Reviewer's report

Title: Ageing and long-term smoking affects KL-6 levels in plasma, sputum and lung with significant correlations to COPD severity

Version: 2 Date: 2 February 2011

Reviewer: Ruth tal-singer

Reviewer's report:

Major Compulsory Revisions

1) The authors have demonstrated the effect of smoking on the levels of Plasma KL6 in older subjects yet COPD patients have not been separated based on their smoking status. Are they all former smokers? if so, please note in the text but otherwise I suggest splitting the data by smoking status to evaluate whether KL6 is affected by age and smoking status as opposed to disease (Figure 1)

2) Is it possible to explore a correlation between pack year and plasma level of KL6 after adjusting for age? given the age-related differences in plasma levels of KL-6, the 10 years difference between COPD and older smoking controls could be attributed to age and not disease?

3) Are the differences between younger and older subjects gender related? there are more women in the older population. If differences are observed when analyzing data obtained in men, it would be useful to note that in the text.

4) Sputum analysis in Figure 2: I am concerned about the interpretation of the data due to the presence of 3 outliers in the COPD population. Is there a characteristic that might explain the findings in the three individuals? e.g. smoking status, age, pack years, worse lung function? it would be worth discussing.

5) In Table 4, these correlations with lung function are impressive (and different from observations in IPF), have correlations been observed when adjusted for age and smoking status?

Minor essential revisions:

1) Methods: it is not clear whether GOLD IV patient were prescribed medications (oral and/or inhaled corticosteroids) after the study assessments were taken. Would be useful to make it clear as therapy may impact KL6 levels.

2) Figure 3 A: utilize the same magnification to better illustrate the observed differences

Discretionary Revisions:

1) A box plot may be a more informative display of the data on plasma and
sputum

2) A Scattergram of the strongest correlation in Table 3

3) Provide assay sensitivity information (e.g. range, lower limit of detection). May help explain differences between values reported by others

4) Would be useful to note whether plasma levels of KL 6 are correlated to sputum levels.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests