Reviewer’s report

Title: Valproic Acid Decreases Urothelial Cancer Cell Proliferation and Induces Thrombospondin-1 Expression

Version: 1 Date: 27 June 2012

Reviewer: Gan Wang

Reviewer’s report:

Bladder cancer is one of the most commonly diagnosed cancer types, and the prevention of bladder cancer recurrence is an integral challenge in the management of this disease. Valproic acid (VA) is a well-known HDAC inhibitor. The VA is an attractive candidate of anticancer drugs that displays some anti-cancer activity. The underlying mechanism, however, is not fully understood. The work presented in this manuscript investigated the role of VA in inducing expression of TSP1, a natural inhibitor of angiogenesis, as a possible mechanism for its anticancer action. The results of the studies demonstrated that the VA treatment caused a reduced cell proliferation in both UMUC3 and T24 bladder cancer cells. The study further revealed that the VA treatment resulted in a reduced expression of TSP1 gene in both UMUC3 and T24 bladder cancer cells using a quantitative PCR assay. Although the results are interesting and may explain an important mechanism utilized by VA in its anticancer action, the results are too preliminary and more studies are needed before publication.

Major compulsory revisions:

1. Although the work suggested that the VA treatment caused reduced cell proliferation in the tumor cells, no statistical analysis was done to show the statistical significance between the untreated and the VA treated cells in the cell proliferation in the study.

2. The increased expression of the TSP1 in the VA-treated UMUC3 and T24 cells was only determined by quantitative PCR assay. Some western blots data to show an increase in expression of the TSP1 protein in the VA-treated cancer cells would be necessary for the work. Again, statistical analysis is lacking for the qPCR data.

3. In order to provide a better understanding for the mechanism of VA in inducing expression of the TSP1, some studies, such as a ChIP assay that can directly determine if the VA treatment would cause altered binding of the HDACs at the promoter region of the TSP1 gene, would provide more convincing evidence explaining the mechanism of VA in its anti-cancer action via inducing expression of TSP1.

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

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