Reviewer’s report

Title: Assessing Known Chronic Kidney Disease Associated Genetic Variants in Saudi Arabian Populations

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Reviewer: Paolo Manunta

Reviewer’s report:

This paper evaluates the prevalence of eight genetic variants retrieved from previous GWA studies on Chronic Kidney Disease (CKD) in Saudi Arabians and their association with markers of chronic kidney disease.

Methods

Recruitment of healthy population DNA control samples is ethnically-matched. What does it mean? Different ethnic populations are considered? As well discussed, ethnic- and population-based differences in regional linkage disequilibrium (LD) can create associations with opposite directions of effect and biased results may be obtained.

NO clinical characteristics are described. I think you should add a table

Results

Variant rs4821480 in MYH9 was the only significantly associated with increased risk of development of chronic kidney disease, particularly with OR = 0.59 (95% CI 0.42-0.82, P = 0.002). Theoretically, an OR<1 reflects a protective role of the variant instead of an increased risk.

The multivariate model was built using the clinical demographic information including age and gender, biochemical and genetic information. Why rs4821481 was also included despite its not significant association with presence of CKD, as reported in Table 2?

Discussion

"Functional variants in APOL1 are found on two different G1 and G2 haplotypes that are common in African populations (10-25%), but not observed to date in other populations.”

This sentence should be referred with a citation; moreover, which kind of functional variants does it mean?
Similarly, ethnic- and population-based differences in genome LD must alert to translate genetic effect of specific variant among populations from different ethnicities. As reported in Figure 2 (Hodgson et al, 2014 PLoS Genet10(6): e1004393.), ADMIXTURE clustering patterns between European (such as CKDGen consortium) and Saudi Arabia is quite different, with diverse inferred ancestry components.

Declarations

Why no datasets were generated or analysed? Which data all Tables and Figure refer to?

Figure and Tables

Figure 1 did not report any statistic significance. Please add.

Table 1.

Please correct Sex (M) as Sex M (%)

Table 2

As no data about LD parameters are available for Saudi Arabians, SNPs reporting the same Freq are in strong LD (r2>0.8)?

MYH9 gene:

<table>
<thead>
<tr>
<th>SNP</th>
<th>r2</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs4821480</td>
<td>0.24</td>
</tr>
<tr>
<td>rs4821481</td>
<td>0.25</td>
</tr>
<tr>
<td>rs2032487</td>
<td>0.25</td>
</tr>
<tr>
<td>rs3752462</td>
<td>0.25</td>
</tr>
</tbody>
</table>

SHROOM2 gene:

<table>
<thead>
<tr>
<th>SNP</th>
<th>r2</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs9992101</td>
<td>0.26</td>
</tr>
<tr>
<td>rs17319721</td>
<td>0.26</td>
</tr>
</tbody>
</table>

A Legend reporting meaning of OR and Beta has to be added.
Supplemental Table 2, 9 out of 10 described biochemical assays are reported (EGFR missed).

Analogously, in Figure 1 only 9 graphs of biochemical assays comparison are reported (serum Calcium missed).

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

No

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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Please indicate the quality of language in the manuscript:

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