

April 26th, 2017

**Xiu-Xia Song, PhD.**  
**Science Editor**  
**World Journal of Transplantation**

Dear Dr. Xiu-Xia Song (Academic Editor) and Editor-in-Chief,

The authors of the manuscript entitled "A Historical Perspective of Cell Transplantation in Parkinson's disease" (32710) would like you to consider the reviewed manuscript for publication in World Journal of Transplantation. We thank the reviewer for their constructive comments. We think that we have successfully addressed the suggested minor revisions to our manuscript. Following is the point by point response to the Reviewer' comments, indicating the modifications done (red in text) to the manuscript when it applies.

We look forward for your response.

Sincerely,

Dr. René Drucker-Colín

Reviewer 1:

We thank the reviewer for his comments that have allowed us to present the section 5 (General Discussion) more clearly and correctly. We believe the changes have improved our manuscript.

Comment 1:

"Well written and informative; I can say that as a non-neuroscientist I actually enjoyed reading this manuscript and learned quite a bit from it. The only question that I would like the authors to consider is that of the lifespan or durability of the engrafted cells. Most of the studies cited show that engrafted cells improve function for only a limited period of time. It is unclear to me if this is because the animals were not observed for an extended period, or because the engrafted cells died, became senescent, lost function, etc. I would ask the authors to consider adding a paragraph to "Section V: General Discussion" to address cell viability and durability, and express an opinion for last-lasting symptom control in PD animals/patients."

The reviewer pointed out an important question. Grafted cells have been shown to survive and to improve function when grafted in animal models of PD. Unfortunately, there are no specific studies following long-term survival in animals, probably due to the cost of maintenance over a long period of time and also because the relatively short lifespan of the most used models (rat and mouse). On the other hand, clinical trials have shown that patients with significant functional improvement could maintain the improvement during long periods of time (from some years to twenty years after grafting). These studies undercover

the potential of these cells as a treatment of motor symptoms. However, because only a small proportion of grafted patients show significant improvement during long periods of time, we mention the need of unveiling the underlying factors associated with the high variability observed (see Page 19 2nd paragraph). We now added a paragraph with the requested information on the General Discussion Section (see Page 20 last paragraph).

Comment 2: Grade B: Minor language polishing

We have sent the article to language editing. The Licensed in Translation Adelaida Monjaraz Fuentes (Professional ID 2344716) has provided a Certificate indicating that the manuscript has reached the highest level required for World Journal of Transplantation (Certificate attached on line). All changes done to the manuscript text have been performed using the track-changes function of Word, so they can be easily recognized and assessed.

We have done the following additional modification to the text that do not change the main content, ideas or conclusions:

1. In the Acknowledgments section we added **Ruth Rincón Heredia** who participate in the initial review of the manuscript but that we have mistakenly omitted.
2. In the Acknowledgments section we removed the IN20471 and ICyTDF/170/2012 support grants.