ANSWERING REVIEWERS

July 2, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 3929-review.doc).

Title: Interaction between COX-2, Snail, and E-Cadherin in gastric cancer cells

Author: Xiaojun Liu, Zhaofeng Chen, Hailong Li, Zenan Hu, Min Liu, Aiping Tian, Da Zhao, Jing Wu, Yongning Zhou, Liang Qiao

Name of Journal: *World Journal of Gastroenterology*

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The manuscript has been improved according to the suggestions of reviewers:

1. Reviewer 1 (02523299):

Comment 1.1. I found some of the dialogue slightly confusing, however.

Answer 1.1. The regulatory mechanisms between COX-2 and NF-κB were heterogeneous in different cancer cell lines. Therefore, some of the conclusion was inconsistent in our discussion part. Our data suggested that COX-2 may function upstream E-cadherin pathways in SGC-7901 cells, in which COX-2 was high expressed.

Comment 1.2. Table 1+2 are of no relevance to the reader and could be removed.

Answer 1.2. Table 1 and Table 2 showed the sequences of siRNAs and primers for RNAi and qPCR, respectively. These nucleotide sequences may provide useful information for readers, and we believe they are worthwhile to keep.

Comment 1.3. Figures 1, 2+3 could be more polished and user friendly. They do not reproduce well.

Answer 1.3. These figures have been modified for better presentation.

2. Reviewer 2 (02461125):

Comment 2.1. Although the detailed experiments and data may vary significantly, the purpose and conclusion of this study is very similar to the corresponding author's published results (Chen et al. Int J Mol Med, 2013; 32:93-100). Authors should address the major difference between the two studies.

Answer 2.1. The authors research team has been focused on the role COX-2 in the development of gastric cancer, and the underlying molecular mechanisms. Both papers were accomplished by same study group. The former paper used Celecoxib to block the activity of COX-2 whereas the current study adopted a RNAi based approach to further explore the regulatory mechanism of COX-2 on E-cadherin in gastric cancer cells. The paper by Chen et al (Int J Mol Med, 2013; 32:93-100) has been cited in the current work (reference 12).

Comment 2.2. Fig. 3 contains data which may be inconsistent with the suggested Cox-2/PGE2/NF-κB/Snail/E-cadherin pathway. For example, given that NF-κB acts downstream of PGE2, when comparing lane 5 with lanes 3 and 1, decreased Snail and upregulated E-cadherin are anticipated; when comparing lane 3 with lane 1, Snail should be increased while E-cadherin should be down-regulated. Neither of these alterations was actually observed in Fig. 3.

Answer 2.2. We completely agree with this reviewer. Another figure has been uploaded, in which the difference between each groups is displayed more clearly.

Comment 2.3. In addition, "scramble siRNA" is not a definitive label

Answer 2.3. In revised manuscript, "scramble siRNA" was replaced with "control siRNA" in relevant figures.

Comment 2.4. "PEG2" should be "PGE2".

Answer 2.4. We apologize for this mistake. It has been corrected.

Comment 2.5. Statistical analysis should be performed from Fig. 1 to Fig. 3.

Answer 2.5. A * has been added on qPCR data in Figs. 1 to 3 to indicate the statistic significance. The differences in Western blot bands was so obvious that a statistic mark may not be necessary. In addition, data for the statistic analysis were showed in main body of manuscript.

Comments 2.6. It is unnecessary to present the sequences of each of the 2 strands of siRNA which are completely complementary.

Answer 2.6. Please refer to the Answer 1.2.

The authors are grateful to the reviewers and editors for handling our manuscript and considering publishing our work in the *World Journal of Gastroenterology*.

Sincerely yours,

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