Reviewer’s report

Title: Genome-wide association study identified ATP6V1H locus influencing cerebrospinal fluid BACE activity

Version: 0 Date: 12 Feb 2018

Reviewer: Karol Estrada

Reviewer’s report:

Hu et al report a GWAS using on CSF BACE activity on 357 samples from ADNI. One genetic variant (rs1481950) reached genome-wide significance. There are key major issues that need to be addressed before this paper can be accepted for publication.

1. Report PCA plot of the 357 samples, using Hapmap or 1000 genomes samples to anchor the samples, and a second plot without the Hapmap samples to see the cluster of samples.

2. Report a QQ plot and a lambda inflation factor

3. Upload higher resolution figures for the figure 2a and 2b, it is impossible to see current version.

4. Don't report Bonferroni correction, it is well established that a P < 5x10^{-8} is considered genome-wide significant

5. Page 10, line 190 and tables, change P < 0.01 to the actual p-value. Add Beta and 95% CI

6. Add in discussion why ATP6V1H is an interesting gene to drive BACE

7. Add in results what is the p-value, beta and 95% CI of rs1481950 with AD and AD-related phenotypes.

8. Describe power settings for this study to identify a genetic variant with a MAF=5% on 357 samples.

9. Divide Table 2 into GWS variants (1) and the rest. Only list independent signals, i.e. remove markers with correlation > 0.30 with any other marker on the table.

10. Create similar plots like Figure 3, stratified by gender and on age categories.

11. Report a resource where authors will make genome-wide summary statistics of their GWAS result.

12. Add a forest plot of rs1481950 in the 3 disease states in ADNI.
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.

No

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:

Needs some language corrections before being published

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