Reviewer’s report

Title: TRAIL signals through the ubiquitin ligase MID1 to promote pulmonary fibrosis

Version: 1 Date: 29 Jul 2018

Reviewer: Riitta Kaarteenaho

Reviewer's report:

Thank you very much for offering me the opportunity to review the revised version of the interesting manuscript by Adam Collison and co-authors. I have still some questions regarding the methods, especially the diagnostic procedure of the patients whose lung biopsies were used in this study.

Methods (pages 4-5):

More detailed representation of the patients who had undergone the transbronchial lung biopsy operation would be informative since these 8 cases constituted the human lung biopsy material of the present study.

It would important to state in the manuscript that the histological confirmation for UIP/IPF of the patients was performed by analyzing the transbronchial lung biopsy samples, but not surgical lung biopsies, which causes some uncertainty in the diagnoses of IPF. In both ATS/ERS guideline (Raghu G et al Am J Respir Crit Care Med 2011) and the more recent suggestion ("White paper", Lynch DA et al Lancet Respir Med 2018) it has been straightforwardly informed that the transbronchial lung biopsy samples are not large enough for the diagnosis of IPF. Thus, the diagnostic procedure of the patients suspected for IPF was not performed according to the current international guidelines for the diagnosis of IPF, which fact would be appropriate to inform in the manuscript.

Were the HRCTs of all biopsied patients categorized as possible UIP, and not definite UIP?

Fig E1:

Higher magnification and arrows would be demonstrative. Hyperplastic pneumocytes are not visible in the Fig E1 C. Moreover, intra-alveolar fibrotic lesions in the Fig E1 E may as well represent organizing pneumonia (OP) pattern, and not UIP.
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.

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 recommend additional statistical review

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Please indicate the quality of language in the manuscript:

Acceptable

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