

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 58649

**Title:** Autophagy related protein 9A increase in hepatitis B virus-associated hepatocellular carcinoma and the role in apoptosis

**Reviewer's code:** 00504486

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** South Korea

**Author's Country/Territory:** Thailand

**Manuscript submission date:** 2020-07-31

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-07-31 22:02

**Reviewer performed review:** 2020-08-06 11:02

**Review time:** 5 Days and 12 Hours

|                                 |   |
|---------------------------------|---|
| <b>Scientific quality</b>       | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| <b>Language quality</b>         | <input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing<br><input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>               | <input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority)<br><input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| <b>Re-review</b>                | <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No   |
| <b>Peer-reviewer statements</b> | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous<br>Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No   |

#### **SPECIFIC COMMENTS TO AUTHORS**

This letter reported that ATG9A is upregulated in HBV-associated hepatocellular carcinoma, and provides resistance to apoptosis. Their previous study (World Journal of Gastroenterology, 2016) Upregulation of ATG9A was already reported in hepatoma cell lines but clinical samples were added to support their issue in this letter. 1. It seems like that suppression of ATG9A decreases HBV DNA replication in Fig2.B. Therefore, statistical analysis should be added in Fig2.B although they described no difference HBV copies between ATG9A-knockdowned and control cells. 2. The author described the text as “ In order to search for the effect of autophagy in HBV-associated hepatocellular carcinoma, we investigated apoptosis “. For performing Fig4 experiment, rationale is lack. This description seems to be inappropriate. For example, we recommend to describe “ In order to search for the effect of ATG9A on apoptosis, we performed a flow cytometry

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 58649

**Title:** Autophagy related protein 9A increase in hepatitis B virus-associated hepatocellular carcinoma and the role in apoptosis

**Reviewer's code:** 02538092

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Thailand

**Manuscript submission date:** 2020-07-31

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-08-03 14:17

**Reviewer performed review:** 2020-08-10 11:02

**Review time:** 6 Days and 20 Hours

|                                 |   |
|---------------------------------|---|
| <b>Scientific quality</b>       | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| <b>Language quality</b>         | <input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing<br><input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>               | <input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection             |
| <b>Re-review</b>                | <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No   |
| <b>Peer-reviewer statements</b> | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous<br>Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No   |

## **SPECIFIC COMMENTS TO AUTHORS**

The author presented interesting findings in the letter entitled “Autophagy related protein 9A increase in hepatitis B virus-associated hepatocellular carcinoma and the role in apoptosis” that ATG9A expression is up-regulated in HBV-associated HCC tissue, and silencing it could trigger cell apoptosis. However, the scientific importance or clinic significant of these findings have not been well address. Firstly, the author has reported that ATG9A was upregulated in HBV related-HCC and associated with apoptosis[ref1]. The only progress here is tested these results in HCC tissue. Secondly, author’s data showed that neither HBx could affect ATG9A nor ATG9A could affect HBV replication. These results disproof that ATG9A were connected with HBV. Thirdly, ATG9A is the only transmembrane protein of the core autophagy machinery. The domain-swapped homotrimer ATG9A has membrane-bending properties and internal cavities for lipid transportation[ref2]. Why the author pursues its role in apoptosis other than autophagy? In conclusion, rejection for amending was suggested. Reference: 1. Kunanopparat A , Kimkong I , Palaga T , et al. Increased ATG5-ATG12 in hepatitis B virus-associated hepatocellular carcinoma and their role in apoptosis[J]. World Journal of Gastroenterology, 2016, 22(37):8361-8374. 2. Carlos M.G, Xiao-FengT, Tengfei L, et al. Structure of Human ATG9A, the Only Transmembrane Protein of the Core Autophagy Machinery[J]. Cell Reports, 2020,31(13):107837. DOI: 10.1016/j.celrep.2020.107837