Author's response to reviews

Title: Therapeutic effects of STAT3 decoy oligodeoxynucleotide on human lung cancer in xenograft

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Author's response to reviews:

July 11, 2007

Melissa Norton, MD
Editor-in-Chief, BMC Cancer
BioMed Central Ltd,
Middlesex House,
34-42 Cleveland Street,
London W1T 4LB, UK.

Dear Dr. Norton,

Thank you very much for your response and reviewers' comments to our manuscript (MS number 3170052101292317) entitled "Therapeutic effects of STAT3-decoy oligodeoxynucleotide on human lung cancer in xenograft mice ."

We are pleased with the overall opinion and comments of three Reviewers and feel confident that we have successfully addressed the concerns made by the reviewer (Dr. Brent Cochran). To ensure no duplicate figures from our recent publication (Oncol Rep 2007, Jun;17(6):1377-82), we just cited this publication as a reference29 in the text. Furthermore, we accordingly corrected the errors and typos in the manuscript.

Enclosed pleased find the responses to reviewers' comments point by point and the final revised version of the manuscript and figures. We hope this version is now suitable for publication in BMC Cancer.
Sincerely,

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Responses to Reviewers' Comments

Manuscript number: 3170052101292317

First, we would like to thank the reviewers for their time and effort spent evaluating our manuscript. We feel these revised changes have significantly improved the quality of our manuscript.

Reviewer#1.
No major comment

Reviewer#2.
No major comment

Reviewer#3. Dr. Brent Cochran

1. It is still not clear what the relative contributions of apoptosis vs reduced proliferation are to the growth inhibition observed in the lung cancer cells. They have added new data on thymidine incorporation, but cells that are dead or undergoing apoptosis will also show reduced thymidine incorporation compared with control cells just as well as cells that are stuck in G0/G1. Is the cell cycle profile of living STAT3 ODN treated cells different from scramble ODN treated cells after annexin V stained cells are excluded? This is likely the case, but the authors haven't demonstrated this. If they can't show this, then they should soften their conclusions with regard to effects on proliferation.

Thanks for reviewer making the valid point. We added this into the discussion section and accordingly rewrote the conclusions with regard to effects on proliferation (Page 11) as following:
"Given cells that are dead or undergoing apoptosis may also show reduced thymidine incorporation compared with control cells just as well as cells that are stuck in G0/G1, further study are necessary to clarify what the relative contributions of apoptosis vs. reduced proliferation are to the growth inhibition observed in the lung cancer cells" (Page 11).

"In summary, we have provided evidence that STAT3 decoy ODN suppresses growth of lung cancer cells in vitro and in vivo through affecting the balance between cell proliferation and rate of apoptosis." (Page 11)

2. On page 9 they state that their data on the decrease of cyclin D1 and bcl-xl expression demonstrate that this is how the effect on proliferation is mediated. This is correlative data and thus this conclusion is too strongly stated. They should change these data demonstrate to these data suggest that...

To address this important point, we accordingly corrected this in Conclusion as the following:

"In summary, we have provided evidence that STAT3 decoy ODN suppresses growth of lung cancer cells in vitro and in vivo through affecting the balance between cell proliferation and rate of apoptosis. This inhibitory effect may be correlated to blockade of STAT3-regulated cell cycle genes or anti-apoptotic genes" (Page 11-12).

3. The grammar and awkward word usage continue to be a problem with this paper. There are eight errors of various sorts in the abstract alone. There are also typos and misspellings. Since I don't think BMC Cancer copy edits papers prior to publication, the authors should send this paper to any of the numerous online editing services such as http://www.bioedit.com prior to publication.

We carefully corrected the errors and typos in the manuscript. In addition, we invited Dr. Xiao Yi Yang at NCI/NIH to critically review this paper.