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Rostock, Nov. 6, 2017

Dear Editor,

Thank you and the referees for the constructive review of our paper entitled

"Antifibrogenic effects of vitamin D derivatives on mouse pancreatic stellate cells" (Manuscript No: wjg/2017/36512). To meet the reviewer's concerns, we have thoroughly revised the manuscript according to the suggestions. The format was updated and typesetting was corrected. The changes are highlighted in yellow. Please find enclosed the edited manuscript in Word format. Subsequently, we provide specific point-to-point replies to each reviewer's comments.

Furthermore, we would like to respond to three editorial comments:

- 1- Language Certificate: We have thoroughly revised the manuscript and ask for another check-up. Several authors of the paper have a long standing experience in publishing articles in the English language (together more than 100 PubMed-listed articles).
- 2- Supportive Fondation: There was no funding through external sources. The FORUN program is an internal program of the Rostock University Medical Center, and all forms are in German. Furthermore, the grant application also contains unpublished experimental plannings and ideas (unrelated to this paper) that are confidential at this stage. If more information is required, we ask for a specification.
- 3- Institutional review board statement and institutional animal care and use committee statement: As stated now on the title page, these informations are not applicable to our study. The use of mice for no other purpose than cell isolation is not an animal experiment as defined by the law, and does not obtain numbers as requested. Please contact the corresponding author for more information, if necessary.

We hope that our manuscript, in its revised form, is now acceptable for publication in the World Journal of Gastroenterology.

Sincerely yours,

Robert Jaster



(corresponding author)

## Point-to-point reply to the referee's comments

We thank the referees for their constructive suggestions and helpful advices.

### Reviewer 1:

1. p4, *Two decades ago, pancreatic stellate cells (PSCs) were...*--> "*Two decades ago*" corrected in the end of this sentence.

The correction has been performed as suggested.

2. p4. *..great detail (reviewed in[1])*--> *detail reported by xxx [1]*

We have changed the text accordingly.

3. p5, *Although they displayed slightly different molecular effects, the general efficiency of the three vitamin D derivatives was similar.* --> *This was results of your study or from reference?*

We apologize for this lack of clarity. The finding was the result of our studies, not from reference. This is now stated clearly in the respective sentence.

4. p11, *..reduced DNA synthesis rather slightly (data not shown).* --> *data not shown, how to prove? or you can neglect this points. the next "...too low for reproducible results (data not shown)*

Thank your for the advices.

First point (DNA synthesis): We have deleted the sentence since the point can indeed be neglected.

Second point: Here, we have deleted the phrase "data not shown", since it was misleading.

5. *The section of Discussion*--> *need to add more discussion according to the points in the results in a different paragraph.*

Thanks a lot for this suggestion. On page 12, we have now expanded the section "Discussion" (end of paragraph 2).

6. p13, *In this regard, the applicability of <sup>18</sup>F-proline as a molecular probe for positron emission tomography (PET) might be of particular interest.* --> *What you mean or you can delete this sentence because not related your manuscript.*

Thank you for the comment; the sentence has been deleted.

7. p15, *The section "Comment" not a normal format in a manuscript and delete it.*

We have substituted this section by a section "Article Highlights" (as requested by the journal).

### Reviewer 2:

1. *Please reconcile the nonsignificance of the data of calcipotriol in Fig.6. A statement in this regard will be helpful to the readers.*

Thank you for the comment. The nonsignificance of the effect of calcipotriol is the result of two influencing factors: (1) the small sample size (n=6), and (2) the need for a Bonferroni correction, since multiple testing was performed. Without such a correction, the p-value would be 0.044, with the correction it is 0.141. Taken these aspects together, we believe that the differences

between vitamins D2 and D3 (significant effects) and calcipotriol (no significant effect) need to be interpreted cautiously. From a biological point of view, the relevance of these statistical differences remains, in our opinion, questionable.

To meet the reviewers concerns, we have added one sentence to the legend of Fig. 6 and expanded the discussion of the respective findings (p. 12).

*2. Also please provide a statement of what methodological differences contrasted the antiproliferative effects of vitamin D3 on a published report on murine PSC's?*

Thank you for this advice. We have added a sentence on page 12 (end of paragraph 2) to outline the differences.

*3. Finally the author's statement of recognizing the follow-up studies in animal models to evaluate the antifibrotic effects of vitamin D in vivo will be of great interest for future studies.*

Thank you for this encouraging comment.