Re-submission of the revised manuscript (Manuscript NO: 48323), entitled "Identification of hepatitis B virus and liver cancer bridge molecules based on functional module network".

Dear Lian-Sheng Ma

Thank you for your editorial efforts for our manuscript. Per your instructions for resubmission, we are submitting the revised manuscript of the above article. We also thank very much the anonymous reviewer for the constructive comments to strengthen this manuscript.

The detailed responses on a point-by-point basis are described below and the reviewer's critiques have been accommodated fully in various parts of the revised version (shown in BLUE color).

We hope that you and the reviewer will now find the paper suitable for publication in World Journal of Gastroenterology.

Sincerely yours,

Jing Li

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2 Peer-review report

Reviewer #1: the the title reflect the main subject of the manuscript, the abstract summarize and reflect the work described in the manuscript, but please: expand the method section, explain more regarding the hub-bottlenecks in your results, discuss the following articles in your discussion: 1-Safaei A, Oskouie AA, Mohebbi SR, Rezaei-Tavirani M, Mahboubi M, Peyvandi M, et al. Metabolomic analysis of human cirrhosis, hepatocellular carcinoma, non-alcoholic fatty liver disease and non-alcoholic steatohepatitis diseases. Gastroenterol Hepatol bed bench. 2016; 9(3): 158-73. 2-Zamanian-Azodi M, Peyvandi H, Rostami-Nejad M, Safaei A, Rostami K, Vafaee R, et al. Protein-protein interaction network of celiac disease. Gastroenterol Hepatol bed bench. 2016; 9(4): 268-77.

Reply: Thank you for your comments. We give a detailed description of the relevant methods and added some discussion content in the manuscript.

In the revised materials and methods section:

"…and 122 diseases and 6 control samples were included. The expression data of microRNAs (GSE33857) included 4 disease samples and 12 control samples**…"**

In the revised result section:

"…module intranet, while PLTP and FABP5 were also linked to 15 other genes, respectively. In addition, the variation multiples of BCHE, PLTP and FABP5 were also in front of the differential genes, and BCHE was negative disorder, PLTP and FABP5 were positive disorder**…**The higher the connectivity, the more important the role of the gene in the whole regulatory network. However, PIK3CD is not a persistent disorder gene. We speculate that PIK3CD may play a central regulatory role in the progression of disease**…"**

In the revised discussion section:

"…by PPI network and Cytoscape visualization software [29] **…**Identification of biomarkers based on key factors is an effective index for clinical diagnosis of different types of hepatocellular carcinoma [47]**…"**

Reviewer #2: The research question is quite interesting and the study is so extensive that it deserves to be divided into multiple smaller manuscripts. The manuscript needs to comply with the standard organization for original research articles; so the study material and methods section needs to come just after the study introduction and objectives. The results section would better to be based-on and arranged in accordance with the methods section without redundancy or repetitions referring to tables and illustration in-order to keep reader more attracted and aiming for simplification and readability.

Reply: Thank you for your review. We have reordered the manuscript structure to achieve better reading results.

Reviewer #3: An interesting study about the pathogenesis and therapeutic mechanism of HBV related HCC.

Reply: Thank you for reviewing the manuscript.