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Name of journal: World Journal of Gastroenterology

Manuscript NO: 45299

Title: Mechanism of exosome miR-224 in the development of hepatocellular carcinoma and the diagnostic value evaluation

Reviewer's code: 02953994

SPECIFIC COMMENTS TO AUTHORS

This is an interesting study. The manuscript is very well written. In this study, Cui Yao et al evaluated the mechanism of exosomal miRNA-224 in the development of HCC and its diagnostic and prognostic value for HCC patients. The methods are detail described and the results are very interesting. The authors found that the serum exosomal miR-224 does have some ability to differentiate patients with HCC from healthy controls, with an AUC of 0.910, and HCC patients with higher serum exosomal miR-224 expression had lower overall survival. And the results showed that the exosomal miR-224 can inhibit the expression of GNMT and may be used as a marker for the diagnosis and prognosis of patients with HCC. 1 In table 1, how about the P value about the Cirrhosis, T classification and Tumor size? 2 Figures are very good and interesting. 3 The references are updated and well discussed. 4 Some minor language revisions are required.

Dear PEER-REVIEW, there is no P value about the Cirrhosis, T classification and Tumor size in table 1 because the only one dieases group.

Reviewer's code: 02953927

SPECIFIC COMMENTS TO AUTHORS

Very interesting study about the biomarkers related to the development of HCC. Nucleic acids in exosomes are another molecule that can act as a biomarker. There are many



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reports on exosomal miRNA, which is an ideal biomarker for the early diagnosis of cancer. However, there are few reports on the role of exosomal miRNAs in the diagnosis and prognosis of HCC. In this study, the authors found that the biomarkers can be used for the diagnosis and prognosis of HCC. Overall, the study is well designed, and the manuscript is excellent. 1 The title reflects the main subject of the manuscript. 2 Methods are described in adequate detail. 3 The research objectives are achieved by the experiments used in this study. 4 The results are well discussed. The most recent references are listed and discussed also. 5 Are there any limit for this study? The authors can make a statement about the limit of the study, and make further research in the future. 6 Some minor language polishing should be checked and corrected.

Dear PEER-REVIEW, the limit for this study was added into the DISCUSSION of the manuscript. The content is as follows "However, in this study we only compared the expression of exosome miR-224 in the serum of HCC and healthy controls. It is not clear whether it is different that the expression of exosome miR-224 in cirrhosis, hepatitis or other liver cancer, so the ability of miR-224 to distinguish between HCC and other liver diseases is needed further verification."

Reviewer's code: 02953931

SPECIFIC COMMENTS TO AUTHORS

The manuscript is very well written. Interesting findings which is useful to the clinicians. I have no specific comments.