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Manuscript title: Barriers in contribution of human mesenchymal stem cells to murine muscle regeneration

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Dear Dr. De-Ling Kong,
Editor-in-Chief

We are very pleased that our manuscript was considered 'Grade B: very good' by all three reviewers. We also appreciate the recognition by reviewer 1 and 2 that the study is 'well designed, well organized and carefully conducted' and so 'the research rationale was clear and the research question was driven by practical experimental needs'.

We have addressed both comments made by the reviewer 00504030, marked in red. No claims were made by reviewer 00503926. The questions posed by reviewer 00504024 did not require adaptation of our manuscript. The figures have been adjusted to the resolution requested. Please find enclosed the revised version of our manuscript in Word format.

Looking forward to hearing from you,
Yours sincerely,



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Reviewers' comments

Reviewer 00504030

1. The reviewer suggests "Title needs to be revised to accurately state murine and human tissues are examined in this study." We have changed the title to: "Barriers in the contribution of human mesenchymal stem cells to murine muscle regeneration"
2. The reviewer expressed concerns that "The issue of cell cryopreservation appears to be critical in the described model system. This issue needs to be further discussed in full details in the Discussion section". As suggested by the reviewer, we added a paragraph (marked in red) addressing this issue to the Discussion section and we included an additional reference (#24).
3. The reviewer mentioned that "there are grammatical mistakes throughout the manuscript." We have revised the manuscript accordingly and corrected grammatical mistakes.
4. The reviewer pointed out that "the resolution of most of the figure pictures is not acceptable for publication purpose". We have included higher resolution figures in the re-submitted document.

Reviewer 00504024

The reviewer concerned:

1. "If you use immunosuppressant, can it overcome species difference?"
The recipients of the implants were immunodeficient NOD/SCID mice as reported in the materials section.
2. "What is effect of irradiation on the stem cells to overcome species-specific barrier?"
Irradiation causes impairment of proliferation and differentiation of both satellite cells and MSCs as previously reported (Cho-Lim JJ et al. Radiat Res 2011; de Andrade AV et al. J Cell Mol Med 2014; Li JKD et al. Pediatr Transplant 2007). Therefore irradiation would kill the satellite cells in the minced muscle implants and thus invalidate the model.