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y Políticas de Salud
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Lian-Sheng Ma,

Science Editor,
Company Editor-in-Chief,
Editorial Office
World Journal of Diabetes

Esteemed Editor Lian-Sheng Ma,

First of all, we would like to thank you and the reviewers for enriching the content and the scope of this publication, as well as to let you know that the manuscript has been extensively revised and edited in response to the observations made by yourself and the reviewers.

We highlighted all the modifications made to the manuscript. Here, we comment on some of these modifications.

Reviewer #1

A separate analysis (in methods, results and discussion) between type 1 and type 2 diabetes is mandatory+++. At the present time the paper is complex and a little confusing. Other specific types of diabetes can be omitted but this must be indicated in the methods; I am surprised by the lack of genetic / genomic biomarkers Rem: to my knowledge most of B cells and in the tail and not in the head of pancreas

We thank the reviewer for the suggestion of making a separate analysis for T1DM and T2DM. In response, we have included the classification of the research articles in all the tables (1-3), in which T1DM appears in green and T2DM in violet. This allows the readers to identify immediately which biomarker corresponds to each type of DM. Furthermore, we incorporate new paragraphs —in the introduction, methods, results and discussion— to point out the classification. All the new text is highlighted in yellow.

In table 2, we added a new column with the chronic complications, since we demonstrated that the biomarkers play a role in T1DM to predict complications, as well as to prevent metabolic syndrome in TDM2.

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Our main focus is in the early and late damage of the β-cells, with the purpose of addressing the physiopathology of the diabetes, and the evolution of complications and comorbidities in pediatric population. Beyond the type of diabetes, the essential thing is to identify the mechanisms of damage to understand the pathophysiology, and to be able to control and prevent complications in the short, medium and long term.

The challenge is to find a target molecule that serves as a biomarker of early beta cell failure and, simultaneously, as a therapeutic target. Currently there is intense research being carried out with the hopes of finding this type of biomarker; also, in the clinical practice there are up to 22 different laboratory studies being used to evaluate patients at risk of metabolic syndrome.

This study presents the advances in research on β cell failure biomarkers, so that there is a scientific panorama of the subject, including the novelties such as the RIAO biomarker.

Through our search strategy, the only genetic biomarkers that were found are reported in Tables 1-3. It should be remembered that our objective is the study of biomarkers related to beta cell failure in the pediatric population.

We appreciate the clarification that β cells are found primarily in the tail and not the head of the pancreas. We have updated the introductory paragraph containing this data.

As for the suggestion of the science and the company editors, we include the article highlights, we sent the original figures in TIFF and added the DOI number to the references and all the observations made by them.

Considering all of the above, we believe that the manuscript has evolved significantly, and that it meets your expectations and those of our reviewers. We would like to ask you to consider this updated version of the manuscript for publication in the *World Journal of Diabetes*.

Once again, we thank you for your support.

Best regards.

Myriam M. Altamirano-Bustaman