



PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 78029

Title: Noncoding RNAs as additional mediators of epigenetic regulation in nonalcoholic fatty liver disease

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 01805500

Position: Editorial Board

Academic degree: CCST, MD

Professional title: Adjunct Professor, Professor, Research Scientist, Senior Researcher, Senior Scientist, Teacher

Reviewer's Country/Territory: Italy

Author's Country/Territory: France

Manuscript submission date: 2022-07-15

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-07-15 10:34

Reviewer performed review: 2022-07-15 16:47

Review time: 6 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 Grade E: Do not publish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 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

Author should be congratulated for approaching an interesting topic, but to give readers a broader view of the issue, some points should be added. Recent findings link the mitochondrial sirtuin SIRT4 with cellular senescence, skin aging, and mitochondrial dysfunction, one of the main mechanisms inducing and worsening NAFLD. Authors observed that inhibition of miR-15b, in a SIRT4-dependent manner, increased generation of mitochondrial reactive oxygen species, decreased mitochondrial membrane potential, and modulated mRNA levels of nuclear encoded mitochondrial genes and components of the senescence-associated secretory phenotype ...as evident in....MicroRNA-15b regulates mitochondrial ROS production and the senescence-associated secretory phenotype through sirtuin 4/SIRT4. Aging (Albany NY). 2016 Mar;8(3):484-505. doi: 10.18632/aging.100905. PMID: 26959556; PMCID: PMC4833141. Recently, several human and animal studies have emphasized the involvement of senescence in the pathogenesis and development of liver steatosis including the progression to NASH as characterized by the additional emergence of inflammation, hepatocyte ballooning, and liver fibrosis, as evident in....The Role of Senescence in the Development of Nonalcoholic Fatty Liver Disease and Progression to Nonalcoholic Steatohepatitis. Hepatology. 2020 Jan;71(1):363-374. doi: 10.1002/hep.30834. Epub 2019 Dec 18. PMID: 31230380. This aspect raises much interest in the light that sirtuin 4 plays a central role in the manic-morbidity of NAFLD. In fact, up-to-date study shows low circulating levels of SIRT4 in obese patients with NAFLD mirroring its reduced mitochondrial expression in an attempt to increase the fat oxidative capacity and then the



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mitochondrial function in liver and in muscle. SIRT4 modulates the metabolism of free fatty acids reducing their high circulating levels but, unfortunately, increasing ROS production. Great concentration of free fatty acids, released by adipose tissue, coupled with oxidative stress, directly results in endothelial dysfunction, early atherosclerosis, and coronary artery disease risk factor.



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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: France

Manuscript submission date: 2022-07-15

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-07-15 08:14

Reviewer performed review: 2022-07-16 07:34

Review time: 23 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 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



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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
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SPECIFIC COMMENTS TO AUTHORS

Thank you for the work you have done. I agree for publication of the review.



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Peer-review model: Single blind

Reviewer's code: 00159305

Position: Editorial Board

Academic degree: AGAF, FEBG, FRCP, MD

Professional title: Professor

Reviewer's Country/Territory: Romania

Author's Country/Territory: France

Manuscript submission date: 2022-07-15

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-07-17 19:24

Reviewer performed review: 2022-07-18 04:54

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
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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
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SPECIFIC COMMENTS TO AUTHORS

A concise, comprehensive, complex and well structured manuscript. There are no grammatical/spelling errors throughout the manuscript and the topic debated is of a great interest due to the fact that NAFLD prevalence is increasing and new data regarding the understanding of NAFLD pathogenesis are needed for a better management in the future.