Reviewer’s report

Title: Uric acid induced hepatocytes lipid accumulation through regulation of miR-149-5p/FGF21 axis

Version: 0 Date: 06 Nov 2019

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?

Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?

No - there are major issues

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?

No - there are major issues

STATISTICS - Is the use of statistics in the manuscript appropriate?

No - there are issues with the statistics in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?

No - there are major issues

OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?

Maybe - with major revisions
PEER REVIEWER COMMENTS:

GENERAL COMMENTS:
The proposed study provides insight view and novel strategy potential applicable into the clinical setting for the treatment of NAFLD and hyperuricemia in particular. The study is well-described but important limitations are related to the sole use of cell lines.

REQUESTED REVISIONS:
The proposed study is interesting but requiring additional refinements and supportive data to reach (clinically) relevant conclusions. Both mouse (AML-12) and human (HepG2) cell lines have been tested, while more accurate and clinically relevant results would be collected by the use of primary (human and murine) hepatocytes. The technique to isolate primary liver cells is quite well-established, and cryopreserved primary cells are commercially available. Variability, in particular in human samples need to be considered during such analysis and it would potentially provide a much better insight view and mechanistic outcome. Regarding the in vivo experiments: Interestingly, the authors did not find important to analysis or comment difference between control group (SCD) and the allopurinol-treated group. Moreover, Introduction section is not covering the allopurinol use and the reasons to design the study around such pharmacological treatment only. Large parts of the Results section is actually introductive or commentary to the results. Conclusions and comments on the provided results should be avoided in the Results sections and only address in the final part of the manuscript. miRNA profile and analysis required supportive description and motivation for the cut-off and statistical analysis. Once again, comparison between ctrl and HFD+A group is required and motivated. Transfection experiments in primary liver cells would be the better choice and implemented to give strength to the study. Cell line may be used a preliminary approach to set up technique or only when primary cells have been proved inefficiently in such approach. Long-term expression/effects should also be monitored. Finally, statistical analysis should be motivated and reconsidered. Histological images need to be uploaded to higher resolutions to be evaluated.

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.

No

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:

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.

This reviewer has been recruited by a partner organization, Research Square. Reviewers with declared or apparent competing interests are not utilized for these reviews. This reviewer has agreed to publication of their comments online under a Creative Commons Attribution License attributed to Research Square and was paid a small honorarium for completing the review within a specified timeframe. Honoraria for reviews such as this are paid regardless of the reviewer recommendation.

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.