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OPEN PEER REVIEW

Spironolactone Induces Apoptotic Cell Death in Human Glioblastoma U87-MG Cancer Cells

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1 Original submission

0 comments

No public comments in this round.

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Editor in chief of **International journal of cancer management**

Thanks for considering my manuscript in your journal. I would like also to thank the respected reviewer for their valuable comment. All the comments were revised and you can find the answers bellow. Also the revised version of manuscript was sent in highlighted format.

Sincerely

Dr Marie Saghaeian Jazi

Answer to Reviewer 1:
Spironolactone is used to treat tumor-associated complications in cancer patients. Spironolactone was recently reported to exert anti-cancer effects by suppressing DNA damage repair. Mineralocorticoid receptor signaling is anti-proliferative in GBM cells.

-Contrary to previous evidence obtained in other cancer types, othe Paula Aldaz results in 2021 suggest that spironolactone has no compelling anti-neoplastic potential in GBM. In this study the anti-cancer effect of spironolactone was reported without using in combination with other agents. It is suggested to compare these items in the discussion section.

Answer: thanks for you valuable comment. The reference was added (reference 16) and also a paragraph discussing the difference between our study and results reported by Paula Aldaz 2021 was added to the discussion.

"In contrast to previous studies, Aldaz et al. showed anti-proliferative effect for mineralocorticoid receptor activation by aldosterone in some glioblastoma cancer cell lines but no anti neoblastic effect of spironolactone was reported. However when comparing to our study, they used lower concentration of spironolactone (maximum 10 uM) and they used other glioblastoma cancer cells (T98G, U251, U373, SF188, A172, LN299) but the U87-MG cell line was not tested(16). Although Aldaz et al reported different role with proliferation enhancing for spironolactone as mineralocorticoid receptor antagonist in glioblastoma cancer cells but previous studies has shown that the mechanism related to the apoptosis induction by spironolactone in cancer cell is not through mineralocorticoid receptor antagonism (8). "

-According to the results of early or late apoptotic cells, why is the time of 24 hours not checked?

Answer: Regarding the doubling time of U87-MG (~39h, PubMed=9842975) we selected the 48 and 72 hours for treatment duration.

2 Revision 1

1 comment · 18 Sep 2022

Associate Editor

MINOR REVISION 18 Sep 2022

Dear authors,
Thank you for revising your manuscript according to the reviewer's comments. Please place the methods section before the results section in the manuscript body.

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Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear editor in chief of **international journal of cancer management**

Thanks for considering my manuscript and I am thankful for the helpful comments. I found the minor revision and revised my manuscript according your comments as bellow:

- The method section removed before the results and the heading numbers were revised accordingly
- The key words were checked in Mesh database and it was revised as the following:

Keywords: Spironolactone, glioblastoma, apoptosis, caspase, neoplasm

Sincerely

Dr MSJ

3 Revision 2

0 comments

No public comments in this round.