PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 90673

Title: METT promotes gastric cancer progression via sphingomyelin metabolism

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: 2023-12-11

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-12-17 13:44

Reviewer performed review: 2023-12-26 23:21

Review time: 9 Days and 9 Hours

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<th>Scientific quality</th>
<th>[ ] Grade A: Excellent</th>
<th>[ ] Grade B: Very good</th>
<th>[ ] Grade C: Good</th>
<th>[ ] Grade D: Fair</th>
<th>[ ] Grade E: Do not publish</th>
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<th>Novelty of this manuscript</th>
<th>[ ] Grade A: Excellent</th>
<th>[ ] Grade B: Good</th>
<th>[ ] Grade C: Fair</th>
<th>[ ] Grade D: No novelty</th>
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<th>Creativity or innovation of this manuscript</th>
<th>[ ] Grade A: Excellent</th>
<th>[ ] Grade B: Good</th>
<th>[ ] Grade C: Fair</th>
<th>[ ] Grade D: No creativity or innovation</th>
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I have now reviewed your paper and recognize the importance of your research question. Manuscript NO. 90673 aimed to elucidate the role of METTL5 in the progression of gastric cancer (GC). Here are some suggested revisions and feedback to enhance the “Abstract”: (1) Background: Consider integrating a brief overview of current treatment challenges or gaps in understanding molecular mechanisms in gastric cancer before introducing METTL5. It would be beneficial to specify the importance of m6A methylation in cancer biology to underscore METTL5’s relevance in this context. (2) Methodology: Provide additional details regarding the techniques used for correlating METTL5 with clinicopathological features, in vitro and in vivo experiments. Mention specific assays, cell lines, animal models, and statistical methods employed. Elaborate on the untargeted metabolomics approach used, outlining the methodology and analysis techniques applied. (3) Results: Specify the clinicopathological features significantly correlated with METTL5 expression. Quantify the degree of correlation between METTL5 expression and sphingomyelin metabolism alterations observed in the study. If available, present specific data or statistical analyses supporting findings related to
METTL5’s role in GC cell proliferation, migration, invasion, and cisplatin resistance. (4) Conclusion: Discuss potential clinical implications of targeting METTL5 as a therapeutic strategy in GC treatment, emphasizing its involvement in sphingomyelin metabolism and cisplatin resistance. “METHODS” section: The statement "The patients involved in our study never underwent treatment" lacks detail about the selection criteria or any specific characteristics of the patient cohort. This lack of information might affect the study’s applicability to broader patient populations or limit the understanding of treatment-naive patients' characteristics. Additionally, briefly mention the rationale behind specific assays or experiments where applicable. “RESULTS” section: Strengths: (1) The section covers various aspects of METTL5 in GC, including expression patterns, clinical correlations, functional analyses (knockdown and overexpression), potential mechanisms (sphingomyelin metabolism), in vivo experiments, and chemotherapy response, providing a broad understanding of METTL5's involvement in GC progression. (2) The utilization of multiple techniques such as bioinformatics (TCGA analysis), tissue microarrays, Western blot, qPCR, functional assays, LC-MS, and in vivo experiments adds depth to the investigation, offering a multi-faceted understanding of METTL5’s role in GC. Suggestions for improvement: (1) While the results mention significant findings (e.g., correlations, functional effects), specific statistical analyses, p-values, or measures of significance are not consistently provided. Including these statistical details will strengthen the credibility of the reported associations and findings. “DISCUSSION” section: Strengths: (1) The discussion thoroughly delves into the roles of METTL5 in GC, integrating findings from this study into the broader context of m6A biology, lipid metabolism, and chemotherapy resistance, providing a holistic understanding of METTL5’s potential impacts. (2) This section also effectively links the study's results on METTL5 expression, clinical correlations, functional effects, and sphingomyelin metabolism alterations to the existing literature on m6A modifications, illustrating the
significance of METTL5 in the context of GC biology. Suggestions for improvement: The discussion lacks detailed explanations about METTL5's role in sphingomyelin metabolism, requiring further insights into the mechanisms involved. Expanding on the study's limitations and proposing specific future research directions could strengthen its impact and guide subsequent studies. Additionally, a clearer summary of key findings and their clinical implications for gastric cancer prognosis, therapy, or future research is needed to enhance the conclusion's clarity and significance.