Reviewer's report

Title: Circulating Surfactant Protein D: A Novel Lung-Specific Biomarker of Health Outcomes in COPD?

Version: 1 Date: 4 July 2007

Reviewer: John Hurst

Reviewer's report:

General

This paper by Sin and colleagues examines the associations of surfactant protein D (SPD) and Clara Cell protein-16 (CC16) with clinical variables in COPD. 23 patients were included, who were enrolled in a previously published trial of NIV. The authors are internationally recognised for their important contributions to the field and I found the paper well-written, clear and thoughtful. I raise the following observations:

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. By the authors' own admission (page 3) this is pilot data and certainly if one set out to examine the relationships between SPD / CC16 and outcomes in COPD one wouldn't do this in an way in which half the patients received NIV and half didn't. I note (page 4) that the two groups were 'similar', but it is quite possible that NIV could affect release of these mediators, and also affect health-status. My feeling is that this should be further emphasised, and control and NIV patients might usefully be identified separately in Figures 1 and 2. This would allow a reader to visualise whether the changes in CRQ (occurring over a remarkably short time-scale) are attributable to the NIV intervention.

2. The authors have made an attempt to control their analysis of changes in SPD / CC16 with change in health-status for potential confounding factors. I would add exacerbations to the list that might be considered as it is well described that exacerbations affect both health-status and concentrations of systemic biomarkers. In such a short study, it is possible at least that no patients exacerbated during the course of the study, in which case this may be less important, though an assessment of exacerbation frequency would still be of interest and potential importance.

3. In my opinion, the conclusion (page 8) that "SPD appears to be a better biomarker of COPD severity and symptoms than is CRP..." is a leap too far. This requires considerable further justification, or perhaps toning down a little?

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of
a term, which the author can be trusted to correct)

1. What was the limit of detection of the assays and what values were assigned to any samples falling below this limit?
2. Were both samples from the same patient included in the same assay?
3. Typo page 6. The correlations between the 3 markers appear in Table 4 not 3.
4. Careful with language, associations does not prove causation! Page 6 "CRQ scores did not change in response to..." needs re- wording.
5. Typo page 8, line 12: missing 'with'.

Discretionary Revisions (which the author can choose to ignore)

1. The authors acknowledge the risk of Type I error in this small study. Do they also want to discuss the risk of false conclusions given the relatively large number of comparisons performed?

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

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