

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Hepatology*

**Manuscript NO:** 84188

**Title:** Role of VEGFB in nonalcoholic fatty liver disease and its potential value

**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05270042

**Position:** Editorial Board

**Academic degree:** PhD

**Professional title:** Assistant Professor

**Reviewer's Country/Territory:** Viet Nam

**Author's Country/Territory:** China

**Manuscript submission date:** 2023-03-06

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2023-03-13 10:03

**Reviewer performed review:** 2023-03-20 10:44

**Review time:** 7 Days

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 Grade E: Do not publish
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 type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

<b>Scientific significance of the conclusion in this manuscript</b>	<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
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	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 manuscript contained a good clinically application, which showed the role of VEGFB in nonalcoholic fatty liver disease and its value. 1. In the introduction, the author should write concisely about the epidemiological status of NAFLD, the specific characteristics of NAFLD in each area, complications of NAFLD, mechanisms of complications, introduction of the main mechanisms and roles of VEGFB in the progression of NAFLD. 2. The 'multiple-hit' mechanism was important, but the author did not mention clearly. Instead, the author stated too much about the mechanism of 'first-hit'. The author should not mention old opinions (from 2008) which become inaccurate. Authors should succinctly discuss key points and from new research. 3. In the 'multiple-hit' section, the author should elaborate more on adipocyte dysfunction and cell apoptosis. 4. Some studies provide ideas against the author's opinions such as the regulatory role of VEGFB in obesity, diabetes and other diseases. The author needs to explain more clearly these issues.

**Response 1:** In this review, we first described the role of VEGFB in regulating lipid metabolism in the AMPK signaling pathway, then explained the anti-inflammatory role of VEGFB in NAFLD, and finally elaborated on the role of VEGFB in influencing glucose metabolism by regulating insulin resistance.

**Response 2:** The suggestions of the reviewers have provided us with new ideas. In this review, we have improved the research on the specific mechanism of VEGFB participating in the "multiple hits" of NAFLD. Among them, insulin resistance, as a key point in the "multiple hits", is the first step in the occurrence and development of NAFLD. We will elaborate on the current research about VEGFB participating in insulin resistance via AMPK and PI3K signaling pathways, and further describes the relationship between VEGFB's involvement in lipid metabolism (first hit) and inflammatory response (second hit) in NAFLD by regulating insulin resistance.

**Response 3:** We supplemented the research on the role of adipocyte dysfunction and cell apoptosis in NAFLD in the "multiple hits" theory of NAFLD, and described the role of VEGFB in regulating adipocyte dysfunction and cell apoptosis.

**Response 4:** At present, the role and mechanism of VEGFB in regulating NAFLD are not fully understood and are controversial. In the final part of this review, we concluded the different studies that have not shown a positive role of VEGFB in regulating lipid metabolism and insulin resistance. Based on these views, it will further trigger more research focuses to explore the regulatory mechanism of VEGFB in the occurrence and development of NAFLD, which will provide a new idea for the study of pathophysiological mechanisms and therapeutic targets of NAFLD.

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**Peer-review model:** Single blind

**Reviewer's code:** 03940557

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** Turkey

**Author's Country/Territory:** China

**Manuscript submission date:** 2023-03-06

**Reviewer chosen by:** Geng-Long Liu

**Reviewer accepted review:** 2023-03-28 08:41

**Reviewer performed review:** 2023-04-05 09:41

**Review time:** 8 Days and 1 Hour

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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<b>Scientific significance of the conclusion in this manuscript</b>	<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
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	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

Manuscript is acceptable in present form.

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**Peer-review model:** Single blind

**Reviewer's code:** 03671529

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Assistant Professor, Senior Lecturer

**Reviewer's Country/Territory:** Russia

**Author's Country/Territory:** China

**Manuscript submission date:** 2023-03-06

**Reviewer chosen by:** Geng-Long Liu

**Reviewer accepted review:** 2023-03-28 16:40

**Reviewer performed review:** 2023-04-09 15:51

**Review time:** 11 Days 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
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<b>Peer-reviewer statements</b>	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

A very interesting review. As a small remark, it can be noted that all abbreviations would be deciphered in the text at the first use.

**Response :** Thank you very much for the feedback from the reviewers. We have carefully reviewed the full name issue of abbreviations and made all corrections.