Author’s response to reviews

Title: The antifibrotic drug pirfenidone inhibits spondyloarthritis fibroblast-like synoviocytes and osteoblasts in vitro

Authors:

Julie Stougaard (jkl@biomed.au.dk)

Søren Lomholt (soren.lomholt@gmail.com)

Pernille Ommen (pernille.ommen.andersen@post.au.dk)

Jens Kelsen (jenskels@rm.dk)

Tue Kragstrup (kragstrup@biomed.au.dk)

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Author’s response to reviews:

Dear editor,

Thank you for handling our paper very effectively. We really appreciated the feedback from both you and the reviewers. Below we have addressed your comments.

On behalf of the authors,

Tue

Editor Comments:

I think this paper would deserve to publish in BMC Rheumatology. However, significant revision is still needed to accept for the publication. I would like you to understand how scientists should write the paper. You should describe and interpret the results appropriately based on the facts you have observed and the statistical analysis. Please read my comments below, and revise the manuscript carefully.

Major comments;

1. The results of live/dead staining by flow cytometry would support your statement that PFD does not cause cell death but suppress the proliferation of fibroblasts. Please show
the proportion of dead cells in fig 1, and describe the results in the result section (not material and method section).

Answer: We have added the FCM gating strategy showing the Live/Dead staining and added the percentage of dead cells in the Results section.

2. I think the interpretation of the results in this manuscript is that PFD suppressed proliferation and cytokine production of SpA fibroblasts and mineralization of osteoblasts, but did not alter the differentiation of fibroblasts to myofibroblasts. Please correct all of the related statement in both result and discussion sections. As I wrote in my last comments to you, you should not state that PFD inhibited the expression of aSMA or HLA-DR in the result section, since they are not statistically significant. You can discuss that PFD might have some mild effect to suppress the expression of these molecules in the discussion section though you did not find significant differences due to large inter-donor variation.

Answer: We have changed the Results section describing only moderate suppression of aSMA and HLA-DR (“a modest and non-significant suppression”). We have removed all statements in Discussion, Conclusion and Abstract that “pirfenidone inhibit myofibroblast differentiation”.

3. The results of HOB in fig 4C does not mean anything, since there are no statistically significant differences between the three conditions. You cannot state that inhibition of mineralization by PFD is reversible based on the data. If you think the no differences are due to small sample size, please increase the number of samples.

Answer: We have removed the HOB data entirely.

Minor comments;

1. It was not clear for me what <<causing debris>> means in the first paragraph of result section. I would recommend to remove <<causing debris in the cultures or>> in the sentence.

Answer: We have removed the sentence.

2. In fig 3C, it is hard to see the difference between PFD- and PFD+ in UT condition. Please enlarge the size in 0-10 area in Y-axis so that we can see the difference clearly.

Answer: We have enlarged the lower part of the y-axis in Fig. 3C.