Reviewer’s report

Title: The impact of down-regulated SK3 expressions on Hirschsprung disease

Version: 0 Date: 05 Dec 2017

Reviewer: V.G. Shakkottai

Reviewer's report:

Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format.

Please overwrite this text when adding your comments to the authors.

In this article by Gunadi et al. expression of SK3 channels is assessed in ganglionic and aganglionic segments of cases of Hirschsprung disease. The study is interesting and reproduces findings from a prior report in a different population. The study could be improved with the following changes.

1. It is important to note that the reduction in SK3 occurs in addition to other neurotransmitter signaling in disease. The authors give the impression that the changes are restricted to SK3.

2. The control population demographic information should be provided in table 1. This is important to know in order to determine how well the samples were matched.

3. A major contention of the authors is that SK3 reduction in the ganglionic segment predicts persistence of bowel symptoms. This is not addressed at all as a follow up to the cases. It would be informative to present data on how patients did following surgery and whether the reduction in SK3 in the ganglionic or aganglionic segment in individual cases influences outcome. If long term follow up data are present, these should be included.

4. It could be helpful to show immunostaining from the resection segments for SK3-this would also give the reader more confidence that the appropriate segments of gut were analyzed by qPCR.

5. Some more information about sample preparation would be helpful. Were samples examined by conventional histology and adjacent gut used for RNA extraction? How much tissue was used for RNA isolation? How did the authors ensure that the sample for RNA isolation was from aganglionic (or ganglionic) colon?
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?
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.

I recommend additional statistical review

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

Needs some language corrections before being published

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