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PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

Manuscript NO: 61279

Title: Vascular endothelial growth factor B inhibits insulin secretion in MIN6 cells and reduces Ca^{2+} and cyclic adenosine monophosphate levels through PI3K/AKT pathway

Reviewer's code: 05087664
Position: Peer Reviewer
Academic degree: PhD
Professional title: Senior Scientist
Reviewer's Country/Territory: Italy
Author's Country/Territory: China

Manuscript submission date: 2020-12-08
Reviewer chosen by: Ya-Juan Ma
Reviewer accepted review: 2020-12-24 08:21
Reviewer performed review: 2020-12-30 13:36
Review time: 6 Days and 5 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [ ] Anonymous [Y] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

By using the mouse MIN6 pancreatic cell line, Jia and colleagues describe a potential role of VEGF-B signaling in promoting insulin resistance through suppression of the PI3K/AKT pathway in a paracrine way. They found that administration of VEGF-B to cells impaired insulin secretion, by regulating Ca and AMPc levels, as a possible consequence of reduced activation of the PI3K/AKT pathway. On the opposite, by knocking down the VEGF-B gene, insulin secretion was restored along with increased activation of AKT pathway members. This effect seems to go via the VEGFR1 receptor. To this reviewer, the results are quite interesting and clearly presented. However, a few recommendations might be considered before publication. 1. Some English revision would be beneficial. 2. Briefly explain in the abstract background why the VEGF pathway (specifically VEGF-B) is important in the context of beta-cell function. 3. In the abstract/introduction it would be maybe worth mentioning the pro-proliferative effect that VEGF-B had on these cells. 4. It would be important to verify the specificity of VEGF-B signaling in promoting the observed effects by selective KD of VEGFR1 versus VEGFR2, for example. Also, it could be interesting to see whether stimulation with VEGF-A might have, or have not, similar activity. 5. The authors should check the phosphorylation status of VEGFR1, along with the expression levels. 6. It would be better to use non-saturated WB images to appreciate the differences between samples and control (e.g. Fig 2A and Fig 3D). 7. In all figures, authors should indicate p value significance by asterisk above the graph bars (in comparison to the control) instead of letters. In the figure legend, they should also mention what statistical test was used. 8. In figure 1 it is not clear that 5.5 and 25 mmol/L refer to glucose treatment.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Diabetes

Manuscript NO: 61279

Title: Vascular endothelial growth factor B inhibits insulin secretion in MIN6 cells and reduces Ca^{2+} and cyclic adenosine monophosphate levels through PI3K/AKT pathway

Reviewer's code: 05087664
Position: Peer Reviewer
Academic degree: PhD

Professional title: Senior Scientist

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2020-12-08

Reviewer chosen by: Chen-Chen Gao

Reviewer accepted review: 2021-01-26 09:00

Reviewer performed review: 2021-01-26 09:06

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer statements	Peer-Review: [ ] Anonymous [Y] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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To this reviewer the authors have adequately answered to all raised concerns.