Reviewer's report

Title: Hepatocyte and Keratinocyte growth factors and their receptors are not decreased in human lung emphysema

Version: 1 Date: 31 July 2005

Reviewer: Alvar Agusti

Reviewer's report:

General
This paper investigates if the expression of HGF and/or KGF (and their receptors) in the lungs of patients with emphysema is different from that seen in smokers with normal lung function or never-smokers. Results show that, on average, there are not significant differences between groups. However, the authors found a significant negative relationship between the expression of HGF and the degree of airflow obstruction (FEV1) in patients with emphysema. Overall, I found the paper well written and interesting. However, I think that the authors should improve the following aspects:

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

1. Authors conclude that lung emphysema in humans is NOT associated with a global decrease in the expression of HGF or KGF in the lungs. However, they also report an inverse relationship between FEV1 and the expression of HGF, which suggest the contrary. I think that they need to reconcile these two observations. To this end, I would suggest that: (1) they include in the correlator analysis data from smokers without emphysema; (2) they clarify the “definition” of emphysema. It is unclear if this diagnosis was done on the basis of lung function test, CT scan results or both, or other criteria. Also, it would be very interesting to try to quantify the degree of emphysema present (and to include in the analysis other lung function measurements, such as DLCO) to see if there is any relationship between it and the expression of HGF and KGF. In summary, I think that the authors have to re-think very carefully the interpretation of their results.

2. Authors claim that patients with emphysema had severe airflow obstruction. However, it is obvious from the individual data points shown in Figure 3 that this was not the case in all of them. Actually, it is surprising that some patients with emphysema had normal or only minimally reduced FEV1 values. This should be explained and, probably, has something to do with the point I raised above (interpretation of data).

3. Page 6. Two patients without emphysema were receiving inhaled steroids. Were they asthmatics? Can this bias the results? What if they are excluded from analysis?

4. I found the discussion section too short. For instance, potential limitations of the study are not discussed and I believe they should (small sample size, presence of cancer and, among all, criteria used to classify patients). Above it, however, I think that the authors should resolve the apparent internal contradiction indicated above in point 1, this is, whether HGF expression is abnormal or not in patients with emphysema (mean values being not different but authors showing very convincing negative relationship with FEV1). The conclusion of the paper would then be completely opposite to the current one.

5. Figure 3 needs substantial work-up. First, I would suggest to exchange X-Y axis. I believe that, for
a respiratory audience, it is more intuitive to have FEV1 values on the X axis. Second, if the correlation test used is, as indicated, the Spearman’s rank order test, “r” should be substituted by “Rho” and the line in the figure omitted (it is not a “linear” regression test). Third, and more importantly, I suggest to include in the analysis data on smokers without emphysema (using a different symbol). I think that this may help to resolve the item indicated on points 1 and 4.

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. Ref 18 on page 3 relates to pulmonary fibrosis, not to emphysema

2. Page 5. Last sentence “Increased cumulative …” Unclear meaning. Do you mean that there were significant differences between groups. Please, clarify.

3. Table 1. The expression “non relevant” should not be included here. Why is it “non relevant” to know, for instance, the period since smoking cessation in non-emphysema smokers (while it is in patients with emphysema)?

Discretionary Revisions (which the author can choose to ignore)

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

Declaration of competing interests:

I declare that I have no competing interests