Reviewer's report

Title: Association of genetic variants in the promoter region of genes encoding p22phox (CYBA) and glutamate cysteine ligase catalytic subunit (GCLC) and renal disease in patients with type 1 diabetes mellitus

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Reviewer: Helene Choquet

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Association of genetic variants in the promoter region of genes encoding p22phox (CYBA) and glutamate cysteine ligase catalytic subunit (GCLC) and renal disease in patients with type 1 diabetes mellitus

The present study by Vieira et al. describes the analysis of genetic variants in the CYBA and GCLC genes and their effect on renal disease in patients with type 1 diabetes mellitus. The Authors conducted a case-control study in 401 patients according the diabetic nephropathy status. They found that two variants (-675 T#A in CYBA and rs1788390 in GCLC) modulate the risk for renal disease in type 1 diabetes patients.

The paper is well written and the data clearly presented. However, the current study may be improved.

Minor points:

1. Generally in the manuscript, the official rs numbers should be appeared when it is possible. It is commonly accepted to use the official rs numbers when referring to the SNPs (e.g. GCLC -129 C#T = rs1788390 and GPX3 -65 T#C = rs8177412). This would not only simplify reading the manuscript but also differentiate between the known and the novel SNPs (such as CYBA -675 T#A that is not referenced).

2. The Authors might detail the abbreviations “MDRD”, “UAER” and “ACR”.

3. The sentence “Fifteen percent of the SNPs evaluated by RFLP and by PCR ... were confirmed by direct sequencing and no misgenotyping was detected” might be reformulated. The Authors should give the genotype success rates for each SNPs and if they double genotyped a subfraction of the sample, it may be worthwhile to provide a concordance rate for each SNPs.

4. It may be worthwhile to present briefly the clinical characteristics (sex ratio, age, age at diabetes, arterial hypertension, etc. ...) of the studied subjects according to the case-control status in a table.

5. The Authors might precise which software they used to assess the statistical power.
6. In the Discussion subsection, the authors might name the number of the SNP in the sentence “No previous studies have associated this SNP ...”. Furthermore, the part of this sentence “but a study performed in a Swedish population of type 1 diabetes patients found that those with the CT genotype ...” might be reformulated to improve the understanding.

7. In Table 1, the authors should provide the exact accounts of genotypes distributions.

8. It would be relevant to advert the study of Hodgkinson AD and colleagues in the introduction or discussion part. (Hodgkinson AD, et al. Association of the p22phox component of NAD(P)H oxidase with susceptibility to diabetic nephropathy in patients with type 1 diabetes. Diabetes Care. 2003)


10. Results presented in Table 3 should be more detailed in the Results subsection.

11. The conclusion sentence “The functional SNPs ... require validation in additional cohorts” should be reformulated such as “Furthermore, replication studies for these functional variants will need to be carried out.”

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