

Dear Editor,

we have modified our manuscript ID 38981 entitled “**MICRO-RNAs IN HEPATITIS B VIRUS (HBV)-RELATED CHRONIC LIVER DISEASES AND HEPATOCELLULAR CARCINOMA**” according with the suggestion of the reviewers.

The following changes (shown in red and underlined) have been made in the new manuscript.

Reviewer #1:

Reviewer: Revision manuscript 38981 “MICRO-RNAs IN HEPATITIS B VIRUS (HBV)-RELATED CHRONIC LIVER DISEASES AND HEPATOCELLULAR CARCINOMA” In this review, the authors give an updated overview on the potential pathogenic role of micro-RNAs in hepatitis B related chronic liver diseases. Their role as biomarkers in the management of HBV chronic hepatitis and as therapeutic targets is also addressed. The review is well written, clear and timely. Minor point: Pag. 8, correct “targe” with “target”.

Authors: Done

Reviewer #2:

Reviewer: Evangelista et al discussed ' the role of miRNAs in the pathogenesis of HBV-related diseases and their role as a biomarker in the management of patients with HBV-related disease and as therapeutic targets'.

Some minor issues raised:

1-Page (p),9 line 18: CCAAT or CAAT?,

Authors: CAAT was changed to CCAAT in the revised manuscript

Reviewer: 2-p10, line 7: please explain the effect on HO-1 (a cytoprotective enzyme that decreases HBV cccDNA levels both in vitro and in vivo?

Authors: Besides its hepatoprotective effect, HO-1 has been shown to be endowed with anti-HBV activity in vitro (ref. 45) and in vivo (ref. 46 in the revised manuscript). This point was clarified in the revised manuscript.

Reviewer: 3-p10, line 19: histone deacetylase or histone deacetylases?

Authors: “Histone deacetylase” is correct, since it is referred to the specific HDAC4

Reviewer: 4-p10, line 20 : farnesoid X receptor a or farnesoid X receptor α ?

Authors: “a” was changed to “ α ”in the revised manuscript

Reviewer: 5-p11, line 5: IFN- α or IFN- λ 1

Authors: “ α 1” was changed to “ λ 1”in the revised manuscript

Reviewer #3:

Reviewer: Dear Editor, this is a comprehensive review on association of MicroRNAs with HBV infection. The authors reviewed the effect of MicroRNAs on viral replication and expression of viral proteins and relation of MicroRNAs and HCC. The Authors also discussed the available data suggesting the utility of MicroRNAs as possible clinical biomarker. In my opinion the topic of this manuscript is of interest to the journal readers. There are couple of issues that I will address and I am sure the authors will promptly handle.

i adding references for Table 1 (for every row).

ii effect of miR-205 on HBV infection left blank (table 1)

Authors: Done

We thank the Editor and the Reviewers for helping us to improve our paper. The manuscript has been read and approved by all the authors. We also declare that we have no conflict of interest in connection with this paper.

We sincerely hope that the enclosed new manuscript may be accepted for publication in the “*World Journal of Hepatology*”.

Sincerely yours

Prof. Evangelista Sagnelli