Author's response to reviews

Title: Pentoxifylline sensitizes human cervical tumor cells to cisplatin-induced apoptosis by suppressing NF-kappa B and decreased cell senescence

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Author's response to reviews: see over
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PhD Christina Chap
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Dear PhD Chap:

In April, we sent to *BMC Cancer* magazine for your consideration, our manuscript entitled “**Pentoxifylline sensitizes human cervical tumor cells to cisplatin-induced apoptosis by suppressing NF-kappa B and decreased cell senescence**”. I gladly inform to you that we have finished correcting the observations done by your referees. In this new version, we add in the section of materials and methods the following experiments:

- Analysis of drugs interaction
- Caspase-8 activity
- Analysis of Bcl-2 and Bcl-XL proteins

These experiments also are described in the section of results and further in the section of discussion.

Please accept it as a candidate for publishing in your magazine, our paper has not been submitted to or published in any other journal.

Sincerely yours.

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Response's report

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1.- In general in all assays, we found that the combination of PTX + CIS was better than CIS alone. Indeed, we observed some differences between assays and cervical carcinoma cells lines, when these cells were treated with PTX or PTX + CIS. This can be explained because all these assays, evaluate several cell death processes in different temporal phases. For example, annexin-V visualizes the early apoptosis; while acridine orange and ethidium bromide allows us evaluate the complete morphological profile in the late apoptosis [1]. The clonogenic assays represent the cellular capacity after chemotherapy exposition, to continue to replicate [2]. These observations reflect the complexity of the signal transduction pathways. Due to the heterogeneity and the differences between in HeLa and SiHa cell lines in they lead to apoptosis in response to similar [3]

2.- The doses utilized were chosen based on the result of individual dose-response curves. These doses allow us to observe any further reductions caused by drug combination, because higher doses induce a significant reduction on the cell viability

3.- Results of the clonogenic assays were analyzed with the CalcuSyn software version 2.0 using the Chou and Talalay method to determine the drug interaction nature [4, 5].

4.- The mistake was already corrected in the new version of the article. We completed the redaction of the formula [2].

5.- The caspase-8 activity of already was evaluated.
6.- We consider to know, the intra-cellular location of the studied proteins is desirable but need protocol to study for that. Nevertheless, the experimental design was focused to analyze the NF-κB pathway. In previous works we have demonstrated that the pentoxifylline acts in a direct way avoiding the ser 32 and 36 phosphorylation of the IkB in leukemic cells treated with doxorubicin [6]. The NF-κB pathway plays an important role in the chemoresistance to anti-tumoral drugs like cisplatin [7, 8]. In this sense, this new version, we include the analysis of two anti-apoptotic proteins, Bcl-2 and Bcl-XL both are regulated NF-κB pathway.

Minor points:

All minor points were corrected

References


