Reviewer’s report

Title: MiR-216b inhibits cell proliferation by targeting FOXM1 in cervical cancer cells and is associated with better prognosis

Version: 0 Date: 02 Jul 2017

Reviewer: Noor Hasima Nagoor

Reviewer’s report:

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1) The direct binding of miR-216b to FOXM1 has been demonstrated previously (Zheng et al., Eur Rev Med Pharmacol Sci. 2016;20(12):2541-50 and Sun et al., Cell Biol Int. 2017. doi: 10.1002/cbin.10754). The authors should take note of this.

2) The effects of miR-216b on cervical cancer cells need to be evaluated on more than one cell line.

3) The authors should include the concentration of miR-216b mimics and inhibitors used in each assays.

4) Page 6, Line 19: Has the expression of FOXM1 in HCC94 (low) and SiHa (high) cells been reported previously? If so, please cite the relevant studies.

5) How did the authors arrived at the conclusion that FOXM1 expression was higher in HeLa, C33A and SiHa cells, and lower in Ca Ski and HCC94 cells (Figure 1A)? In comparison to?

6) Page 10, Line 11-15: This statement did not correspond to the results found in Figure 1B. Instead, Figure 1B appeared to be more relevant to the statement found in Line 17-23 (same page). Authors should include another figure for the statement mentioned in Line 11-15.

7) The authors should clarify on what was the "control" used in Figure 1A and 1B and why.

8) The authors should include correlation analysis for miR-216b and FOXM1 expression in cervical cancer cells in Figure 1.

9) Figure 1C mentioned in the figure legend has been left out from the label in the corresponding figure.
10) The results for normalized band intensity (to β-actin) in western blot should be presented (Figure 1A, 3A, 4B, 5A and 5B). If not, it will be very hard to interpret the results, as the band intensity for β-actin was not exactly the same across samples. Statistical analyses should also be carried out to determine its significance.

11) It was mentioned in the Materials and Methods that cell proliferation was detected on day 1, 3, 5 and 7 using MTT, however results shown in Figure 2B contained results for day 1 to 6 and Figure 5C contained results for day 1 to 5. Can the authors please explain this?

12) The lines used in the graph for Figure 2B can be differently coloured (like Figure 2A) for better presentation.

13) The western blot results in Figure 3A should include results for LEF1.

14) Since p21 is negatively regulated by FOXM1, why was p21 excluded from the results in Figure 3B?

15) The authors should specify what is "NC" in Figure 4C (is it cells transfected with mimics negative control?). Were the results compared to cells transfected with mimics negative control or vector control? Did the authors also include cells transfected with negative control inhibitors?

16) Can the authors comment on why luciferase activity was significantly increased in miR-216b-in cells in Figure 4C?

17) The authors should explain and elaborate on the results shown in Figure 5B.

18) Since results showed that miR-216b affects cell cycle related factors, did the authors carried out cell cycle analysis to examine the effects of miR-216b on cell cycle?

19) Others: Page 4, Line 11: cervical caner should be written as cervical cancer. Caski should be written as Ca Ski. Hela should be written as HeLa

**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.

No

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

No
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