Reviewer’s report

Title: Down-regulation of the tumour suppressor κ-opioid receptor predicts poor prognosis in hepatocellular carcinoma patients

Version: 0 Date: 15 May 2017

Reviewer: Shah Walayat

Reviewer's report:

Interesting work about KOR expression in HCC both at protein and mRNA level. However in addition to the extensive editing of English, certain rearrangements in the results section would improve the presentation of the article. For example, from abstract and results at first glance it looks like both proteins and mRNA levels were determined in FFPE tissues which is not the case. So better to mention the main results of IHC first and then followed by real time PCR results from fresh tissue for confirmation of mRNA levels of KOR. Further no clinicopathological data is available for fresh tissue samples patients and also no IHC was performed in the fresh tissue. This area need further improvement. The term peripheral normal tissue may be replaced with adjacent normal tissue throughout the document to avoid confusion.

In the results "KOR is down-regulated in human HCC" both mRNA expression of 64 samples and IHC of 174 FFPE tissue is mentioned together. As suggested before the mRNA expression results should be placed at the end of the IHC results just for validation purpose. The same comments stand for the discussion section as well.

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 am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

**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/](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