

Dear Editor:

Please find enclosed the edited manuscript in Word format (13170-edited MK CHW.docx).

Title: Mesenchymal Stem Cells in the Treatment of Inflammatory and Autoimmune Diseases in Experimental Animal Models

Authors: Matthew W Klinker, Cheng-Hong Wei

Name of Journal: *World Journal of Stem Cells*

ESPS Manuscript Number: 13710

The manuscript has been improved according to the suggestions of reviewers and editorial staff:

1. Format has been updated:
 1. Running title, Keywords, and Core tip have been added.
 2. Properly formatted phone and fax numbers for the corresponding author have been added.
 3. References have been modified to conform to the stated format of the journal, including the addition of PMID for all references and DOI for those for which one was available.
2. Revisions have been made according to reviewer suggestions:
 1. Reviewer 1 (202286):
 - i. Corrected some typos and suggested some minor changes to language. These changes have been incorporated into the revised manuscript.
 2. Reviewer 2 (505327):
 - i. Suggested adding a figure or diagram. We have added a summary table in response to this request. It summarizes the demonstrated *in vivo* immunosuppressive effects of MSCs in each of the models discussed and also points out studies with negative results. We feel this gives a good overview of the literature without simplifying or generalizing the results.
 3. Reviewer 3 (609371):
 - i. Suggested adding a summary table, which we have done.
 - ii. This reviewer suggested that we give more emphasis to the controversial aspects of the field. We agree with the reviewer's viewpoint, and the table added at this reviewer's suggestion helps bring this point across. In this review we have tried to emphasize only the effects that have been demonstrated *in vivo* in large part because much of the controversy in the field of MSC-mediated immune suppression is due to over-interpretation of *in vitro* experiments that have not yet been confirmed *in vivo*.

4. Both reviewer 2 and 3 suggested that we incorporate studies using clinical trial data in human subjects. These studies are certainly important to understanding the MSC field, but for several reasons we have elected to limit this review to animal models only. First, the literature on clinical trials is vast, and incorporating these studies into the current manuscript would greatly expand its scope and size. Second, these studies have recently been reviewed in a very thorough article which we had cited in the previous version of the manuscript. We have added text in the revised manuscript explicitly directing readers interested in a review of clinical studies to this article. Finally, due to our position in the US Food and Drug Administration, our statements regarding the results of clinical trials can be misinterpreted as an endorsement of a particular commercial therapy. It is therefore exceedingly difficult for this manuscript to give a careful evaluation of the clinical data on MSCs, and such statements if included in this manuscript would require significant delays for internal evaluation and clearance, and only if the revision is officially approved can we proceed to publication.

Thank you again for publishing our manuscript in the *World Journal of Stem Cells*.

Sincerely,

Matthew W. Klinker, Cheng-Hong Wei