Reviewer’s report

Title: MiR-663 is down-regulated with promoter hypermethylation in pediatric acute myeloid leukemia (AML)

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Reviewer: hongwei wang

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In this manuscript, the authors sought to evaluate whether miR-663 was inactivated epigenetically in pediatric acute myeloid leukemia, their results indicated that MiR-663 transcript was significantly lower in AML group compared to controls; meanwhile the miR-663 methylation was also investigated. This paper raises several concerns:

1) The meaning of the results need to be further addressed as there no any correlation between the clinical features and the miR-663 methylation. And also the transcript of miR-663 was almost same in patients with methylated and unmethylated miR-663, the author need to investigate whether promoter hypermethylation is a special event in pediatric AML which control the disease development. The author should be careful to give the major conclusion, and the written pattern should be changed accordingly.

2) The author claimed that a high frequency of miR-663 promoter hypermethylation was found in pediatric AML primary tumor cells but not in the control normal cells, but the result might not be enough to support this conclusion as there no any statistic analysis apart from some raw data in figure 2. And also the scale of the control samples is relative small in compared with the AML samples.

3) The author should answer a critical question whether the promoter hypermethylation have any direct effects on the expression of MiR-663, which should be compared not only in the pediatric AML samples, but also in the leukemia cell lines and the control samples.

4) Figure 2 B is not necessary, as this figure do not add further information apart from showing the raw Q-PCR data.

5) In the statistical analysis, the authors should show which method were used to compare the difference between the groups such as the data presented in figure B.

6) The author needs to give a reason why different assay (Bisulfite genomic sequencing V.S methylation-specific PCR analysis) was used to detect the MiR-663 methylation in the leukemia cell lines and the pediatric AML samples. And especially the detected CpG islands by MSP assay need to be indicated, as the results of Bisulfite genomic sequencing assay might not be necessary
consistent with the MSP assay, Bisulfite genomic sequencing data should be very important and need to be included for the pediatric AML samples to clarify the complete methylation status of the miR-663 promoter.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.