ANSWERING REVIEWERS

June 16, 2018

Dear Editor and Reviewers,

Please find enclosed the edited manuscript in Word format (MS. 39864).

Title: **Abnormal Expression of HMGB-3 Significantly Associated with Malignant Transformation of Hepatocytes**

Author: **Wen-Jie Zheng, Min Yao, Miao Fang, Li Wang, Zhi-Zhen Dong, and Deng-Fu Yao**

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

We are truly grateful to your comments concerning our manuscript **MS. 39864**. We also appreciate the reviewers' careful and thoughtful suggestions, since the comments are all valuable and helpful for improving our paper. We have studied comments and made modifications according to the reviewers' comments.

Reviewer 1 comments: The authors investigated the dynamic HMGB3 expression in hepatocarcinogenesis, bioinformatics databases, HCC cell lines, and xenograft model, and to validate HMGB3 as a diagnostic marker or novel target gene for HCC. They HMGB3 mRNA levels were correlated with cell cycle and DNA replication pathways. Knockdown HMGB3 by specific shRNA significantly inhibited proliferation of HepG2 cells with cell cycle arrest, downregulating DNA replication related genes at mRNA or protein level. Furthermore, silencing HMGB3 significantly inhibited xenograft tumor growth with Ki67 reduction in vivo. The authors concluded that HMGB3 involved in malignant transformation of hepatocytes could serve as a useful biomarker for diagnosis and potential target therapy of liver cancer. The results reported in this paper and the conclusions drawn will contribute significantly to this field.

Thanks to Reviewer 1 for your very kindly comments.

Reviewer 2 comments: While HMGB3's possible role as tumor markers has been found in several malignancy, this study is the first to demonstrate the possible role for carcinogenesis in liver tumor. Authors have carried out excellent experiment in vitro and in vivo and demonstrated the possibility of HMGB3 to be utilized as the biomarker for liver cancer, especially in the process of tumorigenesis. They are commended for their remarkable work. It hoped that their findings can soon be utilized as a tumor marker in the clinical setting. A minor typo, RPMI 1640 (not RIPM 1640)

Thanks to Reviewer 2 for your very kindly comments and the mistake has been corrected.

Thank you again for publishing our manuscript in the ***WJG***.

Sincerely yours,

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