Reviewer’s report

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

Version: 0 Date: 04 Sep 2018

Reviewer: Hitendra Chand

Reviewer's report:

In this study authors report that CD147 and MUC5AC expression were higher in COPD patients with smoking history. Using human bronchial epithelial cells or HBEs in-vitro they show that cigarette smoke exposure increased CD147 levels that induced MUC5AC secretion via MMP9 and p38 MAPK signaling pathways. Therefore, they propose that regulation of CD147 could be a promising target for regulating mucus hyper-secretion in COPD. There are several limitations in this study and the manuscript that preclude the enthusiasm and dilute the importance of these studies, as outlined below:

1. The manuscript language needs an extensive revision to make it as an easy and understandable read.
2. Authors should include lung specimen from COPD subjects without smoking history to substantiate that only smoking is correlated with observed elevated CD147 levels and mucus hyperexpression in the studied population.
3. In addition, they should also provide an information whether or not these subjects had a reported history of chronic bronchitis, the phenotype targeted in this study. This phenotype and its relevance in COPD pathogenesis should be included in the introduction and the discussion.
4. The chemical staining used (PAS) for the analyzing airway mucus shows only basic mucopolysaccharides and therefore do not account of acidic mucopolysaccharides. Authors should analyze the Alcian blue stained sections to include the total number of mucous cells in their study.
5. The data presentation of lung tissues analyzed should be reported as mucous cells per mm of basal lamina to avoid inclusion of PAS- and/or MUC5AC-positive submucosal glands. And additional epithelial cell marker should be included to confirm that the signal is only coming from the epithelial cells. For all histological images a magnification or the scale bar should be provided.
6. The in-vitro studies used HBEs and authors should provide their source and origin to help compare the study with other reports.
7. The HBEs are presumed to be grown in a submerged culture model and HBEs do not represent their natural polarity as observed in conducting airways of the lung. Therefore, authors should provide an evidence that CD147, MMP9 and p38 MAPK are involved in mucin regulation of in-vitro differentiated HBEs.
8. The cigarette smoke referred in the in-vitro experiments should be designated as CS extract and not smoking itself. The concentration of CSE (10%) used is pretty high compared to other contemporary in-vitro models and should be discussed in the paper.
9. In the experiment reported in Figure 6, please include the non-treated control sample to show
the levels of all the proteins analyzed present in an unstimulated HBEs.
10. Authors fail to discuss their in-vivo findings of elevated CD147, a metalloproteinase inducer levels in their cohort and should compare the data in light of the protease-antiprotease imbalance in the COPD pathogenesis.

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.

I am able to assess the statistics

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

Not suitable for publication unless extensively edited

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