Reviewer’s report

Title: Distinct molecular etiologies of male and female hepatocellular carcinoma

Version: 0 Date: 09 Aug 2019

Reviewer: Fiona Ruiz

Reviewer's report:

When performing the eQTL analysis to identify germline genetic effects on the tumor gene expression, did you take into consideration effects of race? In your Female and Male cohorts you showed a significant difference in race between the two cohorts. I think it is informative to show whether these germline SNP's are enriched in different racial groups or if they are solely gender specific.

In your eGene results you mentioned POGLUT1 being a male specific eGene and that it is an essential regulator of NOTCH signaling. However, NOTCH1 signaling was found to be a shared pathway between both sexes. Did any of the male specific eGenes contribute to male specific enriched pathways? Making the connection between the differentially expressed genes and pathways in the sexes and the sex specific eGenes would add additional insight into the different underlying biology of male and female HCC tumors.

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.

Unable to assess

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