Reviewer's report

Title: Overexpression of miR-21-5p as a predictive marker for complete tumor regression to neoadjuvant chemoradiotherapy in rectal cancer patients

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Reviewer: Pasqualino de Antonellis

Reviewer's report:

Dear editor

I have read this manuscript with great interest and my first opinion is that this is a good manuscript and potentially identifies new biomarkers for predicting complete responder to nCRT although the number of patients analyzed was a limiting factor.

The workplan is comprehensive, exhaustive and the methodology is based on established published work.

However, at many places authors have not provided enough justification to support their results that require to be addressed.

I have made some suggestions and comments, listed below, which I feel would improve this manuscript.

Major Points:

Firstly in their study the authors in result section (page 7) claim “The number of sequences for each specific miRNA was used to estimate its expression, and low expressed miRNAs were removed in order to increase detection power of statistic tests “ this conceptually should be a correct way to obtain more robust results but the authors didn’t have any explicit control for assume low and high expression. How many miRNAs are down or up regulated in this samples compared to normal tissue?

Their analyses were performed using only complete vs incomplete responder.

In order to define a possible predictive use of these identified miRNA the author must evaluate the expression also in normal samples.

Then the authors claim that “Using this approach, we found a strong negative correlation (r = -0.5 and p-value = 0.03) for SATB1 gene”. These claim implied that only SATB1 gene was found inversely correlated to miR-21. The author should provide data on others genes that were found inversely correlated to miR 21.

Moreover between early recurrence and incomplete response the miR 21 expression was found to be more or less the same. Authors need to discuss this issue on how early recurrence and incomplete response showed potentially the
same molecular signature in their dataset. Are these entities only distinct by physician, but molecularly are the same?

Minor Points:
Page 9 the claim must be reworted “we analyzed the expression pattern of its target genes using whole transcriptome” as “we analyzed the expression pattern of its putative target genes using whole transcriptome” target scan such as other algorithms used for target prediction needs in vitro validation.

Discretionary Revisions
In methods section page 17 “Only miRNAs with a minimum of 20 cpm in at least seven samples were kept in the analyses.”
My suggestion is corroborate this table, with min and max cpm value for each miRNA
And preferably with a table supplementary table, that show cpm for each miR in each sample.
This table could be helpful for the reader.

With kind regards

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:
I declare that I have no competing interests