Reviewer’s report

Title: ROLE OF CATHEPSIN S IN PERIODONTAL WOUND HEALING - AN IN VITRO STUDY ON HUMAN PDL CELLS

Version: 1 Date: 24 Jan 2018

Reviewer: Reinhard Gruber

Reviewer's report:

The authors show that CatS is a mitogen that also supports migration of periodontal fibroblasts. Even though the data are preliminary, the findings are new and of potential clinical value.

What a pity that the authors have not yet published their finding that CatS is found in inflamed periodontal tissue. This putative finding is maybe not surprising considering that CatS mediate the PgLPS induced IL-6 expression in splenic cells PMID: 28769800. This CatS activity required PAR-2 activation. This research cold be inspiring to test FSLLRY-NH2, a PAR2 antagonist, in the study by Memmert et al. Also cysteine protease inhibitor could be used to see if the mitogenic activity of CatS requires the proteolytic activity of the enzyme. Authors could also rule out that faster wound closure is a consequence of CatS-induced cell proliferation, maybe by irradiating the cell or by blocking cell cycle genes. Also, CatK could serve as a nice control for proliferation. To support the hypothesis, important would be to expose the fibroblasts to a TLR stimulus and then measure proliferation and migration - with antisense CatS RNA or better a specific CatS inhibitor Z-FL-COCHO, or at least cysteine protease inhibitors. Maybe the authors want to consider some of the suggestions but they should at least strengthen their introduction and discussion removing all the textbook knowledge that is not directly relevant for the study. Too little is written about the molecular mechanisms how CatS can exert its function in physiology and pathology. Would be nice to do a LPS- or ligature-induced periodontitis model in CatS KO mice.

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.

No

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.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?
2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?
3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?
4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?
5. Do you have any other financial competing interests?
6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons
CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal