



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	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
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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.



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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

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

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

Review time: 3 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No
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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



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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.