Reviewer’s report

Title: CD147 increases mucus secretion induced by cigarette smoke in COPD

Version: 0 Date: 13 Sep 2018

Reviewer: Sunil Nooti

Reviewer's report:

The study "CD147 improves mucous secretion induced by cigarette smoking in COPD" by Qiao Yu et al., is a correlative study between CD147 expression and MUC5AC in human lung specimens. Apart from the human IHC results, the authors show that CD147 regulates MUC5AC expression through MMP9/p38 MAPK signaling in HBE cells in vitro.

I have two major concerns regarding this study

1. Even though the correlations in vivo are obvious, it is not clear why smokers with and without COPD have a differential CD147 and MUC5AC expression, even though these two groups have similar overlapping smoking histories (52.8±8.6 vs 60.3±7.4 pack years). Since this is not clear, it is difficult to interpret that their link is causal in nature. When was the diagnosis of COPD made for the third group with respect to age and smoking history pack years? I would strongly recommend the authors to look for more differences between these two groups, which could have resulted in COPD, like are the blood alpha-1-antitrypsin levels different? Were there no other genetic or environmental factors that could have led to COPD in smokers with COPD vs smokers without COPD? Moreover, if all the lung specimens were from resected pulmonary nodules, what were these due to? How are the authors sure that the pathology behind the nodular disease is not contributing to immune cell infiltration or affecting the clearance of mucus even though the regions studied are 5 cm away from the pathology?

2. As described by the authors in the background section (citation 17 and references therein), it is already known that there is more CD147 in bronchioalveolar fluid and is expressed predominantly by bronchial epithelium from patients with COPD compared with smokers and nonsmokers. It was also shown here that blocking CD147 led to a decrease in MMP-9 mRNA expression and activity. Since this is already known, what would have been interesting to see was whether there was more MMP9 or phosphorylation of p38MAPk in the lung specimens of smokers with and without COPD. This could have added to the mechanistic basis to some extent. The fact that in vitro experiments in this study use CS, the authors should justify why their results are relevant in light of published literature from in vivo, and why this study is novel.

Minor concerns:
1. There are a number of English corrections, which need to be corrected …. I have only highlighted some here from the first half of page 2. Line number6: "hyper-secretion quantitates" ..... revise
Line 6: "However it is remain unclear"…. revise
2. Chemical inhibitors used in fig 6 will need to be corroborated with specific inhibition using RNAi for p38 MAPK and MMP9.

3. Scale bars are missing in Fig 1 and 2. If quantitation was done at 200X, the displayed figures should be the same.

4. The use of the word "improves" in the title is inappropriate…. Should be changed to "increases".

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited
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