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Round 1

Dear Editor

Enclosed please find the **replies to the questions raised by the reviewers** concerning this manuscript. The changes made in the manuscript have been **highlighted in red** on the text of the manuscript.

This manuscript has been proofread by an expert in English language before submission.

I would like to thank the reviewers and editors for their suggestions to improve this manuscript.

In advance, thank you for **conditionally accepting** this manuscript for publication.

Yours sincerely,

Prof. Leandro Bueno Bergantin, Ph.D.

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REVIEWER #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The proposed review manuscript by Bergantin aimed to present an overview of the basic mechanisms and clinical link between diabetes and inflammatory diseases emphasizing the role of Ca²⁺/cAMP signaling. My general opinion on the manuscript is that the review is well written, but some sub-sections of section 2.2. can be extended.

Reply: Your request has been attended (highlighted in red on the text of the manuscript).

REVIEWER #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The author's purpose of the investigation is very interesting, also for scientists from related research fields. I would recommend the suggestions described below:

1) The title should be short and concise. **Reply:** Your request has been attended (highlighted in red on the text of the manuscript).

According to recent studies that would favor future citations to the paper. What is really new in the paper? The role of CCBs? **Reply:** As a novelty, this revised article also included: 1) a timeline of the major events in Ca²⁺/cAMP signalling field; 2) considering COVID-19 is an emerging and rapidly evolving situation, this article also discussed recent reports about the role of Ca²⁺ channel blockers for preventing Ca²⁺ signalling disruption due to COVID-19, including the correlation between COVID-19 and diabetes.

2) At the end of the intro, it also not clear what is the main message and relevant points of the paper that should be emphasize at this stage. **Reply:** Your request has been attended (highlighted in red on the text of the manuscript).

3) I would like to make the following suggestion: a figure or scheme with the chronology or a timeline of the major events in the field would be interesting and usual for a better understanding of the paper. Moreover, this timeline will also reflect the understanding of the authors about these events. This personal view timeline will be interesting and also pedagogical for the others researchers and professors in the field as well as also for medical scientists.

Reply: Your request has been attended (highlighted in red on the text of the manuscript).

4) The review contain about 22% of references in the last 4 years. However this percentage should be higher. For instance, including recent papers about the role of CCBs for preventing calcium disruption due to COVID, among others examples.

Reply: Your request has been attended (highlighted in red on the text of the manuscript).

5) Globally conclusions should followed the order of presentation of the paper with partial conclusions first and then global conclusions. It is not clear why the author include in the conclusion a table with CCBs.

Reply: Your request has been attended (highlighted in red on the text of the manuscript). This table has been moved to section 3.2.

Science editor:

1 Scientific quality: The manuscript describes a review of the common issues among diabetes and inflammatory diseases. The topic is within the scope of the WJD. (1) Classification: Two Grades B; (2) Summary of the Peer-Review Report: The author's purpose of the investigation is very interesting, also for scientists from related research fields. The questions raised by the reviewers should be answered; and (3) Format: There is 1 table and 1 figure. A total of 90 references are cited, including 20 references published in the last 3 years. There are 11 self-citations. 2 Language evaluation: Classification: Two Grades B. No language editing certificate was provided. 3 Academic norms and rules: No academic misconduct was found in the Bing search. 4 Supplementary comments: **This is**

an invited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJD.

5 Issues raised:

(1) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

Reply: Your request has been attended.

(2) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout.

Reply: Your request has been attended.

6 Recommendation: Conditional acceptance.

Round 2

Dear Editor, This author has attended the Reviewer#1 suggestion, the section 2.2 has been extended, please see in the manuscript the section 2.2.7 'Diabetes and COVID-19'. In addition, Reviewer #2 recommended 'Accept (High priority)'. Nonetheless, if the Editor still wants that the section 2.2 be extended, please be more specific, highlighting which sub-section of section 2.2 needs to be expanded. Thank you. Yours sincerely, Prof. Leandro Bueno Bergantin, Ph.D.