Reviewer’s report

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

Version: 0 Date: 10 May 2018

Reviewer: Riitta Kaarteenaho

Reviewer's report:

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Collison A et al have investigated serum TRAIL, midline 1 protein (MID1) and PP2A in (transbronchial) lung biopsy samples from 8 patients with idiopathic pulmonary fibrosis (IPF). In addition, the effects of both FTY720 analogue AAL(s) on bleomycin induced lung fibrosis in mice, and recombinant TRAIL on mouse fibroblasts were investigated.

This is an interesting translational study, which have used diverse methodologies and materials. Some points regarding particularly the demographics and the investigations of the patients with IPF, however, would benefit supplemental information.

1. In the abstract and the first sentence of the Methods (page 5) it was informed that "lung biopsies were collected". In line 95 it was written that "fibrotic lung tissues were removed from patients undergoing transbronchoscopic lung biopsy".

Apparently the investigated tissue samples were small transbronchial lung biopsies, and not larger surgical lung biopsies? It would be more informative if the authors would use the exact name for the transbronchial lung biopsy samples throughout the whole manuscript including the abstract.

2. Were the transbronchial lung biopsies taken as research purposes since these kind of lung biopsy samples are not large enough for the diagnostic of IPF? How many tissue samples per patient were collected and how the lung tissue samples were handled?

3. Information about the categorization of HRCT according to the ATS/ERS 2011 statement would be both interesting and important. How many of HRCTs were categorized as definite UIP, probable UIP and not UIP, and from how many patients the surgical lung biopsy samples were taken for the confirmation of the diagnosis of UIP? The information of HRCT
categorization and the results of spirometry, especially forced vital capacity (FVC), would be useful to add in the Table 1.

4. The detailed information of some reagents is missing.

5. Images of transbronchial lung biopsy sections would be demonstrative.

6. The type of collagen needs to be supplemented. In page 9, line 32 it was informed that collagen alpha 2 was used, and thus the information about the type of collagen is missing (only the chain was informed). It was, however, informed in the Fig 5 (apparently alpha2 chain of collagen type I?)

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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