

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 82127

Title: Insulin resistance and adipose tissue interactions as the cornerstone of metabolic (dysfunction)- associated fatty liver disease pathogenesis

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02536349

Position: Editorial Board

Academic degree: MD

Professional title: Doctor, Professor

Reviewer's Country/Territory: Turkey

Author's Country/Territory: Mexico

Manuscript submission date: 2022-12-06

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-12-06 12:43

Reviewer performed review: 2022-12-08 08:54

Review time: 1 Day and 20 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 Grade E: Do not publish
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
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



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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

Thank you for the understandable update and the appropriate format of the review. Just correct "unseful" to "useful", "preexissting" to "pr-existing" and abbreviation of metabolic syndome to "MetS" instead of "MS".

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03536702

Position: Editorial Board

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Mexico

Manuscript submission date: 2022-12-06

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-01-04 05:01

Reviewer performed review: 2023-01-11 05:44

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 type="checkbox"/> Grade B: Good <input checked="" 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 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
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 manuscript provides a review on MAFLD, its pathogenesis and some related mechanisms. It is well written but I have the following suggestions for the authors: 1. The title of the manuscript did not well cover the content, especially the content about the commodities in MAFLD. Please revise it. 2. Some descriptions or statements are not accurate. For example, "The same effect is achieved through suppression of adipose tissue lipolysis in insulin resistant states, increasing fatty acid influx into the liver", I think it should be 'impaired suppression'; "For instance, alterations in the peroxisome proliferator-activated receptor α (PPAR- α), which serves as a FFA sensor, leads to decreased fatty acid catabolism and intrahepatic lipid accumulation", what do the alterations mean, activated or inactivated? Please make it clear to the readers as activation of PPAR- α promotes to peroxisomal beta-oxidation of fatty acids by promoting expression of the ACOX1 and P450 genes; "An additional feature of irisin is FFA oxidation, which is a method for lipid removal from ectopic tissue; this will later be explained in the IHTC section". 3. The manuscript needs some editing work. There are some typos or grammatic problems. For example, "unseful" should be "useful". Please

carefully check through the manuscript. 4. Some abbreviations are not defined. For example, AT, WNT. Please define it before use.

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Title: Insulin resistance and adipose tissue interactions as the cornerstone of metabolic (dysfunction)- associated fatty liver disease pathogenesis

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06457446

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Mexico

Manuscript submission date: 2022-12-06

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-01-03 11:58

Reviewer performed review: 2023-01-12 09:21

Review time: 8 Days and 21 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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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 review focuses on insulin resistance of different tissues, together support the epidemiological association between insulin resistance and MAFLD. Somehow, this review provides a valuable point on MAFLD. The discussion is comprehensive, however, some parts might be too brief to bring a persuasive point. 1. In Page 6, the authors said “the “glucentric” view of insulin resistance has shifted to the “lipocentric” view”. Please discuss more details and add the references. 2. Browning of adipose tissue showed abundant association with NAFLD, but the discussion in the review is limited. This part could be expanded. 3. Insulin signaling promotes DNL, but how IR promotes this process? The relative discussion about the mechanism could be added. 4. The authors discussed the relationship between MAFLD and CKD, and mainly on the mutation of PNPLA3. Whether other genes involved in the regulation?