

Reviewer 1

In the manuscript, the authors summarized comprehensively the well-established and recent proposed mechanism of HCC development and progression. This is very important for better understanding the carcinogenesis and development of hepacytes and finally making HCC patients benefit from some potential therapeutic strategies. However, some issues should be addressed before possible acceptance.

1. When discussing NAFLD as one of HCC etiological factors, the association between BMI or diabetes and risk of liver cancer should be mentioned. Ref to Cancer Res. 2016;76(20):6076-6083.
2. The association between molecular stratification or mutational signature and risk of HCC should also be mentioned. Such as refs including Gastroenterology. 2017;152(4):745-761. Nat Commun. 2017;8(1):1315.
3. "expert opinion" section should be added in which some controversies about mechanism such as CSC vs CSC-like cells should be mentioned.
4. Brief description on current ongoing therapeutic strategies or clinical trials against specific molecular mechanisms should be added in discussion section.

Response

We appreciate your comments, and have included additional relevant information and references.

Reviewer 2

1. A large proportion of the review article discusses the etiology of HCC, which contributes to the hepatocarcinogenesis but is not closely related to the title "Mechanisms of hepatocellular carcinoma progression". The authors should focus on the mechanism of HCC progression, particularly novel molecular mechanisms. 2. The article did not include recent novel discoveries in HCC progression, such as non-coding RNAs, RNA sequence, gene mutation and epigenetics. 3. There are some mistakes of grammar and spelling.

Response

Thank you for your observations. We have included additional novel information, and have corrected all mistakes of grammar and spelling.

Reviewer 3

It is a better review paper. I would like the paper is more concisely, add some tables or figures to illustrate the problem.

Response

Thank you for your comments. We have included two figures.