Reviewer’s report

Title: MiR-199a-5p is up-regulated in gastric cancer and functions as an oncogene by targeting klotho

Version: 2 Date: 5 January 2014

Reviewer: An-Mei Deng

Reviewer’s report:

General comments
The aim of this study investigated the role of miR-199-5p in gastric cancer initiation and progression. The investigators found that miR-199-5p was up-regulated in the gastric cancer tissues as well as cell lines. The correlation between miR-199-5p and klotho, as well as the clinical characteristics of gastric cancer, was analyzed. The in vitro study demonstrated that miR-199-5p could regulate the migration activity and invasion ability of gastric cell line. Finally, they determined whether klotho was a direct target of miR-199-5p by luciferase reporter assay.

Generally, this is an interesting and well-done study, which extends our knowledge about the role of microRNA in the parthenogenesis of gastric cancer.

Specific comments
1. Is the question posed by the authors well defined?
   Yes, the question is clearly defined.

2. Are the methods appropriate and well described?
   Partially.
   In statistical analysis section, the authors stated that “miR-199a-5p level obtained by In Situ Hybridization and klotho expression level obtained by Immunohistochemical Staining (categorical data) were described by their frequency and analyzed by Chi-square test or Fisher’s exact test. Spearman’s rank correlation coefficient was used to assess the relationship between miR-199a-5p and klotho expression levels”. The statement is generally correct, however, TMN stage and differentiation in Table 1 and 2 are graded data, Mann-Whitney U test should be employed instead of Chi-square test or Fisher’s exact test (The Journal of pathology, 2013, 231(3): 335-341). In table 3, I am rather confused how the investigators calculate the coefficient of miR-199-5p and klotho expression levels? Based on Table 3, it is clearly that either miR-199-5p or klotho expression level is a binary, rather than a continuous or graded variable. Under that condition, it seems Chi-square test is appropriate. Please explain.

3. Are the data sound?
   Yes. The investigators explored the effect of miR-199a-5p on the migration activity and invasion ability of gastric cell line by a gain and loss of function
strategy. The transfection efficiency should be examined first (J Immunol 2009;183:2150-2158).

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   Yes.

5. Are the discussion and conclusions well balanced and adequately supported by the data?
   Yes. The last sentence of discussion section should be revised. The major clinical implication of present study findings is that miR-199-5p is a potential therapy target, rather than discovering a diagnostic and prognostic biomarker, for gastric cancer.

6. Are limitations of the work clearly stated?
   No, the authors did not state the limitations of the study.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
   Not applicable.

8. Do the title and abstract accurately convey what has been found?
   The title should be revised. The authors found that miR-199-5p could affect the migration activity and invasion ability of gastric cell line, and it also target klotho, however, it remains unknown whether klotho can affect the migration activity and invasion ability of gastric cell line, although previous study has partially support their hypothesis. Therefore, they should not concluded that miR-199a-5p functions as an oncogene by targeting klotho. “Up-regulated miR-199a-5p in gastric cancer functions as an oncogene and targets klotho” may be an appropriate title for their work.
   In fact, the work would be better if the investigators explored the effects of klotho on the migration activity and invasion ability of gastric cell lines.

9. Is the writing acceptable?
   Partially. Some sentences were started with Arabic numbers and should be revised.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.