Author's response to reviews

Title: miR-17-5p targets the p300/CBP-associated factor and modulates androgen receptor transcriptional activity in cultured prostate cancer cells

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Author's response to reviews: see over
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The Editor
BMC Cancer

Dear Editor:

Thank you for your letter of August 20, 2012, regarding our manuscript (1984867920629801), entitled “The p300/CBP-associated factor modulates androgen receptor-regulated transcriptional activity and cellular growth in cultured prostate cancer cells.” We were pleased that the reviewers found that our findings “are important to those with closely related research interests” and “an article of importance in its field.” We very much valued your suggestions and those of the reviewers, and appreciate the opportunity to provide you with a revised manuscript for consideration for publication in BMC Cancer.

We believe that we have adequately responded to all the concerns that were raised. Specifically, per suggestions from the reviewers, we have deleted the IHC data and modified the text on expression of miR-17 in vitro and in vivo in the revised manuscript. We have also re-examined the effects of PCAF siRNA on DHT-induced PSA luciferase activity and added new data on miR-17-associated AR signaling in other cell lines (i.e. C4-2B cells).

For ease of review, the revised portions in the manuscript are highlighted in blue. Enclosed please also find a copy of point-by-point responses to the reviewers’ comments. We believe that the manuscript is considerably stronger thanks to the quality of the review. We hope you agree.

Sincerely,

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POINT-BY-POINT RESPONSES TO THE REVIEWERS' COMMENTS

We thank all the reviewers for your positive comments on our manuscript. We appreciate your thoughtful review and have attempted to satisfactorily respond to your concerns and suggestions.

Responses to comments from Reviewer #1

1). The inconsistency in the expression profile of miR-17 between in vivo and in vitro attenuates the importance of this microRNA in prostate cancer, in particular the conclusion that “miR-17-5p could be a target for therapeutic intervention” is questionable. We agree with you that the inconsistency in the expression profile of miR-17 between in vivo and in vitro attenuates the importance of this miRNA in prostate cancer. Accordingly, we have modified the text and deleted the statement of “miR-17-5p could be a target for therapeutic intervention” in the revised manuscript.

2). In Figure 2D, authors stated that knockdown of PCAF by the PCAF siRNA partially abolished DHT-induced PSA luciferase activity. However, it seems that treatment of PCAF siRNA almost abolished all DHT-induced PSA luciferase activity, which needs to be re-examined. Per your suggestion, we have re-examined the effects of PCAF siRNA on DHT-induced PSA luciferase activity. We have revised the text and included the new data in the manuscript (new figure 2D).

3). Since the level of miR17 is low in LNCaP cells (Fig 3C), it seems inadequate to use this cell model to study effects of anti-miR-17 on AR signaling. We want to thank you for pointing out this issue. We agree that cells expressing a higher level of miR-17 are more adequate for the anti-miR experiment. Moreover, cells need to be responsive to AR. We do have data on the effects of anti-miR-17 on AR signaling in C4-2B cells which express a higher level of miR-17 than LNCaP cells (figure 3C). Data with C4-2B cells continue to support our findings in LNCaP cells and thus, have been included in the revised manuscript (new Figure 4E and 4F).

Responses to comments from Reviewer #2

1). There is still insufficient detail to reproduce the IHC in this manuscript. Secondary and tertiary Ab information, antigen retrieval method and primary Ab incubation times should all be stated. Alternatively the IHC should be removed as it is very poor. There is a very high level of background. PCAF should be in the nucleus and it just appears to be everywhere. I doubt very much that the Ab is binding to PCAF in FFPE tissue. For the IHC to remain proper specificity controls must be completed: FFPE cell pellets of overexpression and knock-down cells showing almost complete loss of staining in the knockdown. Per you suggestion, we have deleted the IHC data from the manuscript.