Reviewer's report

Title: Characterization of global microRNA expression reveals oncogenic potential of miR-145 in metastatic colorectal cancer.

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Reviewer: Eva Bandres

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The findings from the study are interesting and may help to provide additional insights about the role of miR in colorectal oncogenesis. The authors confirm several previous data showed that miRNAs are altered in 45 CRC samples comparing with 4 matched normal colorectal tissues. Several miRNAs are differentially expressed between normal and early stage CRC (including miR-145) and others showed significant differential expression between early and late stage (mostly stage III). Then, the authors analyzed the expression of miRNAs in CRC cell lines and they performed functional studies in vitro to identify the role of miR-143 and miR-145 in the metastatic SW620 cell line. The authors show an interesting phenomenon and the authors propose an interesting hypothesis but there is no mechanism behind the finding. Lack of mechanism is a weakness of this study and I would suggest the authors to characterize the mechanism of their hypothesis since at the moment their data do not justify their conclusions.

Major Compulsory Revisions

- The expression of deregulated miRNA in CRC cell lines is very heterogeneous. Only 11 miRNAs were commonly deregulated in CRC clinical samples and CRC cell lines. The authors suggest that the finding in clinical samples is not completely reproduced in cell line models. However, the authors should considerer if altered miRNA in CRC tissues are consequence of epithelial cancer cells or of other cell types. In situ hybridization could help to elucidate this question.
- On the other hand, the authors performed Northern blot analysis on 22 of altered miRNAs in 8 CRC cell lines. However, there are several miRNAs that are validated by Northern but are not represented in Table 5 as differentially expressed in CRC cell lines (for instance miR-221, miR-96, miR-182, and miR-90b).
- Finally, the results of miR-145 overexpression in SW620 metastatic cell line are particularly interesting. These results contradict previous studies which demonstrated that miR-145 over-expression has tumor suppressor effects in non-metastatic CRC cell lines. The authors hypothesized that the differentially status between metastatic and non-metastatic cells might be the cause of different function of miR-145. In my opinion, this is a good hypothesis but it should be verified. However, the authors should demonstrate that miR-145 over-expression in the isogenically matched non-metastatic SW480 cell line
induce the opposite effect than in the metastatic SW620 cell line. Actually, the genetic network analysis of miR-145 targets in metastatic versus non-metastatic cells is not enough to explain the potential dual-effect of miR-145.

Discretionary Revisions
- The introduction is very long. I think that it should be shorter.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.