Author’s response to reviews

Title: The role of epithelial-mesenchymal transition in the post-lung transplantation bronchiolitis obliterans

Authors:

Chong Zhang (haiyanzhangchong@163.com)
Yuequn Niu (nnnyyg@163.com)
Li Yu (3100102511@zju.edu.cn)
Wang Lv (xx00139@126.com)
Haichao Xu (xuhc@zju.edu.cn)
Abudumailamu Abuduwufuer (07301010028@fudan.edu.cn)
Jinlin Cao (15857145569@163.com)
Jian Hu (dr_hujian@zju.edu.cn)

Version: 1 Date: 29 Aug 2017

Author’s response to reviews:

Dear Editor,

Here we are submitting the revised manuscript entitled “The role of epithelial-mesenchymal transition in the post-lung transplantation bronchiolitis obliterans” for your kind consideration. We thank you and the reviewers for the valuable comments concerning our manuscript and in this revised version, we have carefully addressed all the comments and made significant amount of revisions. Our detailed responses and revisions are as follows.

Reviewer #1

We sincerely thank you for your supportive comments, valuable suggestions and providing us helpful literatures. We are very sorry for our confusing English expression in the former manuscript. Now the revisions have been done in the revised manuscript. And we also highlighted the limitations in this study in the Discussion part, including the small sample size and the common factors in animal models. We also revised the Conclusion part and we hope the revised version would be modest, appropriate and objective.
Reviewer #2

Comment 1: The English language is often difficult to understand. The text of the manuscript should be revised.

Answer: We thank the Reviewer for raising this important point and here we are very sorry for our confusing English expression. Massive revisions have been done in the revised manuscript.

Comment 2: The design of the study is not completely convincing. I would suggest a control group using Lewis to Lewis transplantation in order to compare with F344 to Lewis. A thoracotomy in F344 rats does not seem a viable approach to define a control group to transplanted rats that develop OB. The risk is to observe findings that are not related to OPB but rather to other complications of the lung tx procedure itself.

Answer: We appreciate your valuable suggestion and we do agree that adding a Lewis-Lewis transplantation group would increase the reliability of this study. Unfortunately, with the limitation of revision period, we have some difficulties to perform such experiments. In this study, we observed pathological changes that met BO characteristics after the allograft lung transplantation and meanwhile EMT was also found in this process. Thus, we highlighted that EMT took part in the BO airway remodeling. Although using a sham operation group as the only control group may be not perfect, it made all the pathological changes in the transplantation group apparent. Just as that mentioned in your comments, a Lewis-Lewis transplantation control group may bring other complications of lung transplantation itself into the disease model. Thus, we believe such a control group is enough, though not perfect, to support our conclusion that EMT is involved in the BO airway remodeling. We also highlighted this point as a limitation of our study in the Discussion part.

Comment 3: I would suggest revisiting the definition of OB as CLAD. This is an established approach when referring to chronic lung failure after LTX.

Answer: We thank the Reviewer for raising this important point. Following the advice, the terminology of “CLAD” has been referred in the revised manuscript in the Background part.