September 11, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 3893-review.doc).

Title: microRNA-143 suppresses gastric cancer cell growth and induces apoptosis by targeting COX-2

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 3893

The manuscript has been improved according to the suggestions of reviewers:
1 Format has been updated.

2 Revision has been made according to the suggestions of the reviewer:

(1) In the abstract section, the transfection with miR-145-5p in gastric cancer resulted in a greater growth inhibitory effect and a higher apoptosis rate than that with miR-143-3p; Mutation in the binding site of miR-145-5p completely ablated the regulatory effect. Please reconfirm the word with underline.
Reply: What we mean is: Mutation in the binding site of miR-145-5p completely ablated the regulatory effect on luciferase activity, which suggests a direct binding site of miR-145-5p in 3'-UTR of COX-2. I revised the sentence to make it clear.

(2) Why authors did not search miR-143-5p target genes by using miR target prediction programs?
Reply: Actually we used several different programs to search miR-143-5p target genes. The programs include: RNA22, DIANA-MICROT, MICRORNA.ORG, MIRDB and PICTAR-VERT. We got a big number of target genes include COX-2. After preliminary experiment, we focused on COX-2. Since RNA22 is the only program that predicts folding energy of corresponding RNA/RNA complexes, we only mentioned this program in our paper.

(3) Figure 1 showed that by Western blot the expression of COX-2 protein was increased in the five human gastric cancer cell lines, which was inversely correlated with miR-143 level. Which one was compared to the five human gastric cancer cell lines regarding the increased COX-2 protein?
Reply: the expression of COX-2 protein in the five human gastric cancer cell lines was compared to the normal gastric epithelium cell line GES-1.

(4) Hsa-miR-143-3p or miRNA mimic control was transfected using Lipofectamine. Is it a stable transfection of transient transfection?
Reply: It's a transient transfection, which showed significant tumor suppressive effect of miR-143. In further study, we will construct stable transfected cell lines and perform in vivo study to discuss the effectiveness and safety of miR-143.

(5) In the Results section, a paragraph of "This is consistent with reports from other research groups [22, 23]", of which should be moved to the Discussion section.
Reply: This paragraph has been moved to the discussion section.

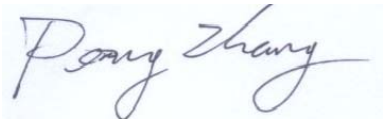
(6) Figure Legends must be separate and in another paragraph.
Reply: Figure Legends has been separated in another paragraph

(7) Why not compare the miR-143 expression in clinical samples between non-cancerous tissues and cancer tissues?
Reply: In a recent report, the authors used real time RT-PCR and chip assay analyzing 70 paired samples of gastric cancers and benign tissues (reference 23). They found that miR-143 is significantly down-regulated in gastric cancer when compared with benign tissue and is associated with progression of gastric cancer. So, in our study, we didn't repeat this part of work.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,



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