Reviewer’s report

Title: Association analysis between the tag single nucleotide polymorphisms of DENND1A and the risk of polycystic ovary syndrome in Chinese Han women

Version: 1 Date: 12 Oct 2019

Reviewer: Lian Deng

Reviewer's report:

Zhu et al., conducted an association study between 5 SNPs in DENND1A and the risk of PCOS in Chinese women, and found that two of them are likely to be the risk variants, which provide clues for further research to fully reveal the mechanisms. The authors carried out adequate comparisons, and made appropriate conclusions. But still, there're several issues to be settled as listed below.

1. The genetic structure of the samples should be evaluated prior to any association test, as Han Chinese is not a homogenous population. The location of samples should be clarified.

2. The sample size used in this study is not large enough, and may lead to limited power of the association test. I understand the difficulties in sample collection, but this issue should be discussed.

3. It is not clear how the 5 tag SNPs were selected. "we systematically studied SNP polymorphisms in the promoter region of DENND1A ...", "... one SNP was selected in each region of the DENND1A gene ..." -- which region exactly? These descriptions are confusing. Also, I suggest they present a full picture of the LD pattern on all the genotyped loci (not just for the 5 SNPs as shown in Figure 1), and reason why these 5 SNPs were chosen as tags in subsequent analyses. They intended to give the details in the second section of Methods "Characterization of LD and selection of tag SNPs", but the whole paragraph is about genotyping experiments, and does not match the subtitle. I suggest they rename this section, and set up a new paragraph for the tag SNP determination.

4. As mentioned in Backgrounds, there are several susceptible loci for PCOS reported in previous study. I think it is necessary to show how these priori candidate loci relate to the 5 tag SNPs, and how they correlate with PCOS in these data here. It is not only a validation, but also show us the similarity and differentiation of populations to the disease risk.

Other minor issues/suggestions:

1. Since all the samples studied are Han Chinese, the title can be more precise, for instance, "Association analysis between the tag single nucleotide polymorphisms of DENND1A and the risk of polycystic ovary syndrome in Han Chinese women".
2. Line 2, Page 9: MAF \(< 0.05\) should be MAF \(\geq 0.05\)?

3. Line 5-6, Page 9: the illustration of Figure 1 (b for case and c for control) is quite different from the figure legend (b for D' and c for R²). I don't understand this figure.

4. One of the 5 SNPs, rs2479102, was misspelled as rs24791902 in quite a lot of sentences in the manuscript. rs24791902 is not an available ID in dbSNP. Also, which version of SNP/gene annotation was used in this study (GRCh37 or GRCh38? Ensembl or Refseq?).

**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.

Yes

**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

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable
**Declaration of competing interests**

Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal.