Reviewer’s report

Title: Islet transplantation improved penile tissue fibrosis in a rat model of type 1 diabetes

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Reviewer: Ana Carolina Santos de Souza Galvão

Reviewer’s report:

The authors affirm that the study was designed to investigate the efficacy of islet transplantation for reversing advanced-stage DMED in rats and to establish whether this treatment is superior to insulin therapy for treating DMED. The study is interesting and show good results. However, in my opinion, some methodological aspects must be reviewed with caution. Twelve weeks was enough time to induce advantage-stage DMED in the rats? Experiments using APO were conducted after the islet transplantation or insulin administration to evaluate the erectile function in the rats but the same were not used before the treatments in order to confirm the establishment of advantage-stage DMED.

The authors mentioned that the effects of islet transplantation in the reversing of DMED were associated with the normalization of glucose blood levels which was not reached with insulin treatment. In addition, it is mentioned that islet transplantation reduces the fibrotic process in penile cavernosum through inhibition of the TGF-β1/Smad2/CTGF pathway. However it seems not appropriate the association of the recovery only to blood glucose levels normalization. Pancreatic islet cells produce other hormone/signaling molecules besides insulin and these could influence the results. It would be better if the authors could discuss a little more such aspects.

Finally, I understand that authors induced a type 1 diabetic model in rats in the present work. Indeed, according to literature pancreatic islet transplantation is a minimally invasive procedure that can restore normoglycemia and insulin independence in Type 1 diabetics. It seems that the results obtained could be associated only to this case since nothing is mentioned about peripheric tissue resistance to insulin in the model established. The same results could be reached in rat models of type 2 diabetes?

In relation to figures:

- It would be better if the authors could insert a title for the legend of figure 1 before describe de each item. The item B, in the same figure, could be better described indicating the dyes used and which parts of the tissue appear stained. For the graphics C and D I suggest the authors change x axis title to "weeks" only. Also, it would be easier if authors use an arrow indicating the 12 weeks as the time of treatment beginning. In addition, authors must describe in the legend the meaning of the "ed" "ins" and "it".

- Figure 2 presents a legend that does not make sense and is very short. Please, review the currently sentence. It would be better if the experiment could be briefly described. The statistic
test used is not mentioned in the legend. As a suggestion, the title of y axis could be changed to "Number of Erections (30 minutes)". As observed in the figure 1, in figure 2 the authors also authors must describe in the legend the meaning of the "ed" "ins" and "it" and indicate the statistic test used.

- Legend of Figure 3 present many problems. The first is the lack of information of which tissues is presented in the figure and the treatments this tissues were exposed. Indeed, the legend's title is the name of a technique which is not adequate. There is no description of the graphics represented as items d, e and f. The authors also authors must describe in the legend the meaning of the "ed" "ins" and "it" and indicate the statistic test used.

- Figure 4 presents the same problems described for figure 3. In addition authors should mention the use of B-actin as loading control and describe the densitometric analysis.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

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I am able to assess the statistics

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