

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 65096

Title: Recent advances in stem cell therapy for neurodegenerative disease: Three dimensional tracing and its emerging use

Reviewer's code: 05734166

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Doctor

Reviewer's Country/Territory: Greece

Author's Country/Territory: South Korea

Manuscript submission date: 2021-02-27

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2021-03-12 14:09

Reviewer performed review: 2021-04-07 02:50

Review time: 25 Days and 12 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" 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 Grade E: Do not publish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 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 checked="" type="checkbox"/> Minor revision <input 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 manuscript coauthored by Il-Kwon Kim, Jun-Hee Park, Bomi Kim, and Ki-Chul Hwang is a well written concise review, covering an interesting original topic with translational value. Indeed, the authors present the majority of data on stem cell transplantation for AD, PD and HD, including most recent data on pre-clinical trials highlighting the need for 3D studies to examine NSC transplantation efficacy and providing an overview of these techniques. Taken together, it is very interesting work for publication. I have two points that I think should be addressed: 1. I believe it would be useful to cover also the use and principles of in vivo imaging and particularly for imaging of transplanted NSCs using a two photon laser scanning microscope. There is bibliography on the subject (e.g. Nature 2016 Nov 10;539(7628):248-253. doi: 10.1038/nature20113.) 2. At the beginning of the sections 'Stem cells and Alzheimer's disease' and 'Stem cells and Parkinson's disease' it is necessary to add a paragraph describing the pathology of each condition with main manifestations regarding aggregation, oxidative stress, inflammation etc. as applicable. It will help the reader to follow the restorative potential of NSC transplantation described next in the section. And a few minor comments on semantics: Pages 15-18 Stem cells derived from pluripotent 'embryonic' stem cells (ESCs), which are more lineage-committed adult stem cells or reprogrammed 'embryonic-like' pluripotent stem cells (PSCs) have been used as a therapeutic source in neurodegenerative diseases [7,8]. more lineage-committed adult stem cells : this is not correct terminology. These are not adult stem cells. What do the authors mean 'more lineage committed'? Pages 160-162 Multifunctional stem cells such as MSCs and progenitor cells can be isolated from various tissues in the adult human body and can only differentiate into cells of the first derived type. Multifunctional stem cells: do the authors mean multipotent stem cells?



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can only differentiate into cells of the first derived type.: It is not clear what the authors mean when they say 'cells of the first derived type' Pages 166-67 Because organizations with ineffective recovery systems cannot easily return after injury or extensive degenerative events Do the authors meant to say recover?

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 65096

Title: Recent advances in stem cell therapy for neurodegenerative disease: Three dimensional tracing and its emerging use

Reviewer's code: 05458765

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Research Fellow

Reviewer's Country/Territory: China

Author's Country/Territory: South Korea

Manuscript submission date: 2021-02-27

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2021-04-06 11:00

Reviewer performed review: 2021-04-07 14:13

Review time: 1 Day and 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 checked="" type="checkbox"/> Minor revision <input 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

SPECIFIC COMMENTS TO AUTHORS

This review focuses on stem cell-based therapy on neurodegenerative diseases and its tracing methods. It has a systemic and broad coverage on this very topic facilitate reading and understating. The up-to-date information and literature summarized and presented in this review are very timely and interesting to the filed. It is educational. However, there are some shortcomings needed to be revised. 1. Tittle. In this MS, the authors used half of the space to introduce the recent progress on stem cell-based therapy on neuro-degenerative diseases, including the Alzheimer's disease, Parkinson's disease, Huntington's disease. However, only small portion of the MS was used to summarize the three-dimensional imaging for stem cell tracking related progress. The tittle should be changed to a more accurate one which will be coincident with the content. 2. The authors did not give a clearer definition about 3D image. Under the subtitle STEM CELL TRACING IN DEGENERATIVE BRAINS, the authors mentioned the imaging technology it is also part of the 3D image field. 3. The structure and flow of this review MS need to be re-organized. Introduce the 3D image on stem cell tracing systematically, including the origin, development, shortcomings and so on.

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 65096

Title: Recent advances in stem cell therapy for neurodegenerative disease: Three dimensional tracing and its emerging use

Reviewer's code: 05384690

Position: Editorial Board

Academic degree: DDS, MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: China

Author's Country/Territory: South Korea

Manuscript submission date: 2021-02-27

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2021-04-07 07:32

Reviewer performed review: 2021-04-19 23:51

Review time: 12 Days and 16 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
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SPECIFIC COMMENTS TO AUTHORS

This review summarized the latest and current approaches to trace and image graft-host relationships for the regeneration of neurodegenerative diseases, which is critical for the clinical translation in stem cell therapy. However, there are some flaws that need to be solved. Firstly, this review has stated the advantages and disadvantages of several stem cell tracing and imaging techniques. However, it is better to make a conclusive suggestion that what kind of stem cell therapy studies are suitable for these techniques. With conclusive suggestion, this review will be more readable and relevant to general audience. Secondly, the authors mentioned that cell tracing strategies help to answer fundamental questions regarding the cell conditions, that is, dose, time, phase. However, the authors lack relevant studies to support this statement. Thirdly, this review lumped nearly all kinds of stem cells in the part of "STEM CELL THERAPY IN NEURODEGENERATIVE DISEASE", however, it is better to discuss which kind of stem cells might be the best choice in therapy for neurodegeneration diseases based on published studies and what the differences are in the therapeutic effects of different kinds of stem cells.