Reviewer’s report

Title: MiR-34a affects dexmedetomidine-inhibited chronic inflammatory visceral pain by targeting to HDAC2

Version: 0 Date: 21 May 2019

Reviewer: Martin Kaczocha

Reviewer’s report:

This is an interesting study that assesses the role of miR-34a in dexmedetomidine-mediated analgesia. Although novel and important, my enthusiasm was dampened by methodological omissions that reduce my confidence in the conclusions of the study. Consequently, the manuscript requires major revisions. My concerns are outlined below:

Major:

1) The methods section is devoid of key details including but not limited to the dose of TNBS, the sequences of the miR-34a inhibitor and scrambled control, the cell-line used for DLRA assay, and the region of the 3' UTR that was amplified.

2) Line 105: The somatic hyperalgesia that occurs with TNBS is not explained. Paw position was assessed following TNBS administration, yet paws were not injected. Please clarify.

3) Figure 3. The interval between adenoviral injections and behavioral testing is not stated in the figure legend nor in the methods. More importantly, the efficacy of the adenoviral transduction in the spinal cord is not shown. Please provide evidence (e.g., GFP fluorescence, immunohistochemistry) showing successful transduction of spinal cord.

4) Since the adenovirus was administered systemically, it is not possible to ascribe the effects to the spinal cord. The authors should perform a follow up experiment using intrathecal viral administration (or alternatively using siRNA/antisense oligos) to knockdown miR-34a.

5) The HDAC2 KD rat is not described in the methods. Is this a new animal model? If not, please provide a reference. If so, describe how it was generated in detail.

6) Page 10: "We found that luciferase activity was suppressed in cells with an miR-34a mimic transfection, which was fused with DHAC2 3'-UTR in 70% of the cases, relative to cells from the control groups". Please show individual points rather than mean +- SEM for this data set. Does this imply that the data were not normally distributed? IF so, why wasn't a nonparametric method employed?

Minor:
1) Line 92: Rats were deprived of food and water?

2) Line 97: vehicle is reported as 5% DMSO. Presumably this is in saline?

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.

Yes

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 am able to assess the statistics

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