Reviewer's report

Title: Evaluation of the potential pleotropic role of AGT polymorphism in atherosclerosis

Version: 1 Date: 10 September 2012

Reviewer: Wassim Y Almawi

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Major Compulsory Revisions

The authors investigated possible associations between several SNPs in AGT gene and atherosclerosis in (presumably) Saudi Arabs. Their conclusion was positive about the differential association of AGT SNPs with CAD traits. Despite the technical aspects of identification and genotyping of AGT SNPs, there are serious concerns that must be addressed before the manuscript can be accepted for publication.

1. The is an association study, and does not address the functionality of the AGT variants with CAD and related traits. This must be reflected in both the title and body of the manuscript.

2. The racial origin of study participants needs to be spelled out. Given that Saudi Arabia, similar to other GCC countries, has a very high proportion of non-Saudi expats, the authors must indicate whether all participants were native Saudis, and means of ascertaining that.

3. Further to #1, and assuming that all participants were indeed Saudis, the authors must provide for the origin of the participants within Saudi Arabia. Were they all from the Riyadh area, or were from other country regions. If so, were the controls matched to cases with respect to their origin.

4. The authors indicate that they included “2292 angiographed controls”. Did they all undergo angiography?

5. My main concern is the heterogeneous nature of the CAD cases. As such, Table 1 is of limited use as is. I would like to see it altered to include the proportion of patients with specific CAD traits. For example, how many obese individuals had diabetes or hypertension? The same applies to the other traits.

6. Combining patients “harbouring a combination of two or possibly three of the cardiovascular risk traits” with other patients with different risk profile in genetic analysis studies is not correct. The authors are strongly to advise to redo the analysis according to the number of risk factors within each strata.

7. The authors need to present biochemical profile of studied participants.

8. Did the authors correct for multiple testing? This must be provided given the borderline association of some of these variants.

9. Power calculation is missing.
Minor Essential Revisions

1. The table footnotes must be restructured and simplified. There is no need to include definition of C, G, A, and T nucleotides.
2. An appropriate figure legend for the haploview must be provided.
3. The manuscript needs to be edited by a professional.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests