Reviewer's report

Title: Blood cells for the differentiation of airway inflammatory phenotypes in COPD exacerbations

Version: 2 Date: 25 Nov 2019

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?

No - there are major issues

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?

Yes - the approach is appropriate

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?

Not sure - key details are missing from the manuscript

STATISTICS - Is the use of statistics in the manuscript appropriate?

Not sure - I am not able to assess the statistics in this study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?

No - there are major issues

OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?

Maybe - with major revisions
PEER REVIEWER COMMENTS:

GENERAL COMMENTS:
In this manuscript entitled "Blood cells for the differentiation of AECOPD airway inflammatory phenotypes" the authors used retrospective data from COPD patients with acute exacerbation (AECOPD) to correlate the percentages of leukocytes from sputum and PBMCs. The data appear to indicate that the tested PBMCs values are poor indicators for the endotypes during AECOPD. However, major problems make it difficult to fully evaluate the study.

REQUESTED REVISIONS:
* Figures: no real conclusion can be drawn from the figures, because:
  - the figures have no legend, and the descriptions of the figures in the main text are not clear;
  - the parts of figure 1 do not even appear in the text; so, one has to make educated guesses on what the figures might show;
  - figures A-G show one or four lines for statistical comparison, but only one number is given - and that number is, puzzling, always 0.08.

* Table 1: There are no human races and I am pretty sure that 'Chinese' is a nationality.

* Table 2: it is not clear to what the p-values at the end of the rows refer to;

* Figure 3: the 'best' predictor in PBMCs for sputum values (%Eos) had an AUROC of 0.67, which is a value for a poor indicator - therefore, I think, one cannot claim (as the authors did in the discussion) that "blood eosinophils … were shown to distinguish patients with sputum eosinophilia". This part of the discussion and the one addressing the limitations appear to contradict each other in the usefulness of the correlation.

* The authors highlight some limitations of their study, however, one major one is not even mentioned: namely the cause of the acute exacerbation. This is usually due to infections, and depending on the infection, changes in PBMCs might be visible that have nothing to do with the COPD. Therefore, the weak correlation they observed between the PBMCs and sputum values could be an indication for the infections, without any relevance to COPD. This is a major caveat that needs to be discussed.

* Finally, the manuscript fails to adequately reference and discuss the vast literature on the topic, which largely showed for COPD what the authors report here (for example, for many others, PMID: 29696728, 29146301, 28482840, 21680942).
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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