

Format for ANSWERING REVIEWERS

October 24, 2014



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 12261-review.doc).

Title : Chronic alcohol consumption potentiates the development of diabetes through pancreatic β -cell dysfunction

Author : Ji Yeon Kim, Dae Yeon Lee, Yoo Jeong Lee, Keon Jae Park, Kyu Hee Kim, Jae Woo Kim, and Won-Ho Kim

Name of Journal : *World Journal of Biological Chemistry*

ESPS Manuscript NO : 12261

Thank you very much for your letter asking to revise our manuscript (#12261). The manuscript has been revised according to the suggestions made by the reviewers. Firstly, this manuscript was reviewed and edited by American Journal of Experts. I believe the revised manuscript has improved satisfactorily and hope it will be accepted for publication in *World Journal of Biological Chemistry (WJBC)*. The following is a synopsis of the changes made as a result of the reviewers' comments:

1. Format has been updated

- (1) In title page, we have changed the address and added the postcode in the address.-----"Division of Metabolic Disease, Center for Biomedical Science, National Institutes of Health, #187 Osong Saengmyeong2-ro, Osong-eup, Heungdeok-gu, Cheongju, Chungbuk 363-700, Korea"
- (2) Co-author Dr. Jae Woo Kim was added. He is contributed for the review and edit of the manuscript.
- (3) We have enhanced the clarity and style of the manuscript by making grammar and spelling corrections and by improving the phrasing.
- (4) We have also edited and corrected the use of preposition, the use of article, and simplification of awkward phrasing throughout the manuscript.
- (5) The manuscript was reviewed and edited by American J of Experts.

2. Revision has been made according to the suggestions of the reviewer

(1) Reviewer 1

	Reviewer comments	
1	a) p.7 it is stated that ethanol increases NADH/NAD ⁺ ratio which is responsible for ROS production by the entry of NADH into respiratory chain. This requires modification because the increase in ROS production is	a) According to reviewer's suggestions, we have changed the sentence to clarify the relationship between the increase of NADH/NAD ⁺ ratio and ROS production via ethanol metabolism and oxidation.

	<p>not due to the oxidation of NADH but due to defect of respiratory chain complexes mainly complex I & III.</p> <p>b) several publications over the past few years have received a lot of attention about a physiological role of UCPs in suppressing oxidative stress and in diabetes. In other words, insulin secretion depends on ATP/ADP ratio & thus mitochondrial coupling. It is worth raising the role of mitochondrial uncoupling (mediated through UCP2 activity), ROS production and insulin secretion.</p> <p>c) p. 15 how can ethanol induces ROS production through mitochondrial dysfunction.</p> <p>d) peroxynitrite (ONOO?) is formed from superoxide anion (O₂⁻) reaction with nitric oxide (NO). The peroxynitrite-mediated regulation raised in this review is attributed only to the NOS activity and lacking the superoxide generation mechanism</p> <p>e) “The peroxynitrite-mediated GSK down regulation or inactivation may induce the perturbation of glucose metabolism and cellular antioxidant defense mechanisms....”. How can down regulation of GSK affect antioxidant defense.</p>	<p>- Page 7, line 8- Page 8, line 8</p> <p>b) As you have suggestions, the physiological role of UCPs, especially, UCP2, in pancreatic beta cells is very important. So, we have described the possibility of UCP2 associated with ethanol consumption-mediated pancreatic beta cell dysfunction and apoptosis (page 16, line 23- page 17, line 12).</p> <p>c) ROS production by ethanol was associated with the mitochondrial dysfunction through the alteration of NADH oxidation, results in defects of respiratory chain complexes. Page 7, line 8- Page 8, line 16</p> <p>d) We have suggested the superoxide generation mechanisms in page 8, line 4-16. As well, we have described the sensitivity of ROS on pancreatic beta cells (page 15, line 21- page 16, line 3).</p> <p>e) According to your pointing, we have demonstrated that ethanol consumption-induced peroxynitrite induced GSK downregulation, which is correlated with the reduction of ROS production. These events are strongly attenuated by the treatment of antioxidants. So, we have suggested that peroxynitrite-mediated GSK downregulation may be associated with the perturbation of antioxidant defense system. Described in pages 23 : line 14-22.</p>
2	The review contains a lot of abbreviations; addition of abbreviation section would be helpful for the reader.	The abbreviation section was added. Page 26
3	typing mistakes	The typing mistakes are corrected over all of manuscript. Reviewed and edited by American J of Experts.

(2) Reviewer 2

	Reviewer comments	Answer for reviewer comments
1	In this review, the authors discussed extensively the potential links among alcohol consumption, type 2 diabetes and beta cell	As your suggestions, we have reviewed and corrected the language including grammar, misused word, and

	function. It is without doubt that the authors have conducted extensive research in this area to make this manuscript potential a valuable contribution to the field of metabolic research. However, the overall article is greatly hindered by the language, including misused word and inappropriate connecting word. The overall article is felt like a direction translation from a Korean article. Clearly extensive editing is needed before this review can be accepted for publication.	inappropriate connecting word. To this, the manuscript was reviewed and edited by American Journal of Experts.
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(6) Reviewer 3

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	Reviewer comments	Answer for reviewer comments
1	<p>The manuscript by Kim et al. reviews recent studies on the association between chronic alcohol consumption and beta cell dysfunction. The manuscript is interesting for the readers of the journal.</p> <p>However, authors should correct the abundant spelling and grammar mistakes.</p> <p>In addition, I recommend the authors to erase the references to Korea, since this is a global issue.</p>	<p>As your suggestions, we have reviewed and corrected the language including grammar, misused word, and inappropriate connecting word. To this, the manuscript was reviewed and edited by American Journal of Experts.</p> <p>As your pointing, we have changed from Korea to Worldwide in abstract and introduction.</p>

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

Won Ho Kim