Author's response to reviews

Title: Regulation of p14ARF expression by miR-24: a potential mechanism compromising the p53 response during retinoblastoma development

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Author's response to reviews: see over
January 10, 2012

Christna Chap, PhD
Executive Editor
BMC Cancer
London, UK

Re: Revised manuscript submission

MS: 1078267248536045
miR-24 contributes to retinoblastoma development by compromising the p53 response to RB1 loss in retina
Kwong-Him To, Sanja Pajovic, Brenda L. Gallie, and Brigitte L. Thériault.

Dear Dr. Chap,

Thank you for considering our important submission for publication. We thank Reviewer 1 for the review of our revised manuscript. We have carefully considered the comments and suggestions from Reviewer 1, and incorporated the specific suggestions into a third revised manuscript.

We detail the exact changes to this manuscript based on the comments from Reviewer 1:

**Reviewer 1:**

*Comment 1:* Figure 4 displays miR-24 levels in four primary retinoblastomas. Two of the four primaries had relatively low miR-24 expression, raising the possibility that high miR-24 levels might be acquired by some tumors (especially those established in culture) but not by others. Additional perspective may be provided by addressing the implication of these “low miR-24 samples in the results or discussion section.

We acknowledge the presence of low miR-24 retinoblastoma tumors in the results section, page 13: “All RB1+/− cell lines, in addition to two out of the 4 primary RB1+/− retinoblastomas (RB 2133 and RB 2362) demonstrated higher miR-24 expression than the RB1+/+ cell lines (Figure 4A).” We also address the implications of “low miR-24” retinoblastoma tumors in the discussion section, page 15: “Some RB1+/− primary tumors showed low miR-24 expression, comparable to RB1+/+ cell lines. These “low miR-24” RB1+/− tumors raise the possibility that the level of miR-24 expression may be insufficient to compromise the p53 response in some retinoblastoma tumors. However other factors besides expression, such as components of the RISC complex, may influence the effect of miR-24 activity in retinoblastoma cells.”
Comment 2: $RB^{+/+}$ retinoblastoma cell lines are cited as “manuscript in preparation”. As $RB^{+/+}$ retinoblastoma is unexpected and potentially controversial, a short additional description of the cells could help to provide insight into their status as a novel retinoblastoma type.

We provide a short additional description of this novel cell type in the results section, page 11: “These $RB1^{+/+}$ retinoblastomas show no detectable mutations in the $RB1$ gene and express full-length pRb protein”. We also provide reference to an abstract presented and published online at the American Society for Human Genetics 2011 Annual Meeting (numbered 16).

Comment 3: The title of the paper may be revised to reflect the still uncertain role of miR-24 in retinoblastoma development in vivo.

We have revised the title to reflect the role of miR-24 in retinoblastoma development: “Regulation of $p14^{ARF}$ expression by miR-24: a potential mechanism compromising the p53 response during retinoblastoma development.”

We have appropriately addressed the comments of Reviewer 1, and made the necessary changes to the manuscript. We thank reviewer 1 for his input.

Thank you for considering this manuscript for publication in BMC Cancer.

With kindest regards,

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