Author's response to reviews

Title: MicroRNA-645, Up-regulated in Human Adencarcinoma of Gastric Esophageal Junction, Inhibits Apoptosis by Targeting Tumor Suppressor IFIT2

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Version: 2 Date: 27 November 2013

Author's response to reviews: see over
TO: Paolo Bruzzi  
Editor-in-Chief of BMC cancer  
National Cancer Research Institute, Italy  

Dear Paolo Bruzzi,

**According to the instructions of editors, we have made several changes in the manuscript as below:**

1. We have added the ‘Competing interests’ section after the “Abbreviations”.
2. We have moved the Abbreviations, Author’s Contribution and Acknowledgement section after Discussion.

On behalf of my co-authors, I am submitting the enclosed material “MicroRNA-645, Up-regulated in Human Adenocarcinoma of gastric esophageal junction, Inhibits Apoptosis by Targeting Tumor Suppressor IFIT2.” for possible publication in BMC cancer. Neither the entire paper nor any part of its content has been published or has been accepted elsewhere. It is not being submitted to any other journal.

An increasing body of evidence indicates that miRNAs have a critical role in carcinogenesis and cancer progression; however, the role of miRNAs in the tumorigenesis of adenocarcinoma of gastric esophageal junction (AGEJ) remains largely unclear. In the present study, we have reported an increased expression of miR-645 in AGEJ clinical specimens compared with paired non-cancerous tissues. We also observed a significant miR-645 up-regulation in two gastric cancer (GC) cell lines, SGC-7901 and BGC-823, which were used as cell models because there was no available AGEJ cell lines established to date. We found that inhibition of miR-645 could sensitize dramatically SGC-7901 and BGC-823 cells to both serum starvation - and chemotherapeutic drug - induced apoptosis by up-regulating IFIT2, a mediator of apoptosis via a mitochondrial pathway, with a potential binding site for miR-645 in its mRNA’s 3’UTR. Further investigation exhibited that IFIT2 expression decreases in SGC-7901 and BGC-823 cells and AGEJ tissues. IFIT2 ectopic expression leads to promotion of cell apoptosis, indicating that IFIT2 may function as a suppressor in the development of AGEJ. Furthermore, inhibition of miR-645
induces up-regulation of IFIT2 and increased caspase-3/7 activity compared with control groups. In summary, our data suggest that miR-645 functions as an oncogene in human AGEJ by, at least partially through, targeting IFIT2.

*Our findings for the first time illustrate the role of miR-645 in the carcinogenesis of adenocarcinoma of gastric esophageal junction, suggesting that miR-645 may inhibits apoptosis by targeting tumor suppressor IFIT2 in AGEJ.*

We believe the paper would be of broad interest to the readers of your journal. Thank you very much for your considering our manuscript for potential publication. I'm looking forward to hearing from you soon.

Best wishes,
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