Reviewer's report

Title: Berberine enhances inhibition of glioma tumor cell migration and invasiveness mediated by arsenic trioxide via the inactivation of protein kinase C

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Reviewer: Sai-Juan Chen

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General
This study demonstrated that arsenic trioxide (ATO) in combination with berberine could inhibit glioma cells metastasis as well as cell viability. Further investigation showed that the mechanism of migration suppression was the inactivation of PKC signal pathway. Though there have already been about 8 in vivo or in vitro studies reported that ATO could reduce metastasis in different solid tumor since 2005, it is still worth to confirm such phenomenon in different system and study more detailed in mechanisms.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1. In this study, it is not suitable that cell viability was determined by MTT assay. The reduction of results after MTT reaction only showed the decrease of viable cells, which could be the result of either proliferation inhibition or decreased cell viability. In fact, cell viability could be determined by trypan blue exclusion. Please check the data of trypan blue exclusion to confirm whether ATO+ berberine inhibited proliferation or induced cell death.
2. The expression pattern of Fig 1C is not quite clear. To confirm the additive effect of combined treatment, it is better to show ATO and berberine treatment alone with the combined treatment in one figure. I was confused about the data of ATO treatment alone in Fig1C, the cell viability of ATO was about 100%, while in Fig1B and 1A, the cell viability was around 80% with the same treatment.
3. Fig 5 is not well done. Please use FITC-conjugated second antibody so that the ratio of signal to noise will be better.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
The results part could be written more concisely since several methods used had already been mentioned in methods part and several time course or treatment had been described in detail in legends.

Discretionary Revisions (which the author can choose to ignore)
Since there are several other paper published also showing that ATO could inhibit metastasis by MMP-9 and MMP-2 reduction (Braz J Med Biol Res,2006, 39:677-85. Gynecol Oncol,2006,103:199-206. J Cell Biochem,2005,95:955-69.), it is not original that the same result obtained in this study. However, in this paper, it was first time to confirm that the combined treatment could inactive PKC. However, since there was no data showing when the inactivation of PKC was released then metastasis restored, it is still not scientific enough to make the conclusion that the inhibition of metastasis was via the inactivation of PKC.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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:
I declare that I have no competing interests.
Sai-juan Chen