Reviewer’s report

Title: The novel histone deacetylase inhibitor, N-hydroxy-7-(2-naphthylthio) hepatonomide, exhibits potent antitumor activity due to cytochrome-c-release mediated apoptosis in renal cell carcinoma cells

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Reviewer: Zhengfang Yi

Reviewer’s report:

In this manuscript, the authors investigated the effect of a novel HDAC inhibitor, HNHA. They claimed that HNHA exhibits potent antitumor activity due to cytochrome-c-release-mediated apoptosis in RCC cells. This is an interesting story.

Comments:

• Major Compulsory Revisions

1. In the first paragraph, author need add more references .”

2. In line 85, page 4, whether “kidney cells” should be corrected as “RCC cells”? Please check it.

3. In line 178, page 8#The author stated “Cell numbers and adhesion abilities were lower in the HNHA treated groups than the control group, and the cells exhibited a more elongated shape”. The authors should explain the relationship between this phenomenon and tumor cell proliferation.

4. In Figure 3, author evaluated whether the anti-growth activity of HNHA was due to effects on cell cycle progression and apoptosis. These results showed that HNHA induced cell-cycle arrest at the G0/G1 phase in RCC cells and FACS analysis showed increased cellular accumulation in the sub-G1 cell cycle fraction. P21 is a cell cycle repressor. In figure 3A, HNHA seems not to be the most potent HDACi in inducing G0/G1 arrest, but HNHA possesses the highest activity in up-regulating p21 level. The author need explain this result. In addition, there are still other G0/G1 phase marker proteins; Please indicate the expression levels of G0/G1 regulators after HNHA treatment.

5# The fonts in all figures need to be consistent.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests: no