

Dear reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Adipose-derived stem cell therapy shows promising results for secondary lymphedema" (ID: 53683). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised parts are marked in the paper. The main corrections in the paper and the responds to the reviewer's comments are as following:

Responds to the reviewer's comments:

Reviewer #1:

1. Response to comment: Core tip and abstract are typical repeated paragraphs from the introduction section.

Response: We have re-written core tip and abstract according to the reviewer's suggestion. We highlight the importance and urgency of ADSC-therapy for lymphedema, and conclude problems that remain to be resolved including the requirement of suitable animal models and safety verification.

2. Response to comment: Table 1 showing the results of animal studies is duplicated in the manuscript.

Response: We are very sorry for our incorrect writing of the results of animal studies. We have re-written this part, deleting the description of Valuation criterias, adding the description of the injectin methods and results.

3. Response to comment: A study of human studies is missing in table 2.

Response: We are very sorry for our negligence of the article entitled "Adipose-derived regenerative cells and fat grafting for treating breast cancer-related lymphedema: Lymphoscintigraphic evaluation with one year follow-up". We have added this article to table 2.

4. Response to comment: English language needs polishing.

Response: We are very sorry for our poor writing, and we have used language editing services provided by biomedical editing companies. Special thanks to you for your good comments.

Reviewer #2:

1. Response to comment: Some description about the characteristic of adipose-derived stem cells to present MHCs without MHC-II may be revised to be more detailed.

Response: We are very sorry for our inexact description about the characteristic of adipose-derived stem cells. The revised part is as following: A prominent characteristic of ADSCs are their low immunogenicity, due to the low levels of expression of Major Histocompatibility Complex (MHC) and costimulatory molecules. ADSCs produce immunomodulatory cytokines including TGF- $\beta$  that block IFN- $\gamma$ -induced MHC expression. The downregulation of MHC can avoid immune surveillance, producing immune-privileged cells ADSCs.

Special thanks to you for your good comments.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. And here we did not list the changes but marked in revised paper.

We appreciate for reviewers' warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.