

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 52092

**Title:** LB100 ameliorates nonalcoholic fatty liver disease via the AMPK / Sirt1 pathway

**Reviewer's code:** 03478516

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Professor

**Reviewer's country:** Italy

**Author's country:** China

**Reviewer chosen by:** Artificial Intelligence Technique

**Reviewer accepted review:** 2019-10-16 09:17

**Reviewer performed review:** 2019-10-18 10:20

**Review time:** 2 Days and 1 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

Authors are kindly requested to compare their results with those below presented:



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SIRT4 could exert its tumor suppressive function in HCC by inhibiting glutamine metabolism and thereby increasing the adenosine diphosphate (ADP)/AMP levels to phosphorylate AMPK $\alpha$  by LKB1, which blocks the mTOR signaling pathway, as evident in Hepatology Volume 69, Issue 4 Sirtuin 4 Depletion Promotes Hepatocellular Carcinoma Tumorigenesis Through Regulating Adenosine - Monophosphate-Activated Protein..... and..... Oxid Med Cell Longev. 2014;2014:920676. doi: 10.1155/2014/920676. Epub 2014 Jun 17. Circulating levels of sirtuin 4, a potential marker of oxidative metabolism, related to coronary artery disease in obese patients suffering from NAFLD, with normal or slightly increased liver enzymes

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

##### ***BPG Search:***

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 52092

**Title:** LB100 ameliorates nonalcoholic fatty liver disease via the AMPK / Sirt1 pathway

**Reviewer's code:** 03664977

**Position:** Editorial Board

**Academic degree:** FAASLD, MD, PhD

**Professional title:** Professor

**Reviewer's country:** Thailand

**Author's country:** China

**Reviewer chosen by:** Artificial Intelligence Technique

**Reviewer accepted review:** 2019-10-19 00:46

**Reviewer performed review:** 2019-10-19 01:24

**Review time:** 1 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

Dear Authors WJG Manuscript ID – WJG 52092 Manuscript Title: LB100 ameliorates

nonalcoholic fatty liver disease via the AMPK / Sirt1 pathway Manuscript type: Basic Study Reviewer's comment 1. The current study focus on the LB-100 which's a serine/threonine protein phosphatase 2A (PP2A) inhibitor, is closely related to IR. Interestingly, in fatty liver mice model, LB100 showed the benefit of improving FFA-induced lipid accumulation in L02 cells through the AMPK/Sirt1 signaling pathway. This's the first finding to demonstrate a probable therapeutic strategy for NAFLD. Currently, there are few studies mentioned about the role of AMPK / Sirt1 pathway and therapeutic potentials in NAFLD.1-4 2. Additionally, previous studies showed that the well-known medication for example Metformin<sup>5, 6</sup> may have a role on Sirt1 and AMPK activations, thus the authors should clarify what's new of the efficacy of LB-100 in comparison to MFM on Sirt1 and AMPK pathways. 3. Regarding on PP2A; there were few information of the<sup>7</sup> Autophagy which played an important role in lipid catabolism (lipophagy). Previous study showed that the elevated levels of methionine and SAME activated PP2A by methylation. Can the author link the association of your results with previous study? Oct 19, 2019 References 1. Zhang J, Zhang SD, Wang P, et al. Pinolenic acid ameliorates oleic acid-induced lipogenesis and oxidative stress via AMPK/SIRT1 signaling pathway in HepG2 cells. *Eur J Pharmacol* 2019;861:172618. 2. Wang Y, Zhao H, Li X, et al. Tangshen Formula Alleviates Hepatic Steatosis by Inducing Autophagy Through the AMPK/SIRT1 Pathway. *Front Physiol* 2019;10:494. 3. Teng W, Zhao L, Yang S, et al. The hepatic-targeted, resveratrol loaded nanoparticles for relief of high fat diet-induced nonalcoholic fatty liver disease. *J Control Release* 2019;307:139-149. 4. Banerjee J, Bruckbauer A, Zemel MB. Activation of the AMPK/Sirt1 pathway by a leucine-metformin combination increases insulin sensitivity in skeletal muscle, and stimulates glucose and lipid metabolism and increases life span in *Caenorhabditis elegans*. *Metabolism* 2016;65:1679-1691. 5. Li Q, Jia S, Xu L, et al. Metformin-induced autophagy and irisin improves INS-1 cell function and survival in high-glucose



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environment via AMPK/SIRT1/PGC-1alpha signal pathway. 2019;7:1695-1703. 6. Doan KV, Ko CM, Kinyua AW, et al. Gallic acid regulates body weight and glucose homeostasis through AMPK activation. Food Sci Nutr 2015;156:157-68. 7. Zubiete-Franco I, Garcia-Rodriguez JL, Martinez-Una M, et al. Methionine and S-adenosylmethionine levels are critical regulators of PP2A activity modulating lipophagy during steatosis. J Hepatol 2016;64:409-418.

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

- ☐ The same title
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- ☐ Plagiarism
- ☐ No

##### ***BPG Search:***

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 52092

**Title:** LB100 ameliorates nonalcoholic fatty liver disease via the AMPK / Sirt1 pathway

**Reviewer's code:** 02941525

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Professor

**Reviewer's country:** Italy

**Author's country:** China

**Reviewer chosen by:** Artificial Intelligence Technique

**Reviewer accepted review:** 2019-10-19 20:54

**Reviewer performed review:** 2019-10-19 22:29

**Review time:** 1 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

In this well designed study, authors demonstrated that LB100 can play an important role



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in liver lipid metabolism to prevent HFD-induced obesity, hepatic steatosis and IR in a NAFLD mouse model. LB100 reduced hepatic lipogenesis and promoted fatty acid  $\beta$ -oxidation via the AMPK/Sirt1 pathway in HFD-fed mice. These findings provide compelling evidence supporting LB100 as a promising therapeutic for NAFLD.

#### **INITIAL REVIEW OF THE MANUSCRIPT**

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- ☐ No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 52092

**Title:** LB100 ameliorates nonalcoholic fatty liver disease via the AMPK / Sirt1 pathway

**Reviewer's code:** 02926997

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Associate Professor

**Reviewer's country:** Iran

**Author's country:** China

**Reviewer chosen by:** Artificial Intelligence Technique

**Reviewer accepted review:** 2019-10-20 04:33

**Reviewer performed review:** 2019-10-20 05:18

**Review time:** 1 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
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## SPECIFIC COMMENTS TO AUTHORS

As a clinician, i need the data on liver histology including quantification of fibrosis at the





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end of experiment. Quantification of fatty acid in liver cell is the primary insult in the NAFLD pathway.

#### **INITIAL REVIEW OF THE MANUSCRIPT**

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