Reviewer’s report

Title: Comprehensive microRNA profiling reveals potential augmentation of the IL1 pathway in rheumatic heart valve disease

Version: 0 Date: 23 Sep 2017

Reviewer: Paola Rizzo

Reviewer's report:

This is a potentially useful study on circulating miRNAs suggesting an involvement of IL1 pathway in rheumatic heart valve disease (RHD).

The authors identified, among others, 2 miRNAs which are downregulated in the serum of RHD patients, compared to normal subjects. They provide in vitro evidence that these miRNAs target IL1 and its receptor and suggest an involvement of IL1, that would be consistent with the already reported inflammatory environment of RDH. To support their findings they show high levels of IL1 and its receptor in diseased valve samples from RHD patients, but not from patients with congenital heart valve disease (CHD).

Before the paper can be considered for publication the author should address the following:

1) To support the claim of specificity of these miRNAs in RHD, the expression levels of these two miRNAs should be assessed also in serum of CHD

2) Provide Methods for the immunostaining and include a negative control of immunostaining shown in Figure 5. Figure 5 is missing a graph cited in the figure legend. Also the authors should mention how many samples were analyzed by IHC.

3) Western blot is cited in the abstract but not shown anywhere

4) The manuscript needs a major revision of English structure and grammar.

5) Normal control seem to be missing from Figure 1. Please explain.
6) Figure 2 A and B are not readable

7) Title and Discussion should downplay the involvement of IL1/IL1R since the downregulation of their expression by the identified miRNAs is inferred only from Luciferase assay.

**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.

No

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Unable to assess

**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:

Not suitable for publication unless extensively edited
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