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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 73148

Title: KAI1/CD82 gene and autotaxin-lysophosphatidic acid axis in gastrointestinal cancers

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00053419
Position: Editorial Board
Academic degree: PhD
Professional title: Professor
Reviewer's Country/Territory: Spain
Author's Country/Territory: China

Manuscript submission date: 2021-11-11

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-11-12 18:14

Reviewer performed review: 2021-11-16 17:45

Review time: 3 Days and 23 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] 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

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors provide an exhaustive review of the evidences supporting the implication of KAI1/CD82 and ATX-LPA axis in gastric cancers. There is a huge number of results enumerated along the manuscript from almost 200 papers. However, despite the details provided, there is a lack of integration, the reader access to an unconnected list of data and it is really challenging to extract a clear physiological/pathological picture. In addition to the lack of integration, there are a few comments for the authors: 1. Critical vision and discussion of the presented evidences is needed to provide the reader with a critical perspective 2. KAI1/CD82 is presented as a factor that can down regulate HGF (page 12) while it induces up-regulation of HGF-induced Sprouty2 (page 13). This apparent contradiction deserves some discussion. 3. The sentence on page 14 "the decreased expression of KAI1 in CRC might be a therapeutic target for CRC" is confuse. The gene/protein might be a target but not the decrease. 4. According to Human Protein Atlas (www.proteinatlas.org), CD82 has no prognostic value in cancer. It might be worth to discuss these evidences as well.

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Reviewer's code: 05849479
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2021-11-11

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-11-12 02:28

Reviewer performed review: 2021-11-29 01:59

Review time: 16 Days and 23 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Main content： In this paper, the molecular composition of KAI1/CD82 gene and ATX-LPA axis, their physiological functions in tumours, and their roles in gastrointestinal cancers and target therapy are reviewed. Method：This article reads and summarizes 198 documents .In chronological order, it reflects the research level and progress of each stage, and explains the current research level and general future research directions. Contribution to the subject： It is much easy to find the literature on the effect of KAI1/CD82 on breast cancer, because there are many studies that have studied and summarized this. The basic attributes of the ATX-LPA axis in the development of various cancers are negative, so for gastrointestinal tumors, the role of KAI1 CD82 is indeed worth studying and summarizing, so as to provide more intuitive information for future research. Advantages of this article： The article describes the similarities and uniqueness of BAI1 CD82 and ATX-LPA axis in pancreatic cancer, hepatocellular carcinoma, gastric cancer, and colorectal cancer in a point-to-point manner, which makes the readers easy to understand. Disadvantages of this article： 1、The typesetting of the description of the abbreviated paragraph is not clear。 2、The article describes the four gastrointestinal diseases separately in the KAI1 CD82 and ATX-LPA axis, but it briefly summarizes the targeted therapy. To make the article top-heavy is the lack of a paragraph in the main content of the article. 3、In the “Comparative analysis of LPAR-mediated signals in tumour”,The description of the receptors is also too general. Although the general attributes may be the same, there are subtle differences between them in different diseases. For example, in hepatocellular carcinoma, the location and role of LPAR2, LPAR6 and other 1, 3, and 5 receptors are

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slightly different, and there are also differences between the 2, 6 receptors, which are all negative effects. If the authors want to narrate, they should also check the literature in detail and describe clearly.[1] Specific details evaluation: 1、In the “Abbreviations”, “Vascular Endothelial Growth Factor C, VAGFC”is wrong. Final conclusion：Accepted after modification

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 73148

Title: KAI1/CD82 gene and autotaxin-lysophosphatidic acid axis in gastrointestinal cancers

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00053419
Position: Editorial Board
Academic degree: PhD
Professional title: Professor
Reviewer's Country/Territory: Spain
Author's Country/Territory: China

Manuscript submission date: 2021-11-11

Reviewer chosen by: Jing-Jie Wang

Reviewer accepted review: 2022-02-03 07:51

Reviewer performed review: 2022-02-03 08:59

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] 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

Some of my questions have been properly addressed. However, there are still a couple of points that must be reviewed by the authors. 1. Regarding the issue: "KAI1/CD82 is presented as a factor that can down regulate HGF (page 12) while it induces up-regulation of HGF-induced Sprouty2 (page 13). This apparent contradiction deserves some discussion", the two sentences in the text are: "KAI1 may inhibit the metastasis of PANC1 and MiapACA-2 PC cells by downregulating Hepatocyte growth factor (HGF)." "Mu et al found that KAI1/CD82inhibits the migration of HCC cells by upregulating HGF-induced Sprouty2[125]." If from the second sentence the reader should understand that Sprouty up-regulation occurs through a mechanisms involving the increase of HGF then, there is an apparent inconsistency, please revise. 2. The Human Protein Atlas is an outstanding initiative associated to the Human Proteome Project that has made available valuable information about functional and pathological aspects of about 17,000 proteins. In particular, based on the expression levels of these proteins in healthy and diseased tissues, they are able to propose scores that suggest the prognostic value of proteins in diseases. As I pointed out in my previous comment, CD82 has not prognostic value in cancer, according to their analysis. My suggestion is to mention this data and to discuss accordingly the data from the author's studies.