Reviewer’s report

Title: Valproic Acid Sensitizes Metformin-resistant Human Renal Cell Carcinoma Cells by Upregulating H3 Acetylation and EMT Reversal

Version: 1 Date: 16 Jan 2018

Reviewer: Prathibha Ranganathan

Reviewer's report:

1. As I had mentioned previously, the rationale for using metformin is not very clear. I agree that the authors have made an attempt to clarify, but the point is still not addressed. Is Metformin given as a treatment for RCC? If not, then what is the physiological relevance of this study?

1. When you say sensitivity to metformin, what happens to the glucose levels in these patients?

2. The bar graphs for determining IC50 in Fig 1, is better than previous one. Tabulation may be a better idea.

3. The changes in the cell cycle profiles are not very convincing. It is better to get a statistician's opinion on the significance of these changes.

4. In figure 3, the differences between VPA alone and combination are not very clear. Again, statistician's opinion may be useful.

5. In figure 6, the effect of TSA is not as apparent as VPA. Please comment on that.

6. Fig 7 legend is missing.

7. Fig 8 is not very clear. Legend is also missing.

8. The language needs to be better before publication.
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 recommend additional statistical review

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

Needs some language corrections before being published

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