Reviewer’s report

Title: GWAS and enrichment analyses of Non-alcoholic fatty liver disease identify new trait-associated genes and pathways across eMERGE network

Version: 0 Date: 19 Apr 2019

Reviewer: Stefano Romeo

Reviewer's report:

The work by Namjou et al is a gwas performed in a pediatric and adult population identifying potential novel loci for fatty liver disease. Following are my questions to the authors:

Authors tested approx 7,200,000 SNPs and based on this threshold for genome wide significance should be 7x10^-9, authors should authors consider genome wide significant only those exceeding this p value?

Do authors see an interaction between the HSD17B13 and pnpla3 common SNPs associated with liver disease?

Authors should seek for replication with liver disease in the UK biobank database available

The MBOAT7 gene locus has been robustly associated with NAFLD (mannica Gastroenterology 2016) it would be i tested to see the effect of this gene locus in the present cohort.

In the gwas on liver biopsy how were coded the cases and control groups for fibrosis (yes/no?), authors should provide more details on what F score they use and how they classified fibrosis

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

Yes

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 recommend additional statistical review

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 organisation 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 no conflict of interest

Statement on potential review bias
Please complete a statement on potential review bias, considering the following questions:

1. Did you co-author any publication with an author of this manuscript in the last 5 years?

2. Are you currently or recently affiliated at the same institution as an author of this manuscript?
If you can answer no to all of the above, write 'I declare that I did not publish with these authors in the last 5 years and also meet the affiliation criteria”. If your reply is yes to any, please give details below.

No

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