Author's response to reviews

Title: High SIRT1 expression is a negative prognosticator in pancreatic ductal adenocarcinomas

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Author's response to reviews: see over
Dear Dr. Solera,

We would like to thank you and the editorial board for reviewing our manuscript (Ms# 4523884429784685) entitled “High SIRT1 expression is a negative prognosticator in pancreatic ductal adenocarcinomas”, which we resubmit anew for your consideration for publication.

We found the additional suggestions of the reviewers very helpful and revised our manuscript accordingly. We think that we have been able to answer all of their points and summarized our responses in the attached text file. We highlighted changes in the manuscript in green colour and left the yellow colour indicating the text passages that have already been changed in response to the previous review.

Please do not hesitate to contact us if we can provide further clarification. We will be happy to consider any further changes that you may deem necessary.

Sincerely yours,

Albrecht Stenzinger
Point-by-point reply to the reviewers’ comments

Ms. No. 4523884429784685

Remarks to the comments of the reviewers
We thank the reviewers for their helpful comments, and we have taken their suggestions into account in our revision of the manuscript. We have reproduced each comment along with our responses and referenced the changes in the manuscript with the corresponding page of the revised manuscript. We highlighted all new changes in the revised version of our manuscript in green colour (formerly revised parts in yellow colour).

Comments to the reviewers’ points

Reviewer Ilse Rooman

The reviewer wrote:

Reviewer's report:
The authors have delivered a satisfactory response to my comments. I have two more remarks to be made:

- The graph in Fig 3b should be in the same order as the Western Blot shown in Fig 3a

Our reply and changes:
We thank the reviewer for this valuable advice and corrected the figure accordingly.

- It would be more informative to replace the Kaplan Meier analysis with Disease specific survival data rather than overall survival.

Our reply and changes:
We fully agree with the reviewer and we are currently compiling additional survival data for this cohort including clinical response and disease-specific survival. However, currently these data are only available for n=5 patients so that we are unable to provide these data for this manuscript yet. However, taken alone we do think that the relation between Sirt1 expression and overall survival is of interest for research groups in the field further underlining the importance of functional work on the role of Sirt1 in tumorigenesis.

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a
Reviewer Younh-Hwa Chung

Minor Essential Revisions

The reviewer wrote:

1. Since the author suggested that SIRT1 is an independent prognosticator in PDACs and plays an important role in pancreatic cancer cell growth, we asked to discuss this matter; Role of SIRT1 between clinical PDAC samples and pancreatic cancer cell lines. We found their discussion that makes their issue more supportable.

2. To support a positive role of SIRT1 in growth, we proposed siRNA or nicotinamide treatment for SIRT1 suppression or inhibition. They followed our suggestion in figure 2 and 5.

3. We asked cambinol effect on SIRT1 in regular figure not in supplementary result. We found their result in figure 9.

In general, the authors followed our suggestions and guidelines but we still found their very minor mistakes such as no consistency of unit: hours and hrs. In addition, we recommend to correct chemical formulation using lower letters instead of H2O, use H2O.

Our reply and changes:
We thank the reviewer for this valuable advice and corrected these two mistakes in the manuscript throughout. We used lower letters for the formula “H₂O” and “hrs” instead of “hours”.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
'I declare that I have no competing interests'