Reviewer’s report

Title: Article miRNA expression profiling in normal breast tissues and hereditary breast tumors from BRCA1- and BRCA2-germline mutation carriers in Brazil

Version: 0 Date: 27 Oct 2019

Reviewer: Carmen Jeronimo

Reviewer's report:

In this study, the authors propose to explore specific miRNA signatures in hereditary breast tumors. The authors performed a global miRNA expression profiling using NanoString technology, a high throughput and sensitive platform for molecular quantification, and identified several miRNAs differentially expressed. Moreover, they explored the potential target genes of each miRNAs.

Overall, the manuscript is well organized and clear. However, there are some issues that need to be addressed by the authors.

Major concerns:

The section "Statistical analysis" is poorly detailed, the authors must clarify it. Indeed, in the section "Results", subsection "miRNA expression profiling of the hereditary breast cancer and normal breast tissues" the authors mentioned an ANOVA test (page 9, line 236) that was not previously referred on section "Statistical analysis" and no data was shown. Moreover, the authors should review the statistical tests performed. The t-test and ANOVA assume a normal distribution of the sample in study, whereas non-parametric tests should be used for non-normal distribution of the sample.

In table 1 it would be more informative if the authors include the tumors' histological subtype. Moreover, the authors should revise the figures presented in the table, because they do not match. For example, in BRCA1 group (n=14) the total described on molecular subtype and the total described for TNM evaluation is 15 cases. Regarding SBC group (n=23) the authors present a total of 47 cases on estrogen receptor evaluation.

The authors present a boxplot in figure 3. This type of graphic is not the most informative to demonstrate the comparison between the different groups. Indeed, no statistically difference seem to be depicted between BRCA1 and BRCA2 breast tumors. The authors should perform a more illustrative graph and present the statistical data.

The authors must include in the "Discussion" a paragraph with the major limitations of the study.

Minor comments:

In authors and affiliations, the authors should key the affiliations listed as number 6 and 9 to the respective author or authors.

In the section "Background", the authors must update the first citation (page 3, line 59) "Cancer
incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012" to the most recent publication from GLOBOCAN "Global Cancer Statistics 2018: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries".

In the study were included 14 hereditary breast cancer patients who did not had pathogenic germline mutations in BRCA1, BRCA2 or other known high-risk genes such as PTEN and TP53. The authors should clarify the inclusion criteria for these patients.

The authors described the statistical analysis performed for miRNAs expression as well as ROC curve analyses on the section "NanoString data analysis". However, it would be more informative and easier to the readers if this information was included on section "Statistical analysis".

The authors must clarify the purpose of the comparison between sporadic breast cancer and normal tissues (page 8, line 231). The reader might not understand the purpose of the analysis.

In section "Discussion" the author should confirm the presence of "DE" abbreviation on page 11 line 308.

In section "Figure titles" the authors should use the abbreviations for normal breast tissues (NBT) as mentioned before (page 22, line 591).

In section "Figure titles" the authors should use the abbreviations for microRNA (miRNA) as mentioned before (page 22, line 591).

**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.

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