BAISHIDENG PUBLISHING GROUP INC
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242 Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com http://www.wjgnet.com

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Answering reviewers

Reviewer #1

The manuscript was well written, providing good information on the trend of iPSC development for modeling neurological disorders.

We appreciate the comments of the reviewer.

In the review, most of the iPSC isolated from patients with each neurological disease seem to express different properties compared to normal cells of healthy control persons. For example, "Further analysis on iPSC-derived DA neurons from the same family, showed increases in mRNA for genes associated with oxidative stress, such as haemoxygenase 2 (HMOX2) and monoamine oxidase (MAO), and when these neurons were exposed to hydrogen peroxide, increased activation of caspase-3 was detected." However, it is believed that there are high possibilities of error and cellular transformation during isolation of cells from patients, induction, and culture of induced cells, and that induction factors may seriously affect the property of iPSC. In other words, I wonder if readers can think that only a few cases of iPSC reported are complete ones, and the different cellular properties fully represent the disease states.

The reviewer pointed out an important point. We agree that in vitro cell could present some cell differences comparing with in vivo cells. However, iPSC for neuronal disease modelling has been consolidated as a good model that mimics the alterations found in post-mortem brain. So, this topic could be a good sign that iPSC modeling disease can bring insights on disease ́s pathophysiology. Moreover, "healthy" cells used as controls are under the same conditions and environment, which could reinforce that some in vitro changes occurs in both cells, patients and controls, so the differences between them may be real and patient characteristics. In addition, one very important point is that cells isolated from patients brings genetic background, specially significant to personalized medicine and drug screening considering particularities on complex genetic conditions and multifactorial diseases.

If the reduced (impaired) functions and different properties of iPSC from patients are real, the patient-derived iPSC may not be suitable as autologous therapeutics, inferior in

the efficacy to allogeneic (normal person's) iPSC or adult stem cells. Therefore, it is recommended that the patient-derived iPSC should be compared with healthy person's iPSC (induced by same procedures), rather than with normal cells. You'd better review under this concept.

The reviewer pointed out an important point, but to our understanding "healthy and normal cells are the same". Moreover, for genetic diseases, unless the defect is previously corrected, an autologous transplant will carry the same alterations, so the cell transplant won ́t work to cure. In our review, we just pointed out iPSC technology to modeling diseases and drug screening for further personalized treatment, transplant is not our focus.

Reviewer #2

This is a nice overview of how iPSC technology can impact treatments of a variety of neurological disorders. Although this draft was not easy to read, careful editing of the manuscript would make a very interesting review to many readers.

We appreciate the comments of the reviewer considering the quality of information presented in our review and we did a careful English edition to improve understanding.

In addition, we did not copy and paste manuscript alterations in this rebuttal letter, because they just concern to English improvement. All of them are highlighted in the edited manuscript (red letters).