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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 89997

Title: FAM53B promotes pancreatic ductal adenocarcinoma metastasis by regulating macrophage M2 polarization

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02543957
Position: Peer Reviewer
Academic degree: PhD
Professional title: Research Assistant Professor
Reviewer's Country/Territory: United States
Author's Country/Territory: China

Manuscript submission date: 2023-11-20

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-12-13 13:35

Reviewer performed review: 2023-12-18 13:39

Review time: 5 Days

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [Y] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The manuscript titled "FAM53B promotes pancreatic ductal adenocarcinoma metastasis by regulating macrophage M2 polarization" attempts to demonstrate that FAM53B promotes pancreatic ductal adenocarcinoma metastasis by regulating macrophage M2 polarization. However there are several major issues that need to be clarified before the manuscript can be considered for acceptance. Though the results presented are interesting the complete lack of methods and details makes this study unacceptable for publication. Although the authors state that the manuscript has undergone language editing, the manuscript still requires significant grammar, language and sentence construction editing to make it more readable and clear. As such the text is very confusing and difficult to read. The methods section significantly lack details in protocols and are confusing. For example, in section 1.1 the authors state"…blown and mixed…" This makes no sense. In the methods section 1.2 the authors state that "… cell suspension was absorbed and added…" this has no meaning. In section 1.3 the authors talk about the addition of serum free media but do not mention how much. Section 1.4 what is 800rmp/min? Section 1.5 details of the CRISPR system are not provided,

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specifically the constructs and sequence of the gRNA. No details are provided about the cell lines used and the culture method. Section 1.6 there is no mention of the macrophage model system used, what cell line? Section 1.7 what is RAPI lysate? Section 1.7 how were the exosomal vesicles collected? And how was the concentrations of the marker proteins adjusted and determined in the lysate. Section 1.8 the animal experiments lack details and make no sense. The details of the mice, age and weight rangers not indicated. Why were the cells digested? How were the animals implanted with the cancer cells? Section 1.9 the usage of future tense is confusing. No mention is the methods about how tissues were collected and processed for ICH and H&E staining. No quantification methods provided. Complete lack of details. Methods are incomplete, no details about the colony formation assay, FACS analysis or the proliferation assay is provided. This makes the results meaningless.

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Peer-review model: Single blind

Reviewer's code: 03060131
Position: Peer Reviewer
Academic degree: MD
Professional title: Doctor
Reviewer's Country/Territory: United States
Author's Country/Territory: China

Manuscript submission date: 2023-11-20

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-12-14 02:05

Reviewer performed review: 2023-12-22 03:02

Review time: 8 Days

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No creativity or innovation

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Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [Y] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

According to the editor's strict regulation, I have carefully read and checked the article described by Yang et al. based on its scientific significance, soundness and novelty. In the present study, the authors have found FAM53B is up-regulated in pancreatic ductal adenocarcinoma tissues, and suppresses the metastasis of pancreatic ductal adenocarcinoma in vivo. According to their results, knockdown of FAM53B attenuated proliferation of pancreatic ductal adenocarcinoma cells. Additionally, immunohistochemical staining showed that FAM53B expression is associated with the polarization of M2 macrophage. Indeed, FAM53B had an ability to induce the polarization of M2 macrophage. Although FAM53B had an undetectable effect on pancreatic ductal adenocarcinoma cell proliferation, knockdown of FAM53B suppressed the metastasis as examined by mouse model. Taken together, the authors suggest that FAM53B could contribute to the development of the novel strategy for the treatment of the patients with pancreatic ductal adenocarcinoma. Although the present study might provide certain advances in the related field, there are several concerns (see below) which should be adequately addressed before reconsideration. Major concerns Their

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description of Results section appeared to be quite different from the standard description (introductive part was too long). To avoid the possible confusion of the readers, the authors have to improve the description of their Results section. The aim of the present study was to confirm their hypothesis whether FAM53B could be implicated in development and/or metastasis of pancreatic ductal adenocarcinoma through the polarization of M2 macrophage. Unfortunately, FAM53B-mediated polarization of M2 macrophage had undetectable effect on proliferation as well as apoptosis of pancreatic ductal adenocarcinoma cells. The authors have to discuss why FAM53B could be involved in the metastasis but not in proliferation. Discussion part was composed on too many introductive descriptions. Discussion part should be described based on their present findings. The present form of Discussion part appeared to be Review article not Original article. English writing did not reach to the standard level. Minor concerns Introduction section is too long. The authors have to focus the points and describe more compactly. In Materials and methods section: The authors have to describe the sources of the primary antibodies used for WB and ICH. All of the figure legends were poorly described. More experimental information should be incorporated. The authors did not describe the results obtained from cell lines in the Results section (Fig. 1D, E, F). In Figure 1D, the size of FAM53B detected in BXPC-3 cells was completely different from that of PANC-1 cells. Which signal could correspond to the native FAM53B? The efficiency of FAM53B knockdown in BXPC-3 and PANC-1 cells should be validated (RT-PCR and/or WB). Although the authors described that “This result highlights the importance of cell interactions for tumor development and provides insights into the underlying mechanisms of the pancreatic ductal adenocarcinoma microenvironment” based on the results shown in Figure 3, there was no direct evidence supporting their conclusion. CRISPR/Cas9-mediated gene silencing should be referred to as “knockout” not as “knockdown”.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 89997

Title: FAM53B promotes pancreatic ductal adenocarcinoma metastasis by regulating macrophage M2 polarization

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03060131
Position: Peer Reviewer
Academic degree: MD
Professional title: Doctor
Reviewer's Country/Territory: United States
Author's Country/Territory: China

Manuscript submission date: 2023-11-20

Reviewer chosen by: Xin-Liang Qu

Reviewer accepted review: 2024-01-22 03:13

Reviewer performed review: 2024-01-24 02:45

Review time: 1 Day and 23 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Based on the answering part of the revised version of the article, I have carefully read and checked the revised version of the article described by Pei et al. Although the revised article might be partially improved, there are several concerns (see below) which have to be adequately addressed before publication. Major concerns: Almost all the Results sections contained the description of results plus the related discussion. In standard article, the Results section should be composed of the description of the results not of the related discussion. The length of the revised Discussion section was still long. The authors have to narrow down the point of discussion. The content of the first paragraph of the Discussion section appeared to be “Introduction” which was not based on the present results. For my feeling, one of the interesting points of discussion might be the different effect of FAM53B on pancreatic cancer from colorectal cancer and liver cancer. Minor concerns: English proofreading is still required.