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PEER-REVIEW REPORT

Name of journal: *World Journal of Hepatology*

Manuscript NO: 87666

Title: Metabolomics in Chronic Hepatitis C: Decoding Fibrosis Grading and Underlying Pathways

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04025443
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Doctor, Senior Researcher
Reviewer's Country/Territory: Russia
Author's Country/Territory: Brazil

Manuscript submission date: 2023-08-22

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-08-30 09:20

Reviewer performed review: 2023-08-30 11:52

Review time: 2 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [Y] Grade E: Do not publish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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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [Y] Grade D: No scientific significance
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 [ ] Major revision [Y] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Dear colleagues! I read with interest your manuscript "Metabolomics in Chronic Hepatitis C: Decoding Fibrosis Grading and Underlying Pathways", which is based on the original research. There are some major problems that does not allow to recommend the manuscript for publishing. 1. There is no description of the studied group (age, gender, BMI, disease duration, necroinflammatory activity, presence and grade of liver steatosis, habits of the subjects, their diet etc). As this information is lacking, the data cannot be reproducible. 2. There is a great number of factors (beside mentioned above) that can have an impact on the metabolite's profile in the subjects. A number of the confounders requires the greater sample size to enhance statistical power. 3. It is not clear, how fibrosis stage was established. In case of liver biopsy - what is the time between liver biopsy and taking a blood samples for metabolic profiling? 4. Selection criteria are not mentioned. Did you applied some? 5. The control group is lacking. This does not allow to judge whether variability may occur in "healthy" population 6. Conclusions are too vague and are not based on the results of the study. As the number of flaws is too high and some of them may hardly be fixed, I cannot recommend this

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manuscript for publishing. However, I hope that my comments will help you to plan further studies.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04072104
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Chief Doctor, Doctor, Occupational Physician, Research Scientist
Reviewer's Country/Territory: Japan
Author's Country/Territory: Brazil

Manuscript submission date: 2023-08-22

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-08-29 13:24

Reviewer performed review: 2023-09-05 13:07

Review time: 6 Days and 23 Hours

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

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] 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

It is an interesting manuscript about "Metabolomics in Chronic Hepatitis C: Decoding Fibrosis Grading and Underlying Pathways" My concern is determined in the following points. Some of the observed biomarkers, once validated, have the potential for application as prognostic biomarkers. Analyses based on liquid biopsy are quite less invasive, and blood plasma, once circulates through the whole body, contains biomarker representative of pathologies that have not yet manifested clinically. It is easier to understand if authors explain with a case example. Multisegment injection-capillary electrophoresis-mass spectrometry (MSI-CE-MS) and nuclear magnetic resonance (NMR) spectroscopy for characterizing the serum metabolome of patients with liver fibrosis in chronic hepatitis C virus (HCV) infection:both instrumental techniques enable rapid yet reliable quantification of serum metabolites in large-scale metabolomic studies with good overlap for biomarker replication. Advantages of MSI-CE-MS include greater metabolome coverage, lower operating costs, and smaller sample volume requirements, whereas NMR offers a robust platform supported by automated spectral and data processing software. Above mentioned methods associated with metabolomics should

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be referred to.