

Format for ANSWERING REVIEWERS



March 26, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: Main manuscript_WJG_9387.doc).

Title: MicroRNA-31 Expression in Serrated Pathway Progression

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 9387

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

To the editor,

Please find our revised manuscript [ESPS Manuscript NO: 9387], which we would like to resubmit for consideration.

We have responded to each of the comments, as indicated below. The reviewers' comments are italicized and in square brackets. Within the revised manuscript, changes to the text in response to the reviewers' comments are underlined, using colored text.

According to the suggestion of the Reviewer (1), we have changed the title "MicroRNA-31 Expression in Serrated Pathway Carcinogenesis" to "MicroRNA-31 Expression in Serrated Pathway Progression".

Thank you very much for the opportunity to respond to the reviewers' comments. We believe that our manuscript has been much improved as a result of these constructive and valuable comments.

Reviewer (1)

[Based on their previous study, the author reported an early invasive colorectal cancer with the HP component, and suggested that miR-31 may contribute to the progression of serrated lesions. Their finding is valuable and interested, which suggested for the first time a possible relationship between a specific miRNA, miR-31, and the serrated pathway in CRC. The relationship had been reported in their previous publication (Carcinogenesis 2013 (in press) [DOI: 10.1093/carcin/bgt374]), so the present case report should focus on the invasive colorectal carcinoma with the HP component other than their previous data. Based only on the miR-31 expression in this case, it is not very convincing to conclude that miR-31 may be an important molecule in serrated pathway carcinogenesis.]

As requested, we have revised the sentences in the Discussion section (page 8, paragraph 2 and page 8, paragraph 3, respectively), as follows:

In this case, higher miR-31 expression was observed in the carcinoma component compared with the HP component, suggesting that not only accumulating epigenetic alterations but also miR-31 expression may contribute to the progression of HP (or SSA). In other words, these findings indicate that HPs (SSAs) with high miR-31 expression may be precursor lesions that progress to SSAs with high-grade dysplasia or CRCs.

Our results suggest that miR-31 may be one of the key molecules in serrated pathway progression.

Because the conclusion was revised, we also have changed the title “MicroRNA-31 Expression in Serrated Pathway Carcinogenesis” to “MicroRNA-31 Expression in Serrated Pathway Progression”.

Reviewer (2)

[In this Case Report the Authors describes the case of a 75-year-old man at a follow-up colonoscopy to have a 7-mm flat-elevated lesion in the cecum that was diagnosed as an early invasive carcinoma with a hyperplastic polyp (HP) component. They reported that the carcinoma and the HP components of the lesion exhibited higher microRNA-31 (miR-31) expression (57-fold increase and 8-fold increase, respectively) compared with the paired normal mucosa. They concluded suggesting that miR-31 may be an important molecule in serrated pathway carcinogenesis This short manuscript is well written and the case reported could be used as basis for further deepened studies aimed to clarify the role of miR-31 in colorectal carcinogenesis correlated to the serrated pathway. It is therefore acceptable for publication.]

We appreciate the reviewer's comments.

3 References and typesetting were corrected

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

Sincerely,

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