

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 81996

Title: ENTPD1-A -miR-144-3p-mediated high expression of CO₂ Y correlates with poor prognosis and macrophage infiltration in gastric cancer

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05754965

Position: Peer Reviewer

Academic degree: PhD

Professional title: Postdoc

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2022-12-07

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-12-14 19:17

Reviewer performed review: 2022-12-17 18:28

Review time: 2 Days and 23 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous
	Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No

SPECIFIC COMMENTS TO AUTHORS

In this manuscript, authors combined bioinformatics with wet lab experiments validation to reveal an ENTPD1-AS1/miR-144-3p/COL5A2 axis in gastric cancer. Firstly, they checked the expression level of COL5A2 in diverse cancer types and found COL5A was upregulated in GC and predicted a worse survival of GC patients. Then, TCGA data proved this point. Next, they identified miR-144-3p was an upstream regulator of COL5A and could be sponged by a lncRNA ENTPD1-AS1. Finally, they demonstrated that COL5A expression was associated with macrophage infiltration. Here I have several comments for the authors. (1) A major issue is that the main regulatory relationships between miR-144-3p/COL5A2, and ENTPD1-AS1/miR-144-3p need to be validated by experiments. Solely in-silico analysis is not enough. (2) How is the physiological function of COL5A in immune cell (particularly macrophage) infiltration? This should be introduced in the background section. (3) The basic information and function of ENTPD1-AS1 and miR-144-3p need to be mentioned. (4) In the sentence of Abstract: The high expression of COL5A2 was positively linked to macrophage infiltration in GC. There should be a space between "COL5A" and "was".

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05754263

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2022-12-07

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-01-07 08:23

Reviewer performed review: 2023-01-09 07:27

Review time: 1 Day and 23 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

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

SPECIFIC COMMENTS TO AUTHORS

1. What is the content of ENTPD1-AS1 -- miR-144-3p and COL5A2 in cells? 2. The discussion focuses on the mechanism research. 3. The analysis of supplementary Table 1 is too simple. 4. Small sample size and sample inclusion criteria.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03769068

Position: Editorial Board

Academic degree: PhD

Professional title: Adjunct Professor, Professor

Reviewer's Country/Territory: Brazil

Author's Country/Territory: China

Manuscript submission date: 2022-12-07

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-01-08 20:50

Reviewer performed review: 2023-01-16 16:35

Review time: 7 Days and 19 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

I have now reviewed your paper and recognize the importance of your research question. Manuscript NO. 81996 aimed to gain insight into the upstream competing endogenous RNA regulatory mechanism and immune microenvironment related to COL5A2 in Gastric Cancer (GC). Manuscript formatting should be revised according to BPG guidelines. The main and short titles accurately reflect the major topic and content of the study. Overall, the Abstract should be further improved. Consider the Abstract as the section that will draw readers' attention to your manuscript. There is no clear delineation of the study's BACKGROUND. It would be interesting to bring data regarding GC itself and the already-established role of miRNAs and ncRNAs in this neoplasm. The "RESULTS" subsection should provide detailed important data from the research findings. Finally, the CONCLUSION subsection of the Abstract should further explore the limitations of the study and future prospects in the research field. The CoreTip should also contextualize the reader in the research question, present the most relevant findings and justify the relevance of the study (all in no more than 100 words).

The INTRODUCTION should be improved. There is a gap between the need to find

biomarkers that could benefit the detection and treatment of GC, the expression of COL5A2, and the aims of the study. The state-of-the-art of already known biomarkers in gastric cancer should be addressed. The study's AIM should also be clearly stated.

Please remember that if you are using an acronym, you must introduce it with full terminology in the first instance so your reader knows what it means. You can do this by giving the full term first and the shortened version in parentheses: "The Cancer Genome Atlas (TCGA)". The MATERIALS AND METHODS could be further detailed. The use of specific approaches and platforms should be justified. Most of the information concerning this section is mentioned alongside the RESULTS section. Which was the threshold criteria for the statistical significance of gene expression? "[RESULTS section] In line with previous studies, significantly high expression of COL5A2 was found in TCGA data and 27 paired specimens (Figures 2A and 2B)" - please cite the studies. Which was the nominal p-value for each enriched signaling pathway in KEGG? This data should be presented in Supplementary Table S2 (interesting results, by the way). Please, also cite the nominal p-value for the correlation between miR-1443p expression and GC survival in the main text. This issue should be addressed in the other sections as well. The DISCUSSION section is well organized. This section describes your main findings based on systematic theoretical analyses of the results. In the CONCLUSION, however, should further explore the limitations of the study and future prospects in the research field.