April 30, 2020

Sami Akbulut, FACS, MD,
Editor-in-Chief
World Journal of Transplantation

Dear Editor:

Please find enclosed our revised manuscript entitled, "**Chronic lung allograft dysfunction post-lung transplantation: The era of BOS and RAS**" (Manuscript ID: 54870), which we wish to resubmit for consideration as an invited review article in *World Journal of Transplantation*.

We are very grateful for the editor's comments regarding the original manuscript, which have enriched the manuscript and enabled us to produce an improved account of the review. We have revised the manuscript in accordance with their suggestions, and hope that it is now suitable for publication in *WJT*. We enclose a point-by-point rebuttal along with the revised manuscript.

Sincerely,

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Itemized modifications to the revised manuscript and point-by-point response to the Reviewers' comments

List of changes

Title: None

Abstract: None

Core tip: None

Introduction: None

Text: P.17, 18: We have added the "article highlights" section at the end of the main text as per the editor's suggestion.

References: None

Figure and Figure Legends:
P.10, 38: We have submitted the original figure 1 and added figure 2 with the legend as per the editor's suggestion.

Audio Core tip：We have added the audio core tip.

Responses to Reviewer

Thank you for reviewing our manuscript and providing valuable advice. The suggestions have helped us to improve the quality of our original paper. We have addressed your comments, provided point-by-point responses (as shown below), and revised the manuscript according to your suggestions.

***Science Editor**:*

(2) Summary of the peer-review report: This review highlighted the most recent development of CLAD definition and phenotypes. Risk factors for RAS and BOS were tentatively differentiated by key features. Considering the complex interaction between lymphoid tissues, pro-fibrosis environment and transplanted lungs, author would consider to present the anatomical changes in a brief manner, following by demonstrating individual immune regulators' role in RAS or BOS.

Response: We appreciate and agree with the editor's comment. For clarity, in the revised version of the main text, we have added figure 2, which demonstrates the anatomical changes with histopathological findings.

Issues raised:

(1) Please write the "article highlights" section at the end of the main text

Response: Thank you for your suggestion. We have written the "article highlights" section at the end of the main text as per the editor's suggestion.

—P. 17, 18; Currently, CLAD is mainly classified into two clinical phenotypes, BOS and RAS. These mechanisms are not clear but considered to involve complex immune-mediated mechanisms such as innate immunity, cellular immunity, humoral immunity and autoimmunity. Finally, tissue remodeling takes place, resulting in irreversible fibrosis. An apparent histological difference between BOS and RAS is the anatomical locations involved: namely, BOS mainly involves small airways while peripheral lung tissue remains relatively intact, while RAS involves multiple anatomical compartments including airways, pleura, interlobular septum, alveoli, and vasculature. Such difference in the distribution of fibrosis may be associated with different magnitude and quality of immune mechanisms including lymphoid neogenesis.

(2) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

Response: We are grateful for your suggestions. We have submitted the original figures 1 and 2.