



PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 88568

Title: Circulating MicroRNA Expression and Nonalcoholic Fatty Liver Disease in Adolescents with Severe Obesity

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02937551

Position: Editorial Board

Academic degree: PhD

Professional title: Professor, Research Fellow

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2023-09-29

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-10-16 00:49

Reviewer performed review: 2023-10-27 03:31

Review time: 11 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 Grade E: Do not publish
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 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 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

This study indicates the differential expression of circulating miRNAs in adolescent NAFLD, suggesting that they may become diagnostic and prognostic biomarkers for NAFLD. However, there are two shortcomings. Firstly, the sample size is small and research needs to be conducted in a larger and more diverse populations. The second issue is that there has been no molecular mechanism validation of differentially expressed circulating miRNAs through cytology or animal experiments.



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Peer-review model: Single blind

Reviewer's code: 02546910

Position: Peer Reviewer

Academic degree: MD

Professional title: Chief Physician, Professor

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2023-09-29

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-11-03 01:54

Reviewer performed review: 2023-11-05 01:49

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
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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

So far, many studies have reported the relationship between microRNA and NAFLD, but there is poor consistency in the global published research and evaluation of human liver miRNA expression. There is limited research on the human liver. This study identified new circulating miRNAs and analyzed their expression in different pathological features of NAFLD, which have mechanisms to promote or alleviate the progression of NAFLD. This is a new exploration and has good innovation. This study is of great significance for the diagnosis and treatment of NAFLD. As a contributor to the pathogenesis of human NAFLD, novel miRNAs are expected to serve as biomarkers for the non invasive diagnosis and staging of NAFLD or hepatocellular carcinoma, or as targets for drug therapy, thereby preventing or reversing disease progression. The novel miRNA discovered in this study provides a new direction for targeted therapy of NAFLD. Due to the different types and quantities of miRNA expression at different stages of NAFLD, as well as differences in gender and whether obesity is present (such as obesity with NAFLD or lean individuals with NAFLD), further research is needed. Due to the relatively small sample size of this study, gender stratification studies were



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not conducted. Additionally, it would be better if specific miRNAs that reflect disease progression or deterioration could be identified.



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Peer-review model: Single blind

Reviewer's code: 03959944

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2023-09-29

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-10-31 08:43

Reviewer performed review: 2023-11-09 01:16

Review time: 8 Days and 16 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
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	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This study investigated miRNAs associated with NAFLD and identified several miRNAs worthy of attention. However, it is necessary to provide additional details about the methods employed and present more robust results to enhance the scientific validity of this study. 1. This reviewer is interested in the methods of acquiring miRNAs from plasma and the approach used for differential expression analysis of miRNAs. 2. Line283, it appears that there is confusion or ambiguity regarding “serum miRNA” and “plasma miRNA”. 3. Could you provide some images related to the histological features of NAFLD? 4. The current study identified several novel miRNAs that may serve as biomarkers for NAFLD. However, as mentioned in the manuscript's limitations, these results were based on a small sample size. Therefore, this reviewer is interested in knowing whether these miRNAs show differential expression at the RT-qPCR level?