Reviewer's report

Title: Caspase 8 and Maspin are downregulated in Breast Cancer Cells due to CpG Island Promoter Methylation

Version: 1 Date: 3 August 2009

Reviewer: Suhu Liu

Reviewer's report:

Major Compulsory Revisions

1. The abstract is too long and lack focus. Need to be reorganized to be more concise.

2. On page 10, the authors chose 4 breast cancer cell lines “with different phenotype” for methylation screening. Please further specify the meaning of “different phenotypes”. Are they cell lines representing different cancer stages or metastasis potential or ER status?

3. Methylation of maspin in breast cancer has been reported previously. So the authors should be cautious about the claiming that they are the first to report this.

4. There are quite a few statements in the paper that require re-iteration. For example, on page 17, the author said they are the first to shown maspin methylation in breast cancer while in fact research about maspin methylation in breast cancer had be published as early as 2000 (Epigenetic silencing of maspin gene expression in human breast cancers. Domann FE, Rice JC, Hendrix MJ, Futscher BW. Int J Cancer. 2000, 85(6):805-10.)

5. There are also some ambiguous and descriptive statements that lack scientific conciseness and clearance and need to be re-phrased. For example, “Methylation of the promoter regions of CpG-rich sites in genes is the major mechanism for the silencing of many genes in tumors” on page 17. “methylation might be an important mechanism of gene silencing but there is no confirmative scientific data to show that “methylation” is the “major” mechanism. Also how many genes can be described as “many” genes?

6. In the second paragraph of discussion, the author listed and described several genes that were reported to be methylated in breast cancer. This part did not related to the content of this paper and not necessary at all and should be shrink back and only keep the first one or two sentences. Also the author gave a small review as to what “caspase 8” is on page 18 for discussion, which was not related to the findings in this research and can be cut back significantly.

7. While there is quite some unrelated discussion, there are also some interesting findings in this paper which the authors seem to fail to notice or give further confirmation and discussion. One of the example is the finding that 5-Fu seems to lead to de-methylation of Caspase 8 promoter. This interesting finding surely require further validation and in depth discussion.
8. Another novel and interesting finding of this paper is that one oncogene, Survivin, is found hyper-methylated in all these breast cell lines. The authors should give further investigation and discussion about this discovery. It is actually recently reported that surviving is also hypermethylated in endometrial cancer (Oncogene. 2009 May 14;28(19):2046-50.)

9. The discussion about Caspase 8 and maspin is mixed up in the “DISCUSSION” part.

**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:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

'I declare that I have no competing interests