Reviewer's report

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

Version: 1 Date: 11 July 2012

Reviewer: Kenneth Iczkowski

Reviewer's report:

This is an interesting article about the use of valproic acid in bladder cancer. This could be potentially clinically useful and promising. It could have a very good impact. However, both the science and the manuscript could benefit from some strengthening along the lines described.

Major Compulsory Revisions:

What was the basis for choosing to use 1 mM and 5 mM valproate? First, are these commensurate with levels attainable in the serum of humans or animals? Second, are these doses that were used before in prior published work? Likewise for SAHA. Also, why the choice of three days to treat the cells? Was a time course study done to show that the effect of valproate is maximal at three days as opposed to 1 or 2 days?

In the Methods it is stated that "t-test using JMP Statistical Software" was used but it is not explained which bar graphs are significantly different from others. These differences should be indicated with a * for p<0.05, or maybe two ** for p<0.01. Likewise, on Figure 3, more explanation of the how the statistics were carried out is needed, as well as indicating which differences are significant.

The paper would be strengthened by adding western blot analysis if at all possible, and if there exists an specific antibody to TSP1. If no specific antibody exists, then please explain this as well.

Finally, the findings are mainly descriptive and would be strengthened by a demonstration of the mechanism of vaproic acid action. For example, ChIP analysis showing whether there is altered binding of HDAC inhibitors to the promoter of TSP1 induced by valproic acid.

Minor Essential Revisions:

Second paragraph last sentence should have a comma not a semicolon.

TCC-SUP, not TCCSUP

4th paragraph increased the percentage--> and increased the percentage

Page 2 Para 2. ...TSP1 expression was enhanced in embryos carried by dams.... This appears to be an unpublished observation. If so, please indicate that it is by adding (unpublished observation).
Place a space between a number and a unit, not 1 mM but 1 mM.

Figure legend number 1 Not--> Note

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

'I declare that I have no competing interests.