PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 72671

Title: Human amniotic fluid stem cell therapy, similar to insulin treatment, can help regain bladder function in type 2 diabetic rats

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 05373202

Position: Peer Reviewer

Academic degree: MD

Professional title: Associate Professor, Chief Doctor, Staff Physician

Reviewer’s Country/Territory: Turkey

Author’s Country/Territory: Taiwan

Manuscript submission date: 2021-10-26

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-11-09 11:44

Reviewer performed review: 2021-11-09 11:48

Review time: 1 Hour

Scientific quality
[ ] Grade A: Excellent  [ ] Grade B: Very good  [ ] Grade C: Good
[ ] Grade D: Fair  [ ] Grade E: Do not publish

Language quality
[ ] Grade A: Priority publishing  [ ] Grade B: Minor language polishing
[ ] Grade C: A great deal of language polishing  [ ] Grade D: Rejection

Conclusion
[ ] Accept (High priority)  [ ] Accept (General priority)
[ ] Minor revision  [ ] Major revision  [ ] Rejection

Re-review
[ ] Yes  [ ] No
SPECIFIC COMMENTS TO AUTHORS
I congratulate the authors for this experimental study. The present results show that, similar to insulin treatment, hAFSCs transplantation can improve STZ-induced diabetic bladder dysfunction and have a protective effect on pancreatic beta cells in type 2 DM rats.
Name of journal: *World Journal of Stem Cells*

Manuscript NO: 72671

Title: Human amniotic fluid stem cell therapy, similar to insulin treatment, can help regain bladder function in type 2 diabetic rats

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 05564298
Position: Editorial Board
Academic degree: PhD

Professional title: Full Professor, Research Scientist

Reviewer’s Country/Territory: Mexico

Author’s Country/Territory: Taiwan

Manuscript submission date: 2021-10-26

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-11-15 18:00

Reviewer performed review: 2021-11-15 21:23

Review time: 3 Hours

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SPECIFIC COMMENTS TO AUTHORS
The authors report in the present manuscript that a human amniotic fluid stem cell transplantation can mitigate diabetic bladder dysfunction similar to insulin therapy in type 2 diabetic rats. There are multiple concerns in their approach. The authors seem to confuse terminology between stem cell transplantation with stem cell therapy. The authors also confuse a hyperglycemia induction with a T2D model. A T2D model follows insulin resistance development, chronic glucose, and lipid metabolism changes, multi*organ deterioration, and, finally, beta-cell exhausting. However, beyond these misconceptions, the work is very interesting, but it needs major revision. Introduction This section is good, but the authors must incorporate information about the model used. SZT-induced hyperglycemia is through an oxidative stress mechanism that affects multiple tissues included innervation, ganglia, and urinary tree. The antioxidant defense at the median- and long-time participates in recovering tissue functions, even structural changes. Although the SZT is a very used model, it is also very common that the mechanism of hyperglycemia and injury be obviated. The cells themselves can recover from the damage caused and are often attributed to the treatment. Materials and Methods Feeding with a high-fat diet is unusual in humans. Hypercaloric diets are based on simple sugars or a high-carbohydrate diet. The time-induction with an HFD is short; therefore, the authors do not observe changes in any measured parameter compared to the control group. It is also relevant to inform the nutrient content of the control diet. The authors say, "a single intraperitoneal dose of 35 mg/kg STZ, dissolved in 0.1 M citrate buffer with pH 4.5 to induce experimental DM, which resembles the condition of human type 2 DM". So, the authors must show insulin resistance, dyslipidemia, glucose
intolerance, hyperinsulinemia, and classical deteriorate tissues metabolism that are T2D features, otherwise, they should mention it as hyperglycemia like-diabetes. The insulin administration was insufficient, thereby the results and assumptions are wrong. The authors forget that rats have nocturnal activity, thereby insulin must be administered between 18 - 21 hrs, even if the insulin has a prolonged effect, such as glargine. Please, define CGRP, MafA, PDX-1, etc., before abbreviating. If the aim was to demonstrate that human amniotic fluid stem cell transplantation can mitigate diabetic bladder dysfunction similar to insulin therapy. Why do authors present pancreatic effects? It seems like two different works. The statistical used to evaluate the effect of hAFSCs among the groups, seems incorrect. Chi-Square test is used to compare 2 variables (non-parametric), in this case, seems to be better to use a Kruskal-Wallis test. Also, a one-way ANOVA does not offer sufficient information, it is recommendable a two-way ANOVA. Result and Discussion Based on the changes made in the methodology, the result and discussion section must be rewritten, focusing to answer and discussing the work hypothesis.