Reviewer's report

Title: Boron neutron capture therapy induces apoptosis of glioma cells through Bcl-2/Bax

Version: 3 Date: 12 October 2010

Reviewer: Rolf Barth

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MS ID No. 2985120603541076

Major Compulsory Revisions

The manuscript as a whole, and more specifically the Discussion, have been significantly improved. However, going back to my previous review, the boron uptake values indicated on page 9 are almost two orders of magnitude greater than we have observed. In our own studies, when F98 glioma cells were exposed to 500 µM (95 µg/mL) of BPA for 24 hours, the resulting boron concentration was 6.6 µg per 109 cells, or 0.066 µg for 107 cells (Barth et al., Cancer Res. 64: 6287, 2004). Similar uptake values were seen with a human melanoma cell line (MRA27) and a mouse cell line (L929). The boron values reported by the authors exceed those reported by others in the BNCT literature by 1 to 2 orders of magnitude. Something seems to be wrong with either the analytical method used or their calculations. I would suggest that the authors contact an Analytical Chemist who can independently run the boron determinations on the cell samples. One possible confounding factor would be if there was a carryover of non-cell associated BPA in the preparations that were analyzed. If the authors wanted this reviewer to carry out the determinations in his laboratory, they could contact either me (rolf.barth@osumc.edu) or Mrs. Tianyao Huo (huo.3@osu.edu).

Another issue relates to the very high concentrations of BPA that were used. 50 µg of 10B is equivalent to approximately 1 mg of BPA per mL, which is a very high concentration and could never be used clinically.

Minor Essential Revisions

Abstract

1. p. 2, l. 3: delete “might be” and insert “is”

2. p. 2, l. 4: The statement that “the mechanisms underlying this therapy…” is a misleading and simplistic statement. It was recognized over 70 years ago by Locher that the production of alpha particles discharging their energy within cancer cells would kill them. Since then, there has developed a voluminous literature on the radiobiologic effects of alpha particles. Therefore, either modify the sentence or delete it.

3. p. 10: Change to “were irradiated with a beam of thermal ( ) [this should be
specified] neutrons at the Xi’an Pulse…”

4. l. 15: in “the” not “a” reactor

5. l. 20: (MTT) cytotoxicity assay

6. p. 3: “strongly” not “potently”

7. p. 3, l. 8: “clonogenicity” not “clone forming ability”

Background

8. p. 4, l. 6: Mention should be made of the numerous studies carried out using syngeneic rat gliomas.

9. p. 5, l. 9: “inductively” not “induced”

10. l. 14: Technical details relating to the cobalt source should be provided.

11. p. 6, l. 6: Details relating to the dose contributions from the various components (e.g., # photons, fast neutrons) of the beam should be provided.

12. p. 6: Was the viability of the cells determined prior to and following irradiation? If so, the percent viabilities should be indicated. If not, in all future studies, viability should be indicated.

13. p. 8, l. 9: “Clonogenic assay” not “Colony formation”

14. p. 8, l. 12: “The cells” not “Developing colonies”

15. p. 10, l. 22: “doses” not “amounts”

Discussion

16. p. 13, l. 20: The Discussion has been significantly improved and there are only a few minor comments.

17. p. 14, l. 6: “irradiated” not “reactor”

18. p. 14, l. 7: “clonogenicity” not “clonal formation capability”


20. p. 16: The last 3 concluding sentences of the Discussion can be improved by making a strong “take home” message about the significance of their study in the context of BNCT.

21. Figure 4: The panels are still too small. I would recommend reducing the number and increasing their size.

Discretionary Revisions

None.
**Level of interest:** An article of importance in its field

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

**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