Dear the editors

We appreciate the opportunity to submit a revision of our manuscript for publication in World Journal of Gastroenterology. It is gratifying that the reviewers consider our study is very interesting and well written with subject to minor revision.

This revised manuscript has been improved as a result of changes made in response to the comments of the reviewers. We have attached a point-by-point response to the comments and have highlighted the changes from the previous version with red color in this revised manuscript.

Thank you for considering this revised manuscript. We look forward to your kind reply.

Best regards,

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Point-by-Point Response to the Reviewers' Comments

Reviewer #1 Evaluations:
Recommendation (Required): Minor revision
Reviewer #1 (Comments to the Author):

The authors have investigated the BAFF-R expression and B cells maturation using peripheral blood samples of 50 cases involving patients of HBV infection (with or without HCC) and healthy controls. They found the expression of BAFF-R was significantly reduced in patients with HCC and decreased BAFF-R expression on B cells was significantly correlated with large tumor size and advanced tumor stage. Thus, they considered the depletion of BAFF-R might play an important role in the development of HBV associated HCC. As the role of B-cells and its maturation on HCC remains unknown and has not been well-investigated, their study design and its results are very interesting. Although the small-sample size is quite limitation in this study, the study itself is well conducted and the manuscript is well-written. I have only one question. The authors insisted that "depletion of BAFF-R is contributable to the development and progression of HBV-related HCC". However, it is also considerable that depletion of BAFF-R may be not "cause" of

HCC development but "result" of HCC development. Namely, developed HCC interfaces the immune system and leads depletion of BAFF-R. How about this hypothesis?

Ans. Thank you very much for the comment. We agree with this motivating hypothesis that reduced BAFF-R and B cell subsets may be a consequence of HCC development. As data regarding this concept are limited in HCC, we select a relevant study in an animal model of lung cancer to support the hypothesis. In that report, it was shown that tumor-derived factors such as pathologically activated myeloid-derived suppressor cells (MDSCs) could potentially regulate B cell subsets in terms of percentages and absolute number reduction (see in Discussion and ref#30).

Reviewer #2 Evaluations:
Recommendation (Required): Accept (High priority)
Reviewer #2 (Comments to the Author):

This is an excellent study that demonstrated the relation between BAFF-R in B cells and HBV associated HCC. Their first observation of reduced BAFF-R expression in B cells correlating with HCC tumor size and advanced stage not only demonstrated the influence of abnormalities of B cell development in the development and progression of HBV-HCC but also may have opened a new path for designing the therapeutic target of BAFF or BAFF-R for management of HCC. The authors' work is highly commendable.

Ans. Thank you for your kind comments, very much appreciated.