Reviewer’s report

Title: The role of HIF-1α-VEGF pathway in bronchiolitis obliterans after lung transplantation

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Reviewer: Sehoon Choi

Reviewer's report:

Dear Authors,

In this study, authors concluded that orthotropic lung transplantation model in rats can mimic human BO after lung transplantation, and HIF-1α-VEGF pathway might be involved in the occurrence and prognosis of BO.

I know the authors did great work to do serial rat lung transplantations more than 30 cases, and to analyze the results using histology, IHC and images. However, I should point out followings;

1. Lung transplantation in rats is a well-established research methodology with a history of more than 30 years, and numbers of simplified methods are reported. (Transplantation Proceedings 1989;21:2601-2, J Invest Surg 2008;21:33-7… etc.)

2. Also, the relationship between HIF-1α and hypoxic environment including chronic lung allograft rejection has been investigated for a long time. In these days, there are the trials to attenuate BO by targeting HIF-1α signaling. (Cell 2012;148:399-408, Proc Am Thorac Soc 2009;6:108-121, Cellular Immunology 2012;273:59-66, Journal of Clinical Investigation 2011;121:2336-49, Journal of Investigative Medicine 2016;64:361-3)

So, I congratulate the authors for establishing the methodology of lung transplantation in rats in authors’ lab, however, I can hardly agree with the opinion of authors that "this is the first report confirming the relationship between the HIF-1α and BO in vivo" as written in the last paragraph in discussion. And I also cannot agree to consider this manuscript for publishing in JCTS.

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