

August 15, 2018

Editorial Board

World Journal of Hepatology

Dear Editor:

Thank you very much for giving us the opportunity to revise our manuscript, titled “**Stem cell transplantation for treatment of end-stage liver disease.**” The manuscript ID is No. 40718.

In this editorial, we provide an overview of the progress made in stem cells and regenerative medicine for various medical conditions, including central nervous system diseases, benign and malignant hematological diseases, and its prospects for treating end-stage liver disease. Indeed, several clinical trials and animal models have pointed to the success of this treatment, and basic research is advancing at a rapid rate to optimize the methods. Nevertheless, we stress the importance of balancing focus on safety issues and regulation with the excitement of innovation in this field. This balance will only be achieved by careful and well-designed clinical trials, along with the cooperation of governments and regulatory authorities to ensure guidelines for the safety of new treatments using an evidence-based approach.

We appreciate the reviewers’ comments, and we have carefully revised the manuscript accordingly. We tried our best to improve the manuscript, and we made some modifications that are marked in red font in the revised manuscript by professional editors. As requested, we have improved the grammar and language, eliminated redundancy, deleted unnecessary data, and revised our conclusion. Our responses to the reviewers’ comments are included following the cover letter.

We hope the revised manuscript and our responses to the reviewers’ comments are satisfactory. If anything is unclear, please feel free to contact us.

Thank you for your hard work reviewing our manuscript.

Sincerely,

En-Qiang Chen

Reviewer 1 (comment 1) suggested us to declare all the authors' contribution. Thanks for the suggestion, we have added the Author Contribution List: Chen EQ and Tang H designed the structure of this paper. Wu DB searched the literature and wrote the paper; Chen EQ critically revised the paper.(**line 10-12, page 1**)

Reviewer 1 (comment 2) suggested that the abstract should be improved because it sound repetitive in the first part. Thanks for the comment. We have revised the abstract to making it clear and not sound repetitive in the first part (**lines 2-17, page 2**). We have revised the sentence “Stem cell transplantation has been performed to treat patients with cancer, nervous system diseases, eye disease, orthopedic disorders, diabetes mellitus, and liver diseases” into “Stem cell transplantation has been performed to treat patients with cancer, liver diseases and various kinds of chronic diseases” (**lines 3-5, page 2**). We have revised the sentence “However, the quality, safety, and efficacy of stem cell transplantation are needed to be ensured from well-designed clinical trials and qualified product approved by the government.” into “Animal models of acute liver failure have also provided important insights into the safety, mechanisms, and efficacy of stem cell therapies. Nevertheless, excitement of this promising field must be tempered with careful and calculated research. In particular, studies on the quality, safety, and efficacy of stem cell transplantation are needed so that qualified products are tested in well-designed clinical trials and approved by governments.” (**lines 11-14, page 2**).

Reviewer 1 (comment 3) suggested that in the sentence “...FDA and government” maybe it is better to add the plural “governments”, We have revised the words “the Food and Drug Administration (FDA) or the government” into “the governments” (**lines 14, page 2**).

Reviewer 1 (comment 4) suggested that we should change the sentence in “Stem cells have the capacity for multiple rounds of self-renewal and differentiation”. We have revised the sentence “Stem cells have the capacity for multiple rounds of differentiation and self-renewal” into “Stem cells have the capacity for multiple rounds of self-renewal and differentiation” (**lines 19-20, page 2; line 2, page 2**)

Reviewer 1 (comment 5) suggested that the word “In reality” may be confuse. Thanks for the comments, we have deleted the words “in reality” (**line 6, page 3**).

Reviewer 1 (comment 6) suggested that the web site “www.clinicaltrials.gov.cn” is not available. Thanks for the comments. We have revised the web site “www.clinicaltrials.gov.cn”into “clinicaltrials.gov” (**line 29, page3**).

Reviewer 1 (comment 7) suggested that the content of the recent meta analysis from the authors could be improved and the side effects and criticisms have been poorly described. Thanks for the suggestion. We have added the discussion about the side effects of stem cell transplantation (**lines 4-8, page 5**).

Reviewer 1 (comment 8) suggested us to add the full URL to the citation from websites. Thanks for the comments. We have added the web site into the **reference 15** (FDA announces comprehensive regenerative medicine policy framework. 2017; November 16,2017:<https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm585345.htm>).

Reviewer 2 (comment 1) suggested that the study is well designed and the authors are to be commended on a nicely written report. Thanks for the comments. We have revised our manuscript marked in red color. We hope these modifications are satisfactory and the revised manuscript has reached the journal’s standard.