Reviewer’s report

Title: Assessing the activity of nonsense-mediated mRNA decay in lung cancer

Version: 0 Date: 19 Jun 2017

Reviewer: DAVID M BEDWELL

Reviewer’s report:

Previous studies have suggested that inhibition of nonsense-mediated mRNA decay (NMD) in tumor cells can suppress tumor growth through expressing new antigens whose mRNAs otherwise are degraded by NMD. Thus, NMD inhibition is a promising approach for developing cancer therapies. The authors of this study developed three metrics using RNA-seq data to measure NMD activity, and apply them to a dataset consisting of 72 lung cancer patients.

They show that these metrics have good correlation, and that the NMD activities in adenocarcinoma samples vary among patients: some cancerous samples show significantly stronger NMD activities than the normal tissues while some others show the opposite pattern. The authors conclude that NMD activity varies among lung cancerous samples, and suggest that this could result in varying efficacy of NMD-inhibition based therapy.

Overall, the data and analysis of this study are reasonable. However, some of the analyses appeared to be better than others. Specifically, the R-isoform analysis appear to be more robust than the other two. However, the authors don't really point this out in the conclusions (or abstract). I suggest that a little more interpretation of the results be done in a manner that clearly states which of these algorithms the authors feel is best.

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.

I recommend additional statistical review

**Quality of written English**

Please indicate the quality of language in the manuscript:

Acceptable

**Declaration of competing interests**

Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license ([http://creativecommons.org/licenses/by/4.0/](http://creativecommons.org/licenses/by/4.0/)). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal