Reviewer's report

Title: Neutrophilic airways inflammation in lung cancer: the role of exhaled LTB-4 and IL-8

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Reviewer: Elisabetta Pace

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This is a study from a well-known research group that addresses the role of exhaled LTB-4 and IL-8 from patients with NSCLC. The authors demonstrate that higher levels of LTB-4 and IL-8 are present in breath condensate and in the blood from NSCLC patients cancer and that LTB4 and IL-8 concentrations increase as the cancer stages progress. Moreover, exhaled IL-8 and LTB-4 correlate with the percentage of neutrophils in the induced sputum. The topic of this paper is of interest and some novel findings are described in this manuscript. There are some points of the manuscript to revise.

1. Introduction.
   a. The Introduction may be condensed. The authors have to simplify and clarify the sentence (page 6): “The aim of the present study was to give further support to the neutrophilic inflammatory signalling in lung cancer investigation, two soluble neutrophilic proteins, the LTB-4 and the IL-8 in the EBC of NSCLC patients and controls with a view to giving further insight into the inflammatory theory of lung cancer pathogenesis”.
   b. Please, add the references to the sentence “often a good number of studies are available in literature proposing the use of this sample for the non-invasive diagnosis and monitoring of lung cancer”.

   a. The authors reported in the statistic section that “Data were normally distributed and therefore non-parametric tests were chosen for analysis”. I think that the authors have forgotten the word not normally distributed because non-parametric tests are preferred for not normally distributed data.
   b. In this study, smokers (without lung cancer) have been omitted. Therefore, while the presented data are interesting, it is not fully elucidated whether IL-8 or LTB4 levels are increased by lung cancer disease or represent a smoking effect only. In this regard it has been demonstrated that immunoreactive IL-8 and LTB4 significantly increased in the supernatant fluids from airway epithelial cells in response to smoke extracts (Masubuchi T, Am J Pathol 1998- Pickett G, Toxicol Sci. 2010). Furthermore the authors of the present study reported that increased levels of both exhaled LTB-4 and IL-8 were observed in heavy smokers (group 2) with respect to group 1 mild smokers. The evaluation of LTB4 and of IL-8 also in exhaled breath condensate from smokers without lung cancer or the presentation
of LTB4 and of IL-8 data in non-smokers, current or ex-smokers lung cancer patients as separate groups might allow to fully elucidate the effect of lung cancer in the levels of these mediators and to support the utility of assessing these mediators in the diagnosis and monitoring of NSCLC.

3. Discussion.

a. In the discussion the authors state that “……. confirmed the increase of LTB-4 and IL-8 systematically and in airways”. This reviewer think that it is better: “confirmed the increase of LTB-4 and IL-8 in the systemic compartment and in the airways” rather than “systematically and in airways”.

b. This reviewer thinks that it is better mollify the concept that the increase in LTB4 and in IL-8 represents a proof that neutrophils or inflammatory cells are the main source of these mediators. Airway epithelial cells may actively contribute to the release of both LTB4 and IL-8 and the correlations between these mediators and the number of neutrophils may be the results of the chemoactractant or pro-survival (Petrin D, Cell Signal 2006-Fudala R, Am J Physiol Lung Cell Mol Physiol. 2007) properties of these mediators.

Minor

1. Present references in a separate section (the Heading “References” is located in the last page of the Discussion section).

2. Add statistic in the legend of figure 1.

3. Add statistic in the figure 2 as well as in the legend of figure 2.

4. Revise further the paper for the English (discussion page 14: “previous” instead of “preceding” results).

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.