Reviewer’s report

Title: Association between PPARGC1A polymorphisms and the occurrence of non-alcoholic fatty liver disease (NAFLD)

Version: 1 Date: 2 February 2008

Reviewer: Anna Baranova

Reviewer’s report:

This is the review of the paper “Association between PPARGC1A polymorphisms and the occurrence of non-alcoholic fatty liver disease (NAFLD)” by Yoneda at co-authors

Authors of this manuscript undertook relatively small case-control study of polymorphisms located in PPARG1C gene in attempt to reveal their possible associations with NAFLD or NASH. 115 NAFLD and 441 controls were genotyped. Significant association of one of the polymorphisms, rs2290602, and NAFLD was revealed (P <0.0143) after Bonferroni correction. Despite significance of these findings, I do not think that this paper should be published in BMC Gastroenterology as it is submitted now. My explanations are given below:

1. Is the question posed by the authors well defined?
   Yes

2. Are the methods appropriate and well described?
   Methods are appropriate, but they could be described better. E.g. In “DNA preparation and SNP genotyping” part first paragraph reads “genomics DNA was prepared from each blood sample according to standard protocols”. First, this phrase implies more than one protocol applied. Second, it need clarification, e.g. what kit has been used?

3. Are the data sound?
   Data are not sufficient. Larger population of cases needs to be tested, especially in case when NASH alone was tested against controls. Rule of thumb for these kinds of studies is at least 400 cases. If it is not feasible, functional (experimental) study of the effect of the rs2290602 on splicing needs to be performed and reported.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   Yes

5. Are the discussion and conclusions well balanced and adequately supported by the data?
   

No. Authors should at least discuss SNP that they found to be associated with NAFLD, give its sequence and location (which is, by the way, interesting it might influence gene splicing).

6. Are limitations of the work clearly stated?
Not.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
Yes

8. Do the title and abstract accurately convey what has been found?
yes

9. Is the writing acceptable?
yes

Major Revision is recommended. Either sample size needs to be increased, either functional (experimental) study of the effect of the rs2290602 on splicing needs to be performed and reported.

Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest
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- An article whose findings are important to those with closely related research interests

Quality of written English
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- Acceptable

Statistical review
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Is it essential that this manuscript be seen by an expert statistician?
- Yes, and I have assessed the statistics in my report. It is fine.

Declaration of competing interests
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- 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 paper, either now or in the future?

No

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

No

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

No

- Do you have any other financial competing interests?

No

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

No

I declare that I have no competing interests

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**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**
I declare that I have no competing interests