Author's response to reviews

Title: The radiosensitizing effects of doranidazole on human colorectal cancer cells exposed to high dose irradiation

Authors:

Li Zhang (tyour19652004@yahoo.com.cn)
Aimin Gong (yinke760109@163.com)
Jun Ji (cancer-1976@hotmail.com)
Yuanyuan Wu (wuyuanyuan9@yahoo.com.cn)
Xiaoyu Zhu (zhuxiaoyu66@yahoo.com.cn)
Suqing Lv (lusuqing341@hotmail.com)
Honazhu Lv (pole163@163.com)
Xizhuo Sun (xizhuomd@163.com)

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Author's response to reviews: see over
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Authors:
Li Zhang: tyouri19652004@yahoo.com.cn
Aimin GONG: yinke760109@163.com
Jun JI: cancer-1976@hotmail.com
Yuanyuan WU: wuyuanyuan9@yahoo.com.cn
Xiaoyu ZHU: zhuxiaoyu66@yahoo.com.cn
Suqing LV: lusuqing341@hotmail.com
Hongzhu LV: pole163@163.com
Xizhuo SUN: xizhuomd@163.com

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Author's response to reviews: see over

The Biomed Central Editorial Team

Object: MS: 8993516871385781 - The radiosensitizing effects of doranidazole on human colorectal cancer cells exposed to high dose irradiation. Dr Li Zhang et al.

Thank you for consideration of our manuscript for publication in your journal. We have reviewed the above manuscript according to your reviewer’s comments.

Reviewer #1 (Halil Kavgaci)
Revise for reviewer’s comments

"The radiosensitizing effects of doranidazole on human colorectal cancer cells exposed to high dose irradiation" titled paper carefully evaluated. In this study, radiosensitizing effect of doranidazole on five colorectal cell line (HT-29, DLD-1, Colo 201, LoVo, and SW 620) were investigated. But except oneparamater (cell killing), only Colo 201 results were reported. If other paramater were not studied, other cellline omitted and manuscript will be revised.

• We have used five colorectal cell line to investigate the radiosensitizing effect and studied all five cell lines in cell killing analysis, please see “table 1”. In other figure, well only presented the data of Colo 201 (the data of other cell lines was not shown).

Table 1 second line is fault. Dornidazole 5 mmol/L will be added.

• Table 1 has been changed as the reviewer indicates. (see the manuscript).

Reviewer #2 (Natsuo Oya)

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1. Page 8 (colony assay) and Figure 2, Page 8 (PI assay) and Table 1;
(1) In page 8, line 7, the SER values in colony assay were described to be 1.26 and 1.79 for low radiation dose and high radiation dose, respectively. The Authors should describe the definition of SER and how these values were calculated.

- Corrected as the reviewer indicates. (see the manuscript, page 6, materials and methods, “5. Colony forming assay and cell survival curve”)

“In both experiments under hypoxic condition, cell surviving frictions were determined by the standard in vitro colony formation assay and cell survival curve. The sensitizer enhancement ratio (SER) was calculated from two radiation doses with or without doranidazole to reduce cell survival to 1%.

\[ \text{SER} = \frac{\text{irradiation D0}}{\text{irradiation + doranidazole) D0}} \]

(2) In Figure 2, the set of plots representing ?Doranidazole plus irradiation? was fit to a straight line. Regression to a linear-quadratic curve would be better.

- Corrected as the reviewer indicates. (see the figure 2)

(3) In page 8, line 19, and Table 1, again, SER was used undefined. The Reviewer’s understanding is that SER is defined as “the ratio of two radiation doses, required to obtain the same effect in different two experimental conditions”. The Authors mentioned in the Discussion section (also in the title of the paper) that the radiosensitizing effect of Doranidazole was more significant in the high-radiation dose range. Therefore, appropriate evaluation of SER is very important.

- Corrected as the reviewer indicates. (see the manuscript, materials and methods, “5. Colony forming assay and cell survival curve” and page 8, line 19), and the table 1 is not the determination of SER, it presented the cell killing assay only.

2. In ?Morphological changes of the cells? and ?Cell migration assay?, no quantitative analysis was performed. Omit them or provide quantitative data.

- We have performed the quantitative analysis of the morphological changes of the
cells and the cell migration assay, please see the manuscript, materials and methods, "6. Morphological observation with fluorescence microscopy" and "7. Cell migration and invasion assays".

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

There are several typographic errors;

page 3, line 4, defection

• Corrected as the reviewer indicates. “transference”

page 7, line 19, show

• Corrected as the reviewer indicates. “present”

page 8, line 20, doranidazoel

• Corrected as the reviewer indicates. “Doranidazole”

page 9, line 16, along

• Corrected as the reviewer indicates. “along” has been deleted.

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