Author’s response to reviews

Title: Survivin selective inhibitor YM155 induce apoptosis in SK-NEP-1 Wilms tumor cells

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Author’s response to reviews:

Dear Editor,

Thank you for your review of our manuscript (MS: 7840940867960173 Survivin selective inhibitor YM155 induce apoptosis in SK-NEP-1 Wilms tumor cells). We appreciate the concerns and suggestions provided by the reviewers, and we have revised our manuscript accordingly. Our point-by-point responses are provided below, and text that has been added or modified from the original text is shown in the revised manuscript in yellow font. We know that your journal has high publication standards, so we have already had the language of this paper corrected by a professional language editing service that specializes in scientific manuscripts.

Upon review of our revised manuscript, we hope that you will find it acceptable for publication in BMC cancer and we look forward to your response.

Sincerely,

Pan Jian, PhD.

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Reviewer’s report: 1

The manuscript entitled “Survivin selective inhibitor YM155 induce apoptosis in SK-NEP-1 Wilms tumor cells” by Dr. Pan et al. studied the antitumor activity of YM155, an inhibitor of survivin, on SK-NEP-1 Wilms tumor cells, and analyzed the differential gene expression profile in YM155 treated or control cells by using Real-time PCR array. The data suggested that Y155 treatment could inhibit cell proliferation, induce apoptosis and decrease cell growth in vivo. This study is well designed, the charts and tables are clear and the conclusion is reasonable. This article can be accepted with minor revision. Here are the comments:

Minor Essential Revisions
1. In Figure 2A and 2B, there is no statistical analysis on both of the apoptosis and cell cycle data.

Following the suggesting, we added the statistical analysis on both of the apoptosis and cell cycle data. The analysis data can be found in the results section.

Discretionary Revisions
1. Why only Sk-NEP-1 cells were selected as the target cells of YM155? Did the author ever test the response of other Wilms tumor cell lines to YM155?

Only SK-NEP-1 cell line was used is because there are only two Wilms tumor cell lines can be purchased from ATCC,SK-NEP-1 and G-401. We purchased SK-NEP-1 from ATCC. We also trying to purchase the G-401, but never succeed. We are now trying to separate the primary tumor cells from the sample of pediatric Wilms tumor, and one day I hope we will establish another cell line of Wilms tumor. Next we will test the response of primary Wilms tumor cells to YM155.

2. In table 1 and 2, some genes were shown to be differentially expressed between the untreated and treated groups with YM155 by using Real-time PCR array. Is there any validation experiment that has been done? The author could consider working on some of the dys-regulated genes in their future study.

Thanks for the suggestion, we are now analyzing the differentially expressed genes with western-blot, and our analysis indicates that there is relationship
between auto phage and YM155 in SK-NEP-1 cells, we are working on this molecular mechanism.

Reviewer's report: 2

This study demonstrated YM155, a survivin suppressant, inhibited the growth and induced the apoptosis of SK-NEP-1 cells in vitro and in vivo. So far there are some studies exploring the role of YM155 in cancer therapeutics. And a phase II study in patients with refractory large B-cell lymphoma showed YM155 was well tolerated but with limited single-agent activity. These studies mainly tried to explain the growth inhibition and apoptosis effects induced by YM155 through certain molecules or pathways. In this respect, I consider this study valuable cause it employed Real-time PCR array to show the expression profile of genes regulated after YM155 treatment, and Ingenuity pathway analysis (IPA) represents new potential targets of YM155. YM155 showed very good anti-tumor effects in Wilms tumor cell lines, SK-NEP-1 cells, like in many other types of tumors. This shows YM155 could be a potential pan-antitumor reagent. Overall I think the study is well designed and the results are presented generally well. But some spellings should be corrected to make it more readable.

Minor revisions:

1. The background in Abstract is repeated described: survivin is described twice as a member of inhibitor of apoptosis protein family.

Following the suggesting, we have formatted our abstract, we have already had the language of this paper corrected by a professional language editing service that specializes in scientific manuscripts.

2. In background, paragraph 2 -line 6: survivin promoter activity should be strongly "activated", but not "expressed" in tumor cells#

Following the suggesting, we have corrected the background section, we have already had the language of this paper corrected by a professional language editing service that specializes in scientific manuscripts.

3. In methods describing “Xenograft assays the treatment effect of YM155 in nude mice”: 10 days after injection, mice were “treated” with PBS… not treatment

Following the suggesting, we have corrected the methods section, and we have already had the language of this paper corrected by a professional language editing service that specializes in scientific manuscripts.