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: 27 August 2008

Reviewer: Hae-Ryong Park

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Major Points

1. Previous studies revealed that BAPTA-AM exhibits the cytotoxic effects on the other cells. Thus, it must be described whether the concentrations of BAPTA-AM for its VP-16-chemosensitive activity are consistent with those for the cytotoxic antitumor activity in NCI-H446 cells.

2. In Fig. 1, could authors comment a little bit on the fact that basal levels of GRP78 are reduced apparently at treatment with 40 #M of BAPTA-AM in A23187-induced stress condition? In similar manner, this is also related with Fig. 3(C). It seems to cell cytotoxicity induced before GRP78 was down-regulated.

3. In Fig. 3, although authors argued that BAPTA-AM was increased the sensitivity which target S-phase of VP-16-induced resistance, it is not seemed to associate with chemotherapy to VP-16. The drug resistance to VP-16 has the involvement of multiple pathways however, consideration for topoisomerase II# which is a molecular target of VP-16 is necessary. Additionally, why did not carry out the effect of BAPTA-AM on A23187-induced cells in absence of VP-16. These questions should be addressed and discussed in the paper.

4. How does DNA fragmentation in the nucleus when treated with BAPTA-AM in VP-16-resistance cells.

Minor Points

1. In Introduction, if the common used inhibitor of GRP78 is thapsigargin, indicate the Reference for that.

2. In all manuscript, consist with SI units.

3. In Results, correct the subheading of title.

4. In Discussion, is it Table 3 or Table 2? Please check.

5. In Fig. 1, correct the style of graph and consist with font.

6. In Fig. 2, there is no data as control of BAPTA-AM only. Please add.

7. Although written reasonably well, the manuscript would still benefit from careful editing for English syntax and particularly for dropped words.

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