Reviewer's report

Title: Gene Polymorphisms in Association with Emerging Cardiovascular Risk Markers in Adult Women

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Reviewer: Jose M Soria

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General Comments

The investigators conducted a classical population-based association study between several genetic variants and some traits in adult women. Although, the strategy used in this study is potentially interesting, their results are not new. They are mainly confirmatory regarding the relationship between some SNPs and some traits (i.e MHFR and Homocysteine levels). In addition, some major concerns should be addressed to clarify the results.

Major Compulsory Revisions

1.- It is not clear how and why these candidate genes have been selected and not others, and how the SNPs has been selected. I assume that the SNPs have been selected based on their potential functional or regulatory effect. However, other SNPs in these genes with low LD among them should be included to capture the genetic variability of those loci. In fact, in this genomic era with the improvement of genotyping technologies, limiting the genetic analyses to only few DNA variants within candidate genes is a poor strategy.

2.- I concern about the selection of candidate gene, since it is not clear the implication of several of these genes in cardiovascular disease risk. The authors should provide with more information about that.

3.- Recently, it has been reported a genome-wide association and replication study to identify genetic loci associated with plasma CRP concentrations. The lack of concordance between the effect on coronary heart disease risk of CRP genotypes and CRP levels argues against a causal association of CRP with coronary heart disease in this study (Elliot P et al JAMA 3002:37-48.2009). In addition, there are also information regarding several genome-wide with fibrinogen levels. It would be convenient that the authors incorporate this information into the manuscript.

4.- Although, I agree with the authors that the investigated traits are influenced by environmental factors which were not adequately captured by the current study (an important limitation), they would incorporate some data about the effect of the environmental factors that they have information with the trait levels.

Minor Essential Revisions
1.- The authors should incorporate in the Material and Methods how these phenotypes (i.e., Plasma c-Reactive, fibrinogen and Homocysteine) were measured.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I have not Declaration of competing interests