Author’s response to reviews

Title: Resveratrol enhances anticancer effects of paclitaxel in HepG2 human liver cancer cells

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Author’s response to reviews:

Dear editor

Thank you very much for your attention and the referee’s evaluation and comments on our manuscript. We have revised the manuscript according to your kind advices and referee’s detailed suggestions. We sincerely hope this manuscript will be finally acceptable to be published on your journal. Thank you very much for all your help and looking forward to hearing from you soon.

Sincerely yours

Prof. Qi Zhang
For Ewa Grzebyk, Dr (Reviewer 1):

Thank you very much for your attention and the referee’s evaluation and comments on our manuscript. We have revised the manuscript according to your kind advices. We have revised the manuscript as red letters.

No information on used measuring devices.

We have revised it in materials and methods section.

Figures 10 and 11 unreadable (too much presented data).

We have revised the Figures 7, 8, 9, 10, 11.

The Conclusion section in the Abstracts should be changed with an indication of the type of research (in vitro).

We have revised the conclusion section in the abstracts, the type of research was added.

For Raghavendra L Hallur, Ph.D (Reviewer 2):

Thank you very much for your attention and the referee’s evaluation and comments on our manuscript. We have revised the manuscript according to your kind advices. We have revised the manuscript as red letters.

1. Maintenance of the cell culture shall be included

We have added the cells culture in the method section in line 130-134.

2. Author shall explain the overall mechanism of Resvestrol with paclitaxel and how it will enhance the activity?

We have revised the overall mechanism in line 396-398.
For Alessandro Di Cerbo, PhD (Reviewer 3):

Thank you very much for your attention and the referee’s evaluation and comments on our manuscript. We have revised the manuscript according to your kind advices. We have revised the manuscript as red letters.

- there are some typing and grammar errors throughout the manuscript that should be revised. The manuscript should be revised by a native English speaker.

We have revised the grammar errors.


We have added these references.

- I have few concerns regarding the statistical analysis chosen by the authors:

1) I'm wondering if the data of each group really follow a Gaussian distribution. If so the better post hoc test would be Dunnett, Bonferroni or Sidak rather Duncan's.

2) Conversely, if the data of each group really wouldn't follow a Gaussian distribution the suitable statistical test would be a Kruskal-Wallis test with a Dunn's multiple comparison test.

So the authors should better clarify the presence of a Gaussian distribution or not and chose the suitable test.

We have revised the statistical analysis using Dunnett method.
For Siwen Chen (Reviewer 4): 1.

Thank you very much for your attention and the referee’s evaluation and comments on our manuscript. We have revised the manuscript according to your kind advices. We have revised the manuscript as red letters.

The text itself contains various grammatical errors, extensively long sentences, confusing statements and disorganisation. A native English speaker should review the document to ensure this is remedied. We only point out few of these mistakes below.

We have revised the grammar errors.

2. Wrong English tenses: In the introduction, "Clinical trials revealed that paclitaxel can treat other diseases to some extent……", the tenses of "revealed" and "can" are different. "In-depth research found that resveratrol can enhance the sensitizing effect of prostate cancer cell line PC-3 in vitro", the tenses of "found" and "can" are different. There are many mistakes like this in the text.

We have revised these mistakes in line 96.

3. In the introduction: "These cancer inhibitors that occur naturally are more safer as having low toxicity……", the expression of "more safer" is wrong.

We have revised the mistake in line 108.

4. For the first time, abbreviations should be accompanied by full names. Such as "Hp", "NF-κB", "CDK" and "ECM" in the discussion. If the word appears only once, do not enclose an abbreviation, such as "tumor infiltrating T lymphocytes (TIL)" in the discussion.

We have added the full names.

5. Some citation formats are wrong, such as "Wong found that a lot of receptor-mediated cell signal transduction……[13]", the citation format should be stated as follows "Wong [13] found that a lot of receptor-mediated cell signal transduction……"

We have revised these mistakes in line 267, 332.
6. In the materials and methods, please confirm that the cell lines are from Kunming in Guangxi? The cell lines were purchased from Conservation Genetics CAS Kunming Cell Bank in Kunming City, Guangxi Province, China.

7. Academic papers should use professional vocabulary. In the background, it is more appropriate to use "proliferation" and "apoptosis" instead of "cell replication" and "die naturally". We have revised these words in line 80 and 83-85.

8. In the background, "In this paper, we study the effects of paclitaxel combined with resveratrol, to reduce the concentration of toxicity and side effects of paclitaxel, Meanwhile observe their joint anticancer effects.", what is the "concentration of toxicity"? Have they observed "side effects of paclitaxel" in cell lines? We have revised this sentence in line 121.

9. In the discussion, "their ratio determines whether the cell is able to accept the apoptotic signal", the correct sentence maybe "heir ratio determines whether the cell is able to accept the apoptotic signal or not". We have revised this sentence in line 284.

10. Some expressions can cause ambiguity. Such as "The 10 ug/mL of Res had no effect on Nthy-ori 3-1 normal cells……", which effect do they mean? In this paper, they only determined the effect of Res on proliferation, apoptosis, and so on. They should be clearly stated. It is growth inhibitory effect, we have revised these sentences in line 32-34.

11. The methods in the abstract is too simple. They only list the methods used, they should point out what these methods are for. We have revised this section in abstract in line 28-31.
12. In the figure legends of Figure 3 to Figure 11, the letters "a", "b", "c", and "d" above the bar were stated as the mean values, but I don't know why the values were not numerical value but the letters? Do they mean the same letter represent the same numerical value?

The letter were not mean values, the different means the values in different group are significant difference, the same different group are no significant difference, we have marked this explanation in the figure legends

13. In the figure legends of Figure 1 and Figure 2, they have not stated the meaning of the letters "A" and "B", please state it.

We have added the letters in Figure 1 and Figure 2.

14. In MTT assay in the materials and methods and in Figure 1, do they only perform the test once?

The experiment were done by 8 wells for one concentration in 96 well once, and repeated three time.

15. The discussion should be rewrite. They only showed the research progress of the gene or protein they had determined. They should discuss their own results.

We have revised the discussion section.

16. The conclusion section should be rewrite. In this paper, the conclusion was written as the abstract. They should conclude the possible therapeutic mechanisms of the combination of Res and PA.

We have revised the conclusion section.