Reviewer's report

Title: Plasma Chemokine Signature Correlates with Lung Goblet Cell Hyperplasia in Smokers with and without Chronic Obstructive Pulmonary Disease

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Reviewer: Maor Sauler

Reviewer's report:

Victor Kim et al., in their manuscript, utilize bronchoscopically obtained lung tissue and plasma samples from a modestly sized patient population to determine the association between systemic chemokines and goblet cell hyperplasia. This study wishes to address the question of what circulating chemokines are associated with goblet cell hyperplasia. The study utilizes human tissue samples, an approach that is the major strength of this study. It is well written and I have no reason to doubt the accuracy of the data being presented. However, I have the following methodologic concerns and questions regarding the relevance of this study.

Major Criticisms:

1) The authors do not clearly justify studying the association between circulating chemokines and goblet cell size. More than "down-stream" consequences of disease, is there a patho-mechanistic hypothesis that is being addressed? For example, can the authors show a relationship between recruited airway cells and goblet cell hyperplasia? At minimum, can the authors offer a more clear rationale for why the study was undertaken?

2) Given that bronchoscopically obtained biopsies are taken with forceps, with variable tissue compliance and applied force, can the authors provide some evidence that ex vivo goblet cell size is related to in vivo size?

3) Why did the authors not perform any multivariate adjustment for confounding variables? At minimum, there is ample patient size to adjust for smoking status (current/former).

4) Given the small sample size, why did you use a Pearson correlation? Would consider non-parametric correlation testing.

Minor Criticism:

1) I would minimize discussion of immune cell trafficking in COPD. This study does not address those question. This study looks at the association between systemic chemokines and goblet cell hyperplasia – it does not evaluate neutrophil or monocyte/macrophage migration.

2) Why is Goblet Cell Hyperplasia not included in Table 2?

3) I would show at least 2-3 examples of goblet cell hyperplasia/condition.
4) Ensure that all statements in the conclusion are clear in suggesting that any positive findings are purely an association.

5) The study would greatly benefit from more patients. Where power calculations used to determine the sample size?

6) Could the author detail where/when a pre- and post-test adjustment for multiple comparisons was used. From the description in the text, it seems as if this did not occur routinely.

Discretionary Revision:

1) As the authors point out, goblet cell size (as opposed to function) is not strongly associated with patient’s symptoms. Did the author obtain information related to symptoms or exacerbations?

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare I have no competing interests