Reviewer’s report

Title: Pathway mapping of leukocyte transcriptome in influenza patients reveals distinct pathogenic mechanisms associated with progression to severe infection

Version: 0 Date: 19 Aug 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)?

Yes - there is a clear objective

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?

Yes - experiments and analyses were performed appropriately

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

Yes - appropriate statistical analyses have been used in the study

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

Yes - the author's interpretation is reasonable

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

Yes - current version is technically sound
GENERAL COMMENTS: In this manuscript the authors were interested in the influenza disease mechanisms associated with progression to severe infection. This was addressed by analyzing the transcriptome of leukocytes from patients and healthy controls. Indeed, changes in the transcriptome were detected and it was possible to find differences between severely affected patients in comparison to patients with a moderate infection. Particular focus was placed on the pathway analysis.

No unusual methods have been used.

The study is rather descriptive, but provides an interesting data set. Particularly, the size of the analyzed cohort is very nice. The study might help others to develop novel hypotheses and to compare their results to the gene expression data presented here.

This is a very clear and well organized study. It is technically sound and well described. I do not see major issues. Below are some suggestions that might further improve the study:

1. It is not clear whether comorbidities are absent in the healthy control group, or whether they have not been analyzed.

2. Similarly, why is there no count for Leukocytes and Neutrophils in the controls?

3. The figure legends are extremely short. More description would be desirable.

4. A table with the full gene expression data should be included in the manuscript as a supplementary file.

5. In several figures, I do not see error bars in the diagrams. Additionally, in the text, when it is stated that something is significant, it would be helpful to include the p-value.

6. Figure 6 appears only in the discussion. I think this could appear also in the results section.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

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

Yes

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

Yes

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 am able to assess the statistics

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

Acceptable

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