Reviewer's report

Title: miR-124a and miR-137 inhibit proliferation of GBM cells and induce differentiation of tumor stem cells

Version: 1 Date: 26 October 2007

Reviewer: Setha Douc-Rasy

Reviewer's report:

Comments for the authors

Manuscript entitled: MiR-124a and miR-137 inhibit proliferation of GBM cells and induce differentiation of tumor stem cells

By Silber et al.

General comments:

It is a very good paper that clearly highlighted the important role of miR-124a and miR-137 in neural stem cells differentiation either in adult neural stem cells or brain tumor stem cells. The studies of these miRNA selected for the present studies following quantitative RT-PCR analyses of 192 mature miR sequence included mouse oligodendroglioma-derived stem cells (mOSCs) and human GBM-derived stem cells. Although the role of miR-124a and miR-137 in neural stem cells has been published elsewhere, the present work is original by the fact that the mechanism by which these miRNA promote neuronal differentiation in cells deprived of growth factors signaling or inhibit proliferation of GBM cells or early passage GMB cells was clearly demonstrated using transgenic mouse oligodendriomas model and GMB cell lines. Moreover, the results from epigenetic regulation mechanism studies using 5-aza-dC and TSA were properly shown.

---------------------------------------

1- in Fig 1C (p10), miR-124a did not change appreciably following with either agent alone or in combination. In fact, the treatment with a combination of 5-aza-dC with TSA augmented more than 2 fold-change in U87 cells. In Fig 1B, the identity of cell line: SV2-NSC cells should be mentioned over the graph. The same remark for Fig 5A: U251 cells should be mentioned over the histogram.

2- The experiments and the results shown in supplementary figure 1 is of prime importance; the authors should show in the text body but not as in the supplementary data.

After taken into account of these minor points, the manuscript entitled “MiR-124a and miR-137 inhibit proliferation of GBM cells and induce differentiation of tumor stem cells” MiR-124a and miR-137 inhibit proliferation of GBM cells and induce differentiation of tumor stem cells” is good for publication and the reference is
adequate.

3- As the results showed the subtle difference between miR-124a and miR-137 relative to epigenetic regulation or the responses of target genes such as CDK6 and pRB, the function of these 2 miRs may not be redundant and may vary in accordance of development time or cells type. Only additional experiments with more targets and more cell types will define clearly the difference but which is not necessary for this paper.

4- On the text of supplementary figure showing Cycle Threshold and Fold change= f(Differentiation time), it must be Supplementary figure 2 (instead of Supplementary figure 1 as indicated because the Supplementary figure 1 in this text before reviewing is the “Expression of luciferase from the…” ) except that the latter will be put in the main text, so it is no need to correct it.

**Which journal?**: Appropriate or potentially appropriate for BMC Medicine: an article of importance in its field

**What next?**: Accept for publication in BMC Medicine after minor essential revisions

**Quality of written English**: Acceptable

**Statistical review**: No

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