

January 15, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 15907-review.doc).

Title: miR-451 Inhibits Proliferation of Esophageal Carcinoma Cell Line EC9706 by Targeting CDKN2D and MAP3K1

Author: Wenqiao Zang, Xuan Yang, Tao Wang, Yuanyuan Wang, Yuwen Du, Xiaonan Chen, Min Li, Guoqiang Zhao

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 15907

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Reviewed by 00724342

The manuscript is basically good. The authors have done designed and guided the study. But what is confusing is that the authors have declared that no competing interest exists, on one side and this study was supported by the National Natural Science Foundation of China (81272188; 81301726) on the other side. One of the important fact in the Conflict of Interest Disclosure Statement is research funding! In this manuscript, there is no strong evidence that the authors have no conflict of interest. Therefore, it is necessary to obtain statements of the author prior to publication in WJG

Answer: We have deleted one of the researches funding in the revised manuscript.

Reviewed by 01213174

GENERAL This is an in vitro study that addressed the mechanism of tumor suppressive functions of a microRNA, miR-451. The authors authentically conducted the required experiments using esophageal cancer cells and revealed that miR-451 targeted CDKN2D and MAP3K1 and worked tumor-suppressively through the inhibition of the two kinases. The findings are expected to contribute to the development of molecularly targeted therapy for esophageal cancer. This reviewer thinks the manuscript is potentially worth publishing in World Journal Gastroenterology after major revisions are made. SPECIFIC In the present study, authors used EC9706 cells only. This reviewer has a question whether the findings shown by the experiments in this study were applicable to many cancer cells of the esophagus or specific for EC9706 cells? The authors should show the results of Fig. 1 using a different cancer cell line that is originated from human esophageal cancer cells.

Answer: In the preliminary experiment, we used three esophageal carcinoma cell lines (EC9706, KYSE150 and EC-1) to identify that miR-451 targeted CDKN2D and MAP3K1. We only used EC9706 cell line to write the paper in the initial manuscript. In the revised manuscript we have added KYSE150 cells in the results of Fig. 1.

Reviewed by 00753027

The authors reported their findings on the roles of miR-451 in proliferation of esophageal carcinoma cell line EC9706 by targeting CDKN2D and MAP3K1. Based on the results showing inconsistency between CDKN2D and MAP3K1, the authors should not ignore the findings. The provided evidence could not fully support the conclusion.

Answer: Thank you for your advices. In the manuscript we found that CDKN2D and MAP3K1 were direct targets of miR-451. The further results showed that miR-451 inhibited the proliferation of EC9706 by targeting CDKN2D and MAP3K1. We don't discuss the relation between CDKN2D and MAP3K1 in the study.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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