

Dear Editor:

Thank you very much for your kind handling of our manuscript by H. Kaneto *et al.* (No. 5271). We have carefully amended the manuscript according to your suggestions, and are herewith sending the revised version of the manuscript.

We would like to thank you for the valuable comments on our manuscript and for having allowed us to revise and improve our manuscript, and hope that the revised manuscript will now be considered appropriate for publication in *World Journal of Diabetes*.

Thank you very much for your kind consideration.

Sincerely,

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Thank you very much for valuable comments.

1. According to your suggestion, to reflect the content of this paper, we amended the title as follows: “Down-regulation of pancreatic transcription factors and incretin receptors in pancreatic β -cells in type 2 diabetes”
2. According to your suggestion, we amended the subtitles so that this review could be coherent (page 3, lines 1-2; page 5, lines 1-3; page 7, lines 3-5; page 8, lines 1-4 from the bottom).
3. According to your suggestion, we amended the illustrations in the revised version. In Figure 1, we added the description “Increase of β -cell volume to compensate insulin resistance” “Deterioration of β -cell function and decrease of β -cell volume due to glucose toxicity”. In addition, we merged the contents of figure 2 and 3 as one figure (Figure 2 in the revised version). We tried to merge figure 4 and 5 as well, but the combined figure seemed to be too busy to convince readers. Therefore, we showed figure 4 and 5 in the revised version as they were in the previous version. As you pointed, TCF7L2 is a transcription factor inside the cell. Therefore, we put the word “TCF7L2” inside the cell in Figure 4 in the revised version.

Response to the reviewer 00506242

Thank you very much for valuable comments.

According to your suggestion, we amended the description and the structure of the text in the introduction as follow so that readers could understand the need for this text and the structure of the manuscript (page 3, lines 1-7).

“Under diabetic conditions, chronic hyperglycemia and subsequent induction of oxidative stress deteriorate pancreatic β -cell function, which leads to the aggravation of type 2 diabetes. Although such phenomena are well known as glucose toxicity, its molecular mechanism remains unclear. In this review article, we describe the possible molecular mechanism for β -cell dysfunction found in type 2 diabetes focusing on (1) oxidative stress, (2) pancreatic transcription factors (PDX-1 and MafA) and (3) incretin receptors (GLP-1 and GIP receptors).”