



The First People's Hospital of Changzhou & The Third Affiliated Hospital of Soochow University

No.185, Juqian Street, Changzhou, Jiangsu 213003, China

January 25, 2019

Editor, World Journal of Gastroenterology

Response to Reviewer #1

1. It is a well written and documented study.

- Thank you for your support and recognition of our study.

Response to Reviewer #2

1. At the light of the following studies, focusing on the main role of genetic and epigenetic control of metabolism and the key role played by metabolic syndrome in inducing HCC, authors are kindly requested to deepen this aspect in the context of recent data of literature. (doi: 10.1016/j.molmet.2013.09.002 and doi: 10.3748/wjg.v20.i28.9217)

- Thank you for your constructive comments. According to your suggestion, epigenetic mechanisms such as DNA methylation is associated with metabolic diseases which are the main risk factors of HCC. Thus, we speculate that the methylation level of NFE2L3 gene may be involved in hepatocarcinogenesis. We have supplemented and cited these two literature **in the first paragraph of the discussion.**

We hope that the revised manuscript has improved substantially and it is now suitable for the publication in World Journal of Gastroenterology.

Thank you very much for your kind reconsiderations,

Sincerely yours,

Guanghua Luo

Comprehensive Laboratory

The Third Affiliated Hospital of Soochow University,

Jiangsu Changzhou 213003, China.

Tel: +86 519 68870619

Fax: +86 519 86621235

E-mail: shineroar@163.com.