Reviewer's report

Title: Down-regulation of GRP78 is associated with the sensitivity of chemotherapy to VP-16 in small cell lung cancer NCI-H446 cells

Version: 1 Date: 19 August 2008

Reviewer: Kim Janda

Reviewer's report:

This paper describes GRP78 expression in lung cancer cells and its down-regulation in the context of sensitivity to chemotherapeutic drugs.

Major Compulsory Revisions:

Overall, the manuscript is poorly written and needs significant improvement in word order and grammar. Relevant citations about targeting GRP78 are missing. The authors use immunofluorescence to assess the expression of GRP78 on the protein level, however, it would be more appropriate to do this by western blotting. The designation of the treated cells is misleading; the group “BAPTA-AM-inhibited cells” should be called “BAPTA-AM-treated cells”. The “A23187-induced group” should be called “A23187-treated group”. The authors should also consider generating a bar graph for the toxicity data. Furthermore, they should not only treat the cells with VP-16 but also with a known drug such as taxol. It would also be interesting to compare BAPTA-AM to another inhibitor of GRP78 expression.

Minor Essential Revisions:

The authors should decide on either “Grp78” or “GRP78” and be consistent throughout the manuscript.

Page 2, line 3: reads “present”, should read “presence”
Page 2, line 5: reads “trough”, should read “through”
Page 2, line 6: reads “which is”, should read “which are”
Page 2, line 8: reads “GRP78/BiP, one of well-”, should read “GRP78/BiP, a well-”
Page 2, line 12: reads “ The common used”, should read “Commonly used”
Page 3, line 29: reads “the cells were washed with PBS for twice”, should read ”the cells were washed twice with PBS”
Page 6, line 5: reads “once within the cell”, should read “once inside the cell”
Page 6, line 14: reads “inhibited”, should read “inhibit”
Page 6, line 29: reads “sensate”, should read “sensitive”

Figure 1 needs major improvements, the background in II should be white and the bars should be black. Error bars are missing. The Y-axis has not title.
In the discussion the authors state: “In this work, we found that BAPTA-AM attenuated the expression of GRP78 significantly. In line with our results, Juliann G, et al. [21] and W hei-meih C, et al. [18] also respectively reported that BAPTA-AM caused a down-regulation of GRP78 in human breast cancer cell line and 9L rat brain tumor cells. But treatment with BAPTA-AM alone did not inhibit the expression of Grp78 mRNA, whereas treatment with BAPTA-AM followed by heat-shock induced could inhibit the expression of GRP78 obviously.” It is not clear who carried out the heat-shock treatment, the authors in this study or the aforementioned works by different groups. This needs to be clarified.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Not suitable for publication unless extensively edited

**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.