:** Bruno G Loos

**Reviewer's report:**

I have read this paper with high interest. The research question is highly valid and the study populations are of excellent size. I have several comments to be addressed by the authors.

1. Please reduce the Introduction section by 30%, it is really long and wordy.
2. Explain in the Methods section ethnic background of the subjects. If you have a mixed racial population, please include this in the logistic regression analysis, since it is known that various races have different allelic frequencies of Fc#RIIa-R/H131. If needed recalculate results for subjects of German background as a subgroup.
3. All background variables between patients and controls in both study groups (Tables 1 and 2) should be statistically tested. Only if you see statistical differences you can make statements in the Results section that the groups are different for certain characteristics.
4. Add in Table 3 a footnote on the results of Hardy Weinberg testing.
5. Add also in Table 3 allelic frequencies and OR and P-values.
6. Add in the top of Table 3 under “cases” and “controls” the n (number of subjects).
7. Combine Tables 4 and 5, similar presentation as Table 3.
8. Could you please reconsider your Discussion; it is quite long/extensive, yet on the other hand several aspects are missing.
9. I think a discussion on Bovine EC is not so relevant in the current context. Omit this completely. Instead include discussion on the role of bacteria in relation to cardiovascular disease. In certain conditions gram-negative bacteria may get into the circulation on a daily basis. This may stimulate IgG2 production and the Fc#RIIa-H131 variant can strongly bind to the bacteria IgG2 complex. In fact, several papers have suggested for example neutrophil and monocytic hyper reactivity, due to this strong binding. Therefore in your Discussion include not only CRP but also IgG2, and view the hypotheses from 2 angles: both in case of strong binding and in case of weak binding. In this respect it is also not brought forward that CRP can opsonise bacteria and that CRP helps to clear bacteria in the circulation.
10. An important aspect missing in the Results section is the statistical power of
the various results. Please perform power calculations and state the power of the current results.

**Level of interest:** An article of importance in its field

**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.