Reviewer’s report

Title: Silencing of miR-182 is associated with modulation of tumorigenesis through apoptosis induction in an experimental model of colorectal cancer

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Reviewer: Anurag Singh

Reviewer's report:

This paper by Perilli et al. describes the oncogenic role of miR-182 in colorectal cancer (CRC). The authors show that miR-182 is highly expressed in a number of CRC cell lines compared to normal colon tissue. The majority of functional studies are performed using an isogenic cell line pair, MICOL-14hTert/tum. The MICOL-14tum cell line is a tumorigenic variant that expresses significantly higher levels of miR-182. The authors show that miR-182 antagonism causes induction of apoptotic, changes in cell cycle progression and reduced tumorigenicity in immunodeficient mice. Overall, the studies are well conducted. A major drawback of the studies is a lack of detail in terms of the mechanisms by which miR-182 promotes anti-apoptotic signaling. Transcriptomic profiling of anti-miR-182 transfected cells indicates upregulation of FOXO and p53 pathways. However, this is not functionally tested. Functional validation of p53 and/or FOXO signaling would significantly strengthen the studies. Some specific comments are noted below:

1. In Fig. 1A, qPCR data is shown for MICOL-S cell line. This cell line is not described in the text. The authors should include a description of the cell line, i.e. how is it related to MICOL-14.

2. For cell cycle analysis in Fig. 2C, the authors should show the raw FACS plots.

3. Lines 50-51: the numbers are written incorrectly, e.g. should be 3,472 not 3.472.

4. The data in Fig. 4A are confusing and not explained in detail clearly. It seems that anti-miR-182 causes downregulation of the predicted miR-182 target genes. This is in contrast to the qPCR data in Fig. 4B, which shows upregulation, confirming the authors hypothesis. Please explain the data in Fig. 4A.

5. The authors should provide some in-depth discussion of the signaling pathways regulated by miR-182. For instance, what are functional roles of the miR-182 target genes, Gadd 45A/B and NABP1.
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.

Yes

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 recommend additional statistical review

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None.

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