Reviewer's report

Title: Primary microRNA 221/222 is strongly overexpressed in the majority of patients with acute myeloid leukemia

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Reviewer: Spencer B Gibson

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Rommer et al has submitted a manuscript entitled “Primary microRNA 221/222 is strongly overexpressed in the majority of patients with acute myeloid leukemia” for consideration for publication. The authors show that there is a higher ratio of pri-miRNA 221/222 compared to miRNA 221 in primary AML cells compared to normal controls. The author conclude that there is a processing rate limiting step in AML cells to allow for this accumulation. The high pri-miRNA 221/222 could represent a novel biomarker for this disease. Even though the data is interesting and could reflect the biology of AML, there are significant issues with interpreting the data and the functional consequence of these miRNAs. Specific comments are listed below.

Major Compulsory Revisions

1. The high level of pri-miRNA 221/222 is likely due to a limitation in processing but it was unclear whether this was due to an increased over expression of miRNAs or a defect in miRNA processing.

2. miRNA 221/222 are increased in AML cells but this increase is somewhat limited by processing of the miRNAs. What is the functional outcome of this? The level of pri-miRNA might not be important unless there were changes in processing. This was not directly addressed by the authors.

3. In figure 4, there was a huge range of expression of pri-microRNAs in the AML samples. It will be hard to interpret the results unless larger number of AML samples was used. Overall, it seems that most pri-miRNAs were increased in some AML cells. This also causes concern over the important of pri-miR-221/222 in AML.

4. In Figure 5 G, why was MCF-7 cells used. This is a breast cancer line and not close to an AML cells. It is hard to interpret these results.

5. In Figure 6, the lower levels of pri-miR221/222 in remission patients is not surprising since the high levels of pri-miR221/222 in AML cells. There was also no major difference in pri-miR221/222 in relapsed patients. The value of pri-miRNA as a biomarker is hard to determine. It would be good to correlated pri-miR221/222 with overall survival to evaluate it as a biomarker. One troubling issue is patients with low pri-miRNA levels still relapsed.

6. The major question not addressed by author is why pri-miRNA is generally elevated in AML. Is this due to changes in DNA methylation or chromatin changes. This is currently unclear and lowers the significance of this work.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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

Declaration of competing interests:

No conflict of interest to declare.