Reviewer’s report

Title: Suppression of microRNA-31 increased the sensitivity of HCT-116 cells to 5-FU at early stage, and affected cell migration and invasion ability in a p53 independent manner in colon cancer cells

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Reviewer: George Yousef

Reviewer’s report:

This is an interesting study that explores the role of miR-31 on different aspects of colon cancer cell line pathogenesis, including cell proliferation, apoptosis, cell cycle, colony formation, migration and invasion. The study results show also that miR31 increases the sensitivity of the colon cancer cell lines to 5-FU chemotherapy.

The results are valid and of clinical and therapeutic significance since it pave the road for more therapeutic applications of microRNAs. The experimental design is solid and the conclusions are justified based on the results.

Major Criticism:

1) The 5-FU dose given is not indicated or justified. There is only a vague statement about a “clinical dose” that was used without further explanation. It would add significantly to the value of the manuscript if the authors have tried different doses of 5-FU in order to obtain the optimal dose that can illustrate the added effect of miR-31 on cell proliferation, apoptosis, etc.

2) In many of the experiments, there is no indication of the reproducibility. I assume that the authors did the experiments in duplicates or triplicates to ensure reproducibility. That has to be indicated in the materials section.

3) It would add significantly to the value of the study if the same experiments are performed on other colon cancer cell lines so that the results are more generalizable and are not unique for one particular cell line.

4) The statement in page 16 of the results section (page 16, first paragraph), is not justified. This is a mere speculation that is not based on strong experimental support or rationale. It is difficult to believe that miR-31 will simultaneously turn on pro and anti-invasion forces.

5) In the discussion section (page 15), there is a mix up of the discussion about the role of miR-31 in cancer. The authors are citing two different examples, one from head and neck cancer and the other from breast cancer. According to the introduction section, the biological rule of miR-31 in these two cancers is opposing (overexpression verses underexpression). It is difficult to mix up the functions from these two cancers into one working hypothesis.
6) Although there is what seems like increasing sensitivity of the cell lines to 5-FU with inhibition of miR-31, the effect is minimal (as seen in figure 2), although statistically significant. This should be highlighted in the discussion section and the author should indicate the need of more experiments on different cell lines to support this phenomenon and further validate it.

Minor Criticism:
1) The author should expand more on discussing the potential targets of miR-31, possibly through bioinformatics target prediction analysis.

2) Few typographical and spelling mistakes have to be fixed. E.g., page 5, line 2: should read: “underexpressed in serous ovarian carcinomas.”

3) Certain paragraphs are redundant and mentioned repeatedly throughout the text. E.g., the first paragraph of the results section.

4) The results (page 11, line 7) should read: “confirming that miR-31 was.”

5) The discussion has very lengthy paragraphs that are sometimes more than a full page in length. This has to be reorganized.

6) The statement in the conclusion (page 17), “not only the expression but also the function of miR-31 showed a cancer specific manner” is not justified. Since the authors are dealing only with one type of cancer, that is colorectal cancer.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
'I declare that I have no competing interests'