Reviewer’s report

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

Version: 0 Date: 30 Oct 2017

Reviewer: Prathibha Ranganathan

Reviewer's report:

1. Metformin is a drug used to treat diabetes. It does have an advantage in treating renal cancers and other cancers as well. But it is not used as a stand alone treatment. The rationale for using metformin and valproic acid to demonstrate synergistic effect is not very clear in the manuscript. metformin alone has very little anti cancer effect as the authors have mentioned.

2. What is the basis of resistance caused by metformin?

3. The concentrations of drugs used is in the milli molar range which seems rather high. The effect seen may be just due to toxicity and may not be a specific effect

Minor points

1. The figure legends need to be more clear

2. Fig 1-- It would be better to represent the IC50s in a tabular form also

3. Fig 2a-- the difference between Met alone and VPA + Met on ACHN cells is very marginal

4. Fig 3d-- the differences in the cell cycle profiles not very significant
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?
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No

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Not relevant to this manuscript

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

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