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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Author's response to reviews:

Reviewer's report

Title: MicroRNA-645, Up-regulated in Human Adencarcinoma of Gastric Esophageal Junction, Inhibits Apoptosis by Targeting Tumor Suppressor IFIT2
Version: 2 Date: 9 December 2013
Reviewer: Young Jung

Reviewer's report:

In this study, authors demonstrate that mir-645 results in increasing apoptosis by targeting Tumor Suppressor IFIT2 in Human Adencarcinoma of Gastric Esophageal Junction. This study is certainly of value for its subject and the information may be important for other investigators in the field. The experimental plan is clearly executed and there are some flaws. And, there are minor points that need to be considered before final acceptance for publication.

To the reviewer:

Thank you very much for your nice suggestions to help us improving the quality of our manuscript. Just as you instructed, we have modified all the points that are not very proper for publication and we really appreciate your valuable time and help. May you enjoy every nice day!

Major

# They make title and explained the role of mir-645 and IFIT2 in the
Adencarcinoma of Gastric Esophageal Junction (AGEJ) tumor but use the gastric cancer cells in vitro. Exploring the role of mir-645 and IFIT2 expression in gastric cancer rather than in AGEJ to be recommended.

Response:
In our study, the role of miR-645 and IFIT2 in the tumorigenesis of AGEJ were examined in two gastric cancer (GC) cell lines, SGC7901 and BGC-823, which were used as cell models because there was no available AGEJ cell lines established to date. Of course, this is not that proper to use GC cell lines substitute AGEJ cell and we also feel very distressing when we had to do so. Even so, we still used 6 GC cellines such as SGC7901, MKN 45, MKN28, AGS, BGC-823, GC9811 to examine the expression of miR-645 and IFIT2 and finally chose SGC7901 and BGC-823 as cell models because the expression of miR-645 and IFIT2 are consistent with that of miR-645 and IFIT2 in AGEJ.

In Fig 1 –Table 1 showed the expression of miR-645 in AGEJ and paired non-cancerous tissues. Because of the idiomatic expression for AGEJ, we used “gastric cardiac adenocarcinoma”, hence, in order to avoid confusion, we used substituted “gastric cardiac adenocarcinoma” with “AGEJ”. (modified table 1 are listed below)

# 2. IFIT expression is dependent on mir-645 in the pattern of linear equations (Fig4 A and E), I wonder that IFIT2 expression is regulated by only one factor, mir-645.

Response:
This question is of great interest. It is possible that IFIT2 is regulated by many factors including miR-645. In this study, reasons of expression level of IFIT2 regulated by miR-645 was studied are as follows: first, bioinformatics analysis showed that IFIT2 is a potential target miR-645; then luciferase reporter assay showed that IFIT2 was regulated by miR-645; and the expression of IFIT2 and miR-645 were negative correlated in AGEJ tissues which further demonstrated that IFIT2 was a target of miR-645. Certainly, there maybe other factors which could regulate the IFIT2 expression, however, they were not studied here because they are beyond the research scope of this manuscript.

# 3. AGEJ tumors were made 2 groups by tumor size (>5 or <5 centimeter). What is the logic to make group by 5 centimeter.

Response:
The tumor size is a key factor for evaluation of clinical stage purpose. According to the criteria of esophageal clinical pathological stage of China, tumors with size >5 centimeter are classified into # stage. Here we adopted this criteria to mark AGEJ patients of ## or ### stage.

Minor
1. In Fig. 4 D b, the +SEM is missing
   Response:
   “+SEM” has been added.
2. Page 8, 1st line from bottom, the reference is missing
   Response:
   There is not ought to be the “[]” and “[]” has been deleted.
3. The full name of IFIT is appeared in the 1st using.
   Response:
   IFIT2 is the abbreviation of “Interferon-induced protein with tetratricopeptide repeats 2” and this full name has been showed when 1ST used (in the PAGE 2, abstract paragraph).