Reviewer’s report

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

**Version:** 2  **Date:** 3 June 2015

**Reviewer:** Hitendra Chand

**Reviewer’s report:**

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This manuscript addresses an important question of how circulating cytokine signatures relate to goblet/mucous cell hyperplasia (GCH) as observed in smokers with and without COPD. The methods followed are appropriate and well described. The data presented clearly shows that smoking upregulates the levels of CXCL8, CCL4 and CCL22, the neutrophil and macrophage chemoattractants in plasma, and the levels strongly correlate with the observed GCH development. Most of the previous studies had established the role of neutrophils and macrophages in the pathogenesis of COPD following smoke-induced exacerbations based on either in-vitro studies or from various animal models.

There is a minor concern with regards to the sample size and more importantly, about the racial variation in the cohort, which dampens the enthusiasm and authors too share this concern. Nonetheless, the readers of this journal will be able to appreciate the merits of the reported findings if the following concerns are addressed. The title and abstract to aptly convey the reported findings.

**Major Compulsory Revisions**

1. The neutrophils and macrophage counts from patient blood or BAL should be presented to ascertain the correlation of these inflammatory cells to the observed chemokine profiles in this cohort.

2. Please discuss your results in the context of findings from ECLIPSE studies (Agusti et al., PLOS One 2012: 7(5):e37483); and the study reported by from Brozyn et al., (COPD 2009; 6: 4-16) on Th1 type chemokines in smokers and COPD patients.

**Minor Essential Revisions**

1. Is it possible to analyze the biopsies from small airways and compare that with large airways reported in this manuscript?

**Discretionary Revisions**

None

**Level of interest:** An article of importance in its field

**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 that I have no competing interests.