Reviewer’s report

Title: Boron neutron capture therapy induces apoptosis of glioma cells

Version: 1 Date: 12 March 2010

Reviewer: Rolf Barth

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General Comments

The authors have posed an interesting question; does BNCT result in enhanced apoptosis of tumor cells? Clearly, they have done a lot of work to attempt to answer this question, and although they present data to support this hypothesis, the manuscript is so poorly written that what could be convincing data becomes much less so. The authors should try to enlist the support of someone who has not only high proficiency in the English language, but also the scientific background to present their data in a clearer and more convincing way.

Major Compulsory Revisions

Materials and Methods/Results

1. There are numerous errors in English usage and spelling. Examples linear not “lineal”; Rysory, not Ryscor; taken up, not “uptaken”; gradually, not gradiently,” etc., etc.

2. It should be made unambiguous that the cells were irradiated in the reactor beam both in the absence and presence of BPA. How was possible elution of BPA controlled for?

3. The boron uptake values seem unusually high: 2.72µg/107 cells would equal 272 µg/g, which is 10 times greater than that observed following in vivo administration to tumor bearing animals. Please verify that there is not an analytical or computational error.

4. Fig. 2. Error bars should be inserted for all of the data points. Even without them, the numbers for cells irradiated in the reactor at 4 and 8 Gy or without BPA seem to be very close. By visual inspection, these differences do not seem to be significantly different from one another. Therefore, how can one conclude that there indeed was killing related to the 10B(n,#)7Li capture reaction? Also, it would be helpful if symbols were paired. For example, 4 Gy irradiated # and 4 Gy BNCT #.

5. Table 2. “Irradiated in reactor for identical time with BNCT 4 Gy and 8 Gy” and “BNCT 4 Gy and 8 Gy” is very confusing both in the table, text and Fig. 2. This needs to be clarified.

6. What is shown in Fig. 5 should be better explained in both the Results and in
the figure legend.

7. Fig. 4. The histograms seem to show significant differences in the “apoptosis rate” in the presence or absence of boron. Please clarify and comment on this.

Discussion

8. The first paragraph is totally irrelevant to the subject matter of this report – induction of apoptosis following neutron irradiation, and therefore should be deleted.

9. The statement that clonogenic survival data “...may be implying a selective eliminating effect of BNCT towards tumor stem cells in glioma cell hybrid” is completely unsupported by the data presented. Either a strong argument should be made to support this statement or it should be deleted.

10. The next to last paragraph is not only poorly written, but is highly speculative to say the very least.

11. Similarly, the last paragraph regarding the down regulation of “Bcl-2 protein and upregulation of Bax is mediated by damage of mitochondrial membrane integrity” is highly speculative, and poorly written. Either the hypothesis better supported by data or it should be deleted Furthermore, it is not a good concluding paragraph.

12. The poor English usage aside, the fact that the pages were not numbered made review of this manuscript even more difficult.

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

**Declaration of competing interests:**

I declare that I have no competing interests.