



January 22, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6974-Review.doc).

**Title:** Proteomic Identification of Tumor Biomarkers Associated with Primary Gallbladder Cancer

**Author:** Hailin Huang, Houshan Yao, Yi Wang, Weijun Wang, Zhiqian Hu, Kaizhou Jin

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 6974

Thank you for giving us the opportunity to revise our manuscript. We greatly appreciate the reviewers for their thoughtful and insightful comments. We have carefully reviewed all the comments and suggestions from the reviewers. Our point-by-point responses are listed below. Changes made to the original manuscript are indicated by underlining.

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:

**Review number (00058419)**

*(1) However, the study, as currently designed and executed, is likely to identify potential biomarkers for PGC, not the biomarkers for the cancer development and progress as stated by the authors in the manuscript (Aim).*

**Our response:** We are sorry for the inappropriate statement of Aim in the manuscript, and it has been replaced with "To identify potential biomarkers for primary gallbladder cancer (PGC)" as suggested by the reviewer (page 2, line 2).

*(2) "Moreover, I believe that the claim in Core Tip "the first comparative proteomic study to use human PGC, cholecystitis and normal gallbladder tissues" is overstated since a similar approach was employed by Tan and colleagues (Proteomic study of gallbladder cancer, with special reference on the expression and significance of annexin A3. Zhonghua Bing Li XueZaZhi. 2010 Jun;39(6):382-6). Those overstatements should be corrected to more accurately reflect the contribution of this important piece of work. It appears that the authors missed the above paper in which Tan et al. have identified annexin A3 as the potential biomarker for PGC using a similar approach. Therefore, it will be important for the authors to discuss the findings in this manuscript and those of Tan et al.*

**Our response:** We sincerely appreciate the reviewer's thoughtful suggestions. And we are really sorry for having missed the publication of Tan et al. The claim has been corrected in Core Tip (page 3, line 4) and the findings of Tan et al. have been discussed in the revised manuscript (page 11, lines 1-5 and page 11, lines 16).

*(3) Fig. 1 The marks for 7 proteins of interests were difficult to see in my copy of the manuscript.*

**Our response:** We are sorry for the carelessness of the quality of Fig. 1, and we have added clear marks of Fig. 1 in our revised figures.

**Review number (02519865)**

*This is quite novel finding about GB cancer using proteomic approach and authors found three biomarkers of the GB cancer. Although the method was very scientific and accurate, the limited patients number doubt the conclusion of this research. Further validation using more samples are warranted for future clinical use, and also functional validation will needed.*

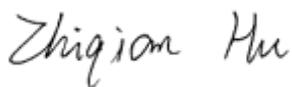
**Our response:** The reviewer raised a very good point here, and we appreciate the reviewer's encouraging comments and thoughtful suggestions. It is true that the patients number was limited for the novel finding about GB cancer, but we had tried our best to collect the limited samples in our previous study. To get more scientific and accurate conclusion, we will absolutely collect more samples and validate the expression and function of potential biomarkers of the GB cancer in the future clinical use.

3 References and typesetting were corrected

We believe that our revisions have significantly improved our manuscript and hope that it is now acceptable for publication in *World Journal of Gastroenterology*.

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

Sincerely yours,



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