Reviewer’s report

**Title:** Major vault protein suppresses lung cancer cell proliferation by inhibiting STAT3 signaling pathway

**Version:** 1 **Date:** 11 Aug 2018

**Reviewer:** Reviewer 2

**Reviewer's report:**

PEER REVIEWER COMMENTS: To view the full report from the academic peer reviewer, please see the attached file.

REVIEWER COMMENTS FROM REPORT: Overall, this is potentially an interesting work that reports on possible role of MVP in lung cancer prognosis. Authors have performed many experiments, including an in vivo experiment, which should potentially help publish this work in a good journal.

I do have some concerns, which, if adequately addressed, should improve the quality of presentation and help get this work published in a good journal -

Authors mention that MVP is over-expressed in drug resistant cells. This would indicate an oncogenic role of MVP in carcinogenesis. However, this study supports a tumor suppressor role of MVP. Thus, there seems to be a context or tissue-specific role of MVP in different cancers. How can this affect any potential therapy. Wouldn't it up-regulation by any means lead to drug resistance?

Adding to the above argument, authors note that they observed higher MVP expression in lung tumors, compared to normal. To me, this supports oncogenic role, and not tumor suppressive. Authors went ahead and analyzed published lung cancer data bases to found that higher MVP correlated with better outcome. However, to me these look like very independent observations that completely contradict each other. A more direct correlation would be to evaluate whether in the patient population that authors themselves studied, did the 99 of 142 patients with higher MVP expression had good prognosis.

Further, of the remaining 43 patients, was the MVP expression significantly lower than normal? Also, did these patients suffer from more aggressive disease? Were these patient associated with poor prognosis? If authors have answers to these questions, there overall conclusion that MVP is tumor suppressor will make more sense.

Another major concern I have is regarding the use of mouse cells. I would highly encourage authors to replicate results in a human cell line. Not many journals and reviewers will like the idea of completing all mechanistic studies in just one cells line, and that it is a mouse cell line is also a concern.

Reference #1 supporting lung cancer statistics is from 2016. Authors should cite the one from 2018.
Editing is warranted for language. For example, the sentence that ends with reference # 14 in the 'background' should read 'Therefore, it seems to….'. Also, the second sentence in Results - 'MVP expression was highly expressed significantly increased..' needs to be revised. There are other such errors as well, which are just too many to list here.

REQUESTED REVISIONS:
Please check my above comments for leads. My one recommendation would be to use human cell lines for mechanistic studies. My second recommendation would be to re-analyze human patient samples with a view to strengthen the tumor suppressive role of MVP.

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.

Not relevant to this manuscript

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

Needs some language corrections before being published

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