Reviewer's report

Title: Investigating the effects of Pirfenidone on TGFbeta1-stimulated Non-SMAD signaling pathways in Dupuytren's disease-derived fibroblasts

Version: 2 Date: 17 Dec 2018

Reviewer: David O'Gorman

Reviewer's report:

The authors have substantially improved the data interpretation in this manuscript. My only additional, discretionary revisions pertain specifically to the results and discussion sections. In all figures (1-4), the format is a comparison between CT and DD cells, treated with TGFß-1 and/or PFD. I suggest that the authors address five basic points in these sections. 1) Are the baseline phosphorylation (activation) levels of these enzymes (AKT, ERK1/2, p38 ) and substrate (MLC2) different between CT and DD?; 2) does TGFß-1 treatment significantly alter these levels within groups (CT and DD)?; 3) does PFD significantly alter these levels within groups?; 4) does PFD significantly impact the effects of TGFß-1 treatments within groups?; 5) did they discern any effects of TGFß-1 or PFD (or both) that are specific to either CT or DD cells?

Some of these points are already addressed in the current manuscript, however some are not, and they would appear to the key discussion points. Perhaps most importantly, if the baseline levels of these molecules in DD and CT cells are not statistically different before treatment (Q1 above), and if PFD has essentially the same effects on both CT and DD cells, does this potentially undermine its utility as a therapeutic for DD without, or with minimal, impact on normal (CT) cellular function? The inclusion of these points in the discussion would substantially enhance the manuscript.

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

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Acceptable

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