Reviewer's report

Title: Clinical significance of mTOR, ZEB, ROCK1 expression in lung tissues of pulmonary fibrosis

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Reviewer: Melissa Piper

Reviewer's report:

Summary: This article by Park et al investigated expression of mTOR, ZEB and ROCK1 in lung tissue from patients with pulmonary fibrosis. The goal of this study is to assess the clinical significance of these biomarkers and their predictive value of outcome. The data from this study should be clinically relevant, however, there the data should be further analyzed to better appreciate these biomarkers in UIP/IPF.

Major Compulsory Revisions:

1) As the authors followed the patients over time, they presented the expression data in the tables as change over FVC. Opposed to using change over time for all patients, it would be very interesting to present all expression data according to severity of disease using FVC, extent of honeycombing by CT scan, DLCO and histologic fibrosis score upon biopsy, as shown for mTOR expression in Figure 2. There is no mention that this analysis was performed for ZEB1 and ROCK1. This information along with the survival curves could further stratify a subset of patients with poor prognosis. By doing this it is possible that ROCK may emerge to be significant marker.

2) The authors mentioned that ANOVA was performed. However, was this performed for each stain with respect to patient samples? It would actually be of interest to do ANOVA across expression of each marker per patient. This would further determine, if collectively together these markers are important.

3) To better appreciate the co-localization of these markers in specific lung tissue, it would be advantageous to co-stain the lung for cell specific markers. Then normalize the staining by immunofluorescence to have a non-bias assessment of the tissue. Also this method would be able to generate a ratio of expression per cell to account for the increase recruitment to the lung tissue.

4) In the discussion (example page 10) and throughout the article, the authors indicate that the role of mTOR in human pulmonary fibrosis is being examined. Much of this is speculative and should be rewritten to reflect that the authors postulate the mTOR role based on existing literature.

Minor Essential Revisions:

1) In the abstract, the authors state that either mTOR or ZEB1 expression was associated with better prognosis, however the survival curves show the inverse.
This should be corrected.

2) In the introduction (paragraph 2, second to last sentence) where the authors described the administration of rapamycin to TGF-a –induced pulmonary fibrosis, the reference by Korfhagen et al should be included.

3) Arrows and magnification should be placed on the IHC images.

4) Please indicate the number of control lung tissue samples used in the comparisons.

**Level of interest:** An article of importance in its field

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests