Reviewer’s report

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

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Reviewer: Leyre Brizuela

Reviewer’s report:

This is a paper from Stougaard and colleagues proposing that « the antifibrotic drug pirfenidone inhibits spondyloarthritis fibroblasts and osteoblasts in vitro». Although the message of the article is interesting, the proposal of a new approach for SpA treatment, manuscript needs a revision and

1. What was the technique used to measure the deposition of hydroxyapatite ? this should be explained.

2. The part « osteblast cultures » has to be rewritten. Culture and mineralization conditions used with osteoblast cell cultures are not explained. The authors have included two references to illustrate the culture conditions for osteoblasts. Nevertheless, mineralization assay has to be detailed and explained because one of the conclusions is that the drug inhibits osteoblast mineralization.

3. Results line 29. …without causing visible cell death, debris or detachment of cells … what « visible cell death » means ? authors seem to conclude quite quickly that their drug has no effet on the cells. The way to confirm the effect of the drug is not sufficient, apoptosis markers can be checked (Clived caspase 3 or PARP) by western blot, flow cytometry or immunocytochemistry. The stats from figure 1 are not correct. Paired t-test has to be done at least when 4 independent experiments have been realized, in this figure there are only 3. A non-parametric Mann-Whitney test would be more appropriate.

4. The most important message of this article for the reviewer is that PFD has an effect in osteoblast mineralization. Authors have presented a new figure with effects of PFD in osteoblast maturation. PFD decreases DKK-1 (and osteoblast inhibitor after treatment of cytokines). This result is interesting but error bars are huge, more experiments have to be done in order to improve the stats because they do not seem correct. OPG (an osteoclast inhibitor) is also decreased. This controversy is well-explained in the discussion. Nevertheless, mineralization figure for HOB has to be improved. Error bars are huge and protocol has still to be explained. What it means « mineralization ratio » ?

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?
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Yes

Are the conclusions drawn adequately supported by the data shown?
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