

Dear reviewer:

Thank you for your comments concerning our manuscript entitled “The emerging role of long noncoding RNAs in recurrence hepatocellular carcinomas” (Manuscript NO.: 67202, Review) Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our manuscript. We have studied comments carefully and have made correction which we hope meet with approval.

1.For the first opinion, we have used the correct references based on your comments. To date, there have been no established criteria to accurately distinguish whether multifocal HCC originates from IM or MO. However histopathological features remain the most convenient strategy.

- 1).Calderaro, J., M. Ziol, V. Paradis, and J. Zucman-Rossi, *Molecular and histological correlations in liver cancer*. Journal of hepatology, 2019. **71**(3): p. 616-630.
- 2).Xie, D., H. Fan, Z. Ren, J. Fan, and Q. Gao, *Identifying Clonal Origin of Multifocal Hepatocellular Carcinoma and Its Clinical Implications*. Clinical and translational gastroenterology, 2019. **10**(2): p. e00006.
- 3).Morimoto, O., H. Nagano, M. Sakon, Y. Fujiwara, T. Yamada, H. Nakagawa, A. Miyamoto, M. Kondo, I. Arai, T. Yamamoto, H. Ota, K. Dono, K. Umeshita, S. Nakamori, Y. Sasaki, O. Ishikawa, S. Imaoka, and M. Monden, *Diagnosis of intrahepatic metastasis and multicentric carcinogenesis by microsatellite loss of heterozygosity in patients with multiple and recurrent hepatocellular carcinomas*. Journal of hepatology, 2003. **39**(2): p. 215-21.

2.For the second opinion, we have removed this part because our focus is not to introduce the pathological process, but to compare MO and IMs in recurrent HCC. We apologize for the pathologically incorrect and misleading statement.

3.For the third opinion, “but it is subjective and limited in accuracy” has changed to “and it is objective and accurate. Pathology remains a cornerstone in the clinical treatment of patients with HCC, as it allows a definitive diagnosis and provides prognostic information.”

4. “In the case of HCC, there are no significant morphological alterations that could be used as a diagnostic markers, therefore various molecular markers are under investigation, including lncRNA.” Although there are currently no significant morphological changes that can be used as diagnostic markers for HCC, we believe that it is necessary to discuss the potential prospects for the application of lncRNA to accurate diagnostic/prognostic biomarkers for recurrent HCC. At present and in the future, we still need to further understand the significance of lncRNAs in the clinical diagnosis and treatment of recurrent HCC, and explore the regulatory mechanism of lncRNAs in the occurrence and treatment of recurrent HCC.

We deeply appreciate your comments of our manuscript, and we look forward to the revised manuscript to your satisfaction.

Thank you and best regards.

Yours sincerely,

HanFei Huang

E-mail: kmhhf@126.com

