Reviewer’s report

Title: MicroRNA-200a confers chemoresistance by antagonizing TP53INP1 and YAP1 in human breast cancer

Version: 0 Date: 29 May 2017

Reviewer: WEI WEI

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Review

In this manuscript, Yu et al investigated the potential oncogenic impact of miR-200a in breast cancer. Overall, this is a well-designed and performed study. The authors have demonstrated that miRNA-200a may induce chemoresistance by inhibiting TP53INP1, YAP1 and consequently p53 family protein mediated apoptosis. The authors further demonstrated the overexpression of miR-200a in chemoresistant breast cancers to suggest the potential clinical relevance. However, this manuscript still contains some gaps in the mechanism studies which need to be addressed by supplying additional experimental data before the consideration of acceptance.

Specific comments:

1. The authors need to declare the matured miRNA sequence - e.g. miR-200a-5p or miR-200a-3p.

2. It is highly recommended the author recapitulate their discovery in Fig. 4D using anatago-miR-200a in the gemcitabine resistant MDA-MB-231 cells.

3. The downregulation of p73 in Figure 4D is not well discussed - please clarify the potential mechanism. It is highly recommended the authors delineate whether the downregulation of p73 is due to the direct targeting effect of miR-200a at RNA level or the destabilization due to the loss of YAP1 at post-translational level. A good starting point is to check p73 mRNA level by qRT-PCR upon miR-200a overexpression.

4. Similarly, the authors need to demonstrate p73 is associated with the alteration of Bim, Bax and PUMA upon miR-200a overexpression.

5. Figure 5A: Since there is no CR patients in this cohort, please remove it from the legend.

Please suggest the statistical method for p-value calculation as well.

6. Figure 5B: Please additionally test the prognostic impact miR-200a by Cox regression model. This avoid the subjective cut-off of a continuous variable (miR-200a expression...
level) used in Kaplan-Meier model, unless the authors can suggest the biological inference of such cut-off.

7. Please discuss whether p53 participated in miR-200a mediated chemoresistance (ZR-75-30 harbors wt TP53)

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.

I am able to assess the statistics

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Please indicate the quality of language in the manuscript:

Acceptable

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