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

Version: 3 Date: 6 November 2007

Reviewer: Yok Lam Kwong

Reviewer's report:

General

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

In this revised manuscript, Lin et al have addressed most of the concerns raised in the last review. Interference of the biochemical pathways involving protein kinase C was postulated to underlie the pharmacological actions of arsenic trioxide and berberine. In most biological systems, to demonstrate the involvement of a biochemical pathway in a biological function, the effects of both activation and suppression of the biochemical pathway should be investigated. In this article, Lin et al presented findings of some of the changes of downstream mediators of protein kinase C subsequent to arsenic trioxide and berberine treatment. However, they did not present any evidence that these pathways were directly related to the observed biological effects of arsenic or berberine, such as cytotoxicity or effects on cell migration. It is disturbing that the authors did not appear to appreciate the deficiency of their data in this aspect. If they truly believe that down-regulation of protein kinase C a and e is the main molecular mechanism of arsenic and berberine, the minimum that they should have done is to demonstrate rescue of the cells from arsenic and berberine by over-expression of protein kinase C a and e. This will be more convincing that further examination of the downstream effectors of protein kinase C.

The problem of this manuscript, as it stands now, is related to inadequate conceptual designs of experiments, rather than poorly executed experiments. If the authors are unable to perform more experiments as suggested above, they should state clearly that the involvement of protein kinase C a and e has not been definitively proven, because rescue experiments of over-expression of these molecules have not been performed.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

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Discretionary Revisions (which the author can choose to ignore)
What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.