

## ANSWERING REVIEWERS



To:

24<sup>th</sup> Dec, 2013

Editor

World Journal of Gastroenterology

Dear Editor,

Thank you for providing the valuable suggestions to improve our manuscript on the role of microenvironment on colorectal cancer. We greatly appreciated receiving the reviewers' comments on our manuscript entitled "*The input of microenvironment regulation on colorectal cancer : A CCN family review of literature*" (5891). Based on reviewer's concern, we've addressed as followed.

We will look forward to your timely response.

Sincerely yours

Dr. Min-Liang Kuo, Ph.D.,

Professor

Institute of Biochemical Sciences, College of Life Science, National Taiwan University,  
Taipei 100, Taiwan

Tel 886-2-33665960; Fax 886-2-23123456 #88607;

Email: kuominliang@ntu.edu.tw

Reviewed by 00504704:

Thank you very much for your kind invitation to review this manuscript.

This is a reasonably well written paper that presents a case of inflammatory myofibroblastic tumor (IMF) involving the omentum. Pathological point of view, IMF is a well known pathologic diagnosis and there were cumulative data about IMF in the literature. So the manuscript has minor significance and novelty.

Response to Reviewer: Thanks for reviewer's comment. Inflammatory myofibroblastic tumor is a solid neoplastic mesenchymal proliferation composed of myofibroblastic spindle cells admixed with inflammatory infiltrates. It was first described in the lung, however, extrapulmonary IMTs have also been described in the mesentery, liver, head and neck, and heart. The most common sites of extrapulmonary IMF occurrence are the mesentery and the omentum. We thanks for reviewer's view and emphasizing.

Reviewed by 00531176:

The manuscript by Chang et al is a brief and an easy to read review on CCN proteins. Despite the efforts of the authors, some aspects of the manuscript should be changed.

1. The title should be more focused on CCN proteins.

Response to Question 1: We've corrected the title as "The input of microenvironment regulation on colorectal cancer : A CCN family review of literature". This title should be more focused on CCN family.

2. The first two paragraphs (introduction and microenvironment in CRC) are extremely summarized and do not properly present the complexity of the tumor microenvironment and all the main actors. Please re-write and extend these parts.

Response to Question 2: Thanks for reviewer's suggestions. We'd re-wrote and added the section of "Introduction" in page 3, line 8-22, and the paragraph of "Microenvironment in CRC" in page 3, line 31-38; page 4, line 1-11.

Reviewed by 01207047:

Dear Editor, Thank you very much for your kind invitation to review this manuscript. It is a review article written on a hot topic.

1. Manuscript is well written manuscript, needs minor English revision.

Response to Question 1: We've completed the English revision by the native English. The attachment is the certificate of English revision.



2. Title of the manuscript does not reflect accurately the major topic and contents of

the manuscript.

Response to Question 2: Thanks for reviewer's suggestion. We've corrected the title as :"The input of microenvironment regulation on colorectal cancer : A CCN family review of literature". This title should be more focused on the major contents in the text.

3. Please give more detail about the data: Correlation of CCN protein with advanced CRC progression, although high expression of CCN2 is the hallmark of good.....CRC and other tumors (33).

Response to Question 3: In order to give more detail about the pathological roles of CCN2 in the progression of well-differentiated CRC and other tumors which were citation from reference 33, we've extended the illustration in page 5, line 33-38; page 6, line 1-4.

4. I would expect to see a pathologist among coauthors of the manuscript.

Response to Question 4: Thanks for reviewer's suggestion. We've added the pathologist, Dr. Yung-Ming Cheng, Department of Pathology, National Taiwan University, Taipei, Taiwan, in the authorship. Dr. Cheng has cooperated with us for more than 15 years, and he is an expert in oncology field.

Reviewed by 00742503:

I have many concerns about this manuscript.

1. The Title does not reflect the focus of the review and is misleading. It is not a review about the regulation of microenvironment on colorectal cancer but a description of some particular proteins. My major concern is that the information given in this review is not, in my opinion very relevant.

Response to Question 1: We're sincerely appreciated with Reviewer's suggestion. We've changed the title as: "The input of microenvironment regulation on colorectal cancer : A CCN family review of literature" to reflect the focus of this manuscript which is the description of some particular proteins, CCN family in CRC's microenvironment.

2. The contribution made is scarce since it is merely a list of data without discussion and in some cases is not updated.

Response to Question 2: We've added the related discussion in page 5, line 33-38; page 6, line 1-4 and 33-38, and also updated the cases and references in the revised text. The revised table was included.

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**Table. The expression of CCN family in colorectal cancer**

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Capital member	Models	Effects	References
CCN1	Periradiated stroma	Positively correlated with metastasis	[29]
CCN1	Clinical sample	Positively correlated with early stage of tumor development	[30, 31]
CCN1	Cultured cancer cells	Promoting cancer cell migration	[33]
CCN2	Clinical sample	1. Positively correlated with early stage of tumor development 2. Negatively correlated with prevalence of peritoneal carcinomatosis 3. Inhibiting invasion and metastasis 4. Negatively correlated with metastasis and patient survival	[36, 37, 40]
WISP-1	Clinical sample	1. Promoting cell cycle checkpoint progression, accelerating cell growth and inhibiting apoptosis 2. Positively correlated with tumor grade	[41-45]
WISP-2	Clinical sample	Negatively correlated with tumor grade	[43, 44]
WISP-3	Clinical sample	Positively correlated with tumor grade	[43, 44]

3. Minor concerns are manuscript contents typing errors and English language should be revised. Figure 1 is not very informative and could be eliminated.

Response to Question 3: Thanks for reviewer's correction, and we had completed the English revision by the native English. The attachment is the certificate of English revision. Moreover, we'd deleted Figure 1 in the revised manuscript.

