Reviewer’s report

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

Version: 1 Date: 13 Nov 2018

Reviewer: Sunil Nooti

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The authors did not answer specifically when the diagnosis of COPD was made for the third group. While CD147 and MUC5AC are increased in smokers with COPD, over and above the levels in smokers without COPD it would only be a correlative evidence. But if CD147 and MUC5AC levels varied with the onset of COPD in the third group, it would be interesting to note whether increase in CD147 preceded the increase in MUC5AC. I don't see why the authors should not show the actual data and discuss at least in brief when they most probably have the clinical data for COPD onset and history.

It is indeed interesting and commendable that the authors were able to get COPD lung tissue, which is a salient feature of this manuscript. However, though the authors reply that "specimens from lung cancer may have influenced the responses", it is not clear why they should not present the data of the diagnosis and reasons for surgical resection of the pulmonary nodule for each patient in the form of a table or supplementary info. All the clinical data summarized in the methods section of "subjects" could be shown in the form of a table for clarity and let the reader decide on their effect.

Smoking and Vaping has been shown to increase MUC5AC secretion (PMID: 29481290). Increase in CD147 and consequent MMP9 regulation is also known (ref 19 in the manuscript). CD147 regulating MUC5AC through MMP9 and p38 MAPK is the main result of this study. However the author's use of non-specific chemical inhibitors is a weak point as I had mentioned earlier. SB-3CT is not only MMP9 inhibitor but also inhibits MMP2 (PMID: 25150065). If the authors cannot use more specific inhibitors they should at least dissect the role of MMP2 and include the same in the discussion about mechanism.

Similarly SB203580 though is commonly used to inhibit p38 MAPK catalytic activity, it is also known not to inhibit the phosphorylation of p38 MAPK by upstream kinases (PMID: 10512765). 10µM SB203580 concentration as used in this study is also known to inhibit phosphorylation and activation of PKB (AKT) by inhibiting the PKB kinase, phosphoinositide-dependent protein kinase 1. Extreme caution has been advised when interpreting data where SB203580 has been used at concentrations above 1-2 µM (PMID: 10702313). Hence the authors should try using lower concentrations for SB203580 or use a more specific inhibition and elaborate mechanistic discussion in light of the above.

The significance notation (* and #) in figure 6 is confusing. It is not obvious and clear unlike in other figures, as to what they are significant to.

The authors have indeed addressed most of the English language concerns of mine.
The authors should also include referring to more recent articles published which are relevant in the role of CD147 (PMID: 30005623) and MUC5AC production (PMID: 29906464).

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

Yes

**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.

Yes

**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:

Acceptable

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