

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 68269

Title: Genome-wide map of N6-methyladenosine circular RNAs identified in mice model of severe acute pancreatitis

Reviewer's code: 03034197

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Serbia

Author's Country/Territory: China

Manuscript submission date: 2021-05-19

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-06-02 06:49

Reviewer performed review: 2021-06-05 09:04

Review time: 3 Days and 2 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 Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input 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 checked="" type="checkbox"/> Accept (General priority) <input 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

This is correctly conducted, well-designed, interesting animal study regarding genome-wide map of N6-methyladenosine circular RNAs identified in severe acute pancreatitis. Manuscript should be published.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 68269

Title: Genome-wide map of N6-methyladenosine circular RNAs identified in mice model of severe acute pancreatitis

Reviewer's code: 03087279

Position: Peer Reviewer

Academic degree: BSc, PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Greece

Author's Country/Territory: China

Manuscript submission date: 2021-05-19

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-05-19 20:57

Reviewer performed review: 2021-06-16 03:39

Review time: 27 Days and 6 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" 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 type="checkbox"/> Minor revision <input checked="" 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 type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Comments to the Authors In this research article, Wu et al. examined the expression of m6A circRNAs in severe acute pancreatitis (SAP), an inflammatory disease that displays a complex and unclear molecular etiology. Moreover, they conducted in silico and in vitro experiments using mice models in order to elucidate their biological roles in this disorder. The findings of the study are interesting, and shed light on the issue of circRNA epigenetics and their involvement in disease development. However, there are several issues that need to be addressed:

- Major issues:

1. Considering that the study was designed using animals (3 mice per group), the Authors need to specify this in the title and be more restrained in their comments regarding the Results of the study, avoiding strong arguments. In addition, generalizing of the conclusions should be avoided, since these results may not be applicable to SAP cases in humans. Authors are advised to conduct conservation analysis of the sequence of the selected circRNAs, in order to suggest that these circRNAs may have similar roles in human SAP.
2. In the “Library preparation” section of the Materials and Methods, the Authors conducted rRNA removal from total RNA. How was the efficacy of this procedure checked, were there any controls?
3. In order to have more robust evidence for the claims in this study, the top 10 upregulated and top 10 downregulated circRNAs according to the level of m6A need to be validated by qPCR experiments.
4. The expression level of ALKBH5 and FTO was measured only through Western blots. In order to further support these results, the corresponding mRNA levels of these molecules need to be examined. On that note, statements such as “These results indicated that ALKBH5 may play a key role in the dynamic process of m6A in SAP” are better avoided.
5. In the Discussion, it is stated that “... m6A circRNAs function in SAP through other mechanisms, such as [...] and interaction with RNA-binding proteins”. However, the interaction with

RNA-binding proteins (RBPs) was not examined in this study. Should the Authors decide to include this claim, at least an in silico prediction of RBP-binding sites needs to be conducted. • Minor issues: 1. Throughout the text, the 6 in N6-methyladenosine (m6A) should be corrected to an exponent 6, as it is the appropriate name structure. 2. In the Introduction, the Authors state that "...we determined the expression of demethyltransferase to deduce the possible mechanism...". This period is very vague and the molecules which are implied should be explicitly mentioned. 3. All abbreviated words (wk, bps etc.) should be replaced with the standard word, since they are not obvious to every reader. 4. In the Materials and Methods, Authors include an amylase and lipase measurement. The specific "commercial kits" used for the quantification should be mentioned. Moreover, the reason for conducting this assay is not clear and is explained only in the Discussion; it needs to be more evident earlier in the manuscript. 5. In the "Distribution of m6A sites in SAP and control groups" of the Results, it is mentioned that "circRNAs can be generated from any region of the genome, and all result in a great diversity of lengths". This statement is vague and can be confusing for the reader. In addition, the relevance of this claim to the genomic distribution of m6A circRNAs that is mentioned immediately after is unclear. 6. The limitations of this study should be clearly stated in the Discussion.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Manuscript NO: 68269

Title: Genome-wide map of N6-methyladenosine circular RNAs identified in mice model of severe acute pancreatitis

Reviewer's code: 03087279

Position: Peer Reviewer

Academic degree: BSc, PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Greece

Author's Country/Territory: China

Manuscript submission date: 2021-05-19

Reviewer chosen by: Yun-Xiaojian Wu

Reviewer accepted review: 2021-07-09 05:13

Reviewer performed review: 2021-07-09 14:49

Review time: 9 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
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
Peer-reviewer statements	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The Authors have adequately addressed the Reviewers' comments; the appropriate corrections were made, and the revised manuscript is significantly improved. The clarifications that are provided contribute to the coherence and quality of the study and all Figures are useful and comprehensible. Overall, the paper is well-written and contributes to the existing knowledge in its field. I have only one additional concern: some information that the Authors provide in their response to the Reviewers is not incorporated to the text; for example, the Table that shows the results of the conservation analysis and the paragraph that describes the rRNA removal efficacy examination need to be included in the manuscript.