Reviewer's report

Title: Induction of autoantibodies against lung matrix proteins and smoke-induced inflammation in mice

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Reviewer: Esmaeil Mortaz

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The manuscript by Brandsma et al trying to described the ongoing smoke-induced specific immune response. They propose that neo-antigens may arise during the chronic inflammatory response in COPD due to lung tissue destruction and/or continued smoke exposure. These neo-antigens are recognized and evoke an antigen specific immune response, characterized by antigen specific T- and B cells in the lung, organized into lymphoid follicles and the presence of autoantibodies. The main objective of study was to answer whether the induction of antibodies against lung matrix proteins can augment the smoke-induced immune response. The manuscript well designed however needs to improve critically before publish as a paper. The big issue of paper is laking of developed emphysema however they referred for own pervious papers (4 and 14) which they have shown high and significant Lmi. I am very interested to know this discrepancy and not reproducing experimental designed?

Comments:

- Why the authors used 2 time points for cigarette smoke exposures and why not longer?
- They obtained samples after 5 days and 1 week but no indication of changes in those days?
- Usually study of BALF is critical as a indicator for lungs and airways, I have not seen any information about data of BAL (cytokines, cells, lgs….). Thus, the presentation of BAL data is very critical for publication and I am strongly asking authors to show data?
- I was wondering to numbers of PMNs in lungs after 3 and 6 months?
- Because the lymph nodes considered as a major source of lymphoid system, it would give impact for manuscripts to show the immunohistiochemistry of LN ?
- I was wondering for staining protocols of lungs cells, the authors used B220 for B cells however we have this receptor in pDCs as well, thus my suggestion is to use CD11c/B220 and B220/CD19 for discrimination of DC and B cells, respectively.
- The discussion wrote as explosively and it is better to make shorter.
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.