Reviewer’s report

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

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Reviewer: Athanassios G. Kotsinas

Reviewer’s report:

The report by Wang and collaborators proposes to assess the activity of nonsense mediated mRNA decay (NMD) in order to predict the possibility of treating cancer through inhibition of this pathway. Specifically, the authors have developed three different metrics based on previously published bioinformatic data obtained from high-throughput expression methods and apply them in a data set of lung adenocarcinoma patients. Their results show a good correlation among the three methods and reveal that in the examined cohort of lung cancer patients NMD exhibits variability from patient to patient in regard to its activity. They further discuss limitations that may apply.

Conceptually, this is a very interesting approach in predicting pathways to be potentially exploited to treat cancer. Yet I have a major concern if I understand correctly the methodological approach. The authors collect data on several genes and from variously published results to generate a "reference pool" against which each patient is examined in regard to its NMD activity status. How can this be applied in everyday practice for each patient? It appears that in order to apply these metrics in a specific type of cancer one would need first to assess various gene targets and next to select the appropriate ones for comparison reasons. This means that ahead of the metrics application a large dataset of information must be available in order subsequently to compare and define which of the involved patient has high/low NMD activity. This seems rather non-practical in terms that this must be adapted for each type of cancer and availability, at least for the moment, of such vast information to define the three metrics. I would suggest discussing potential future implementation of these metrics considering how my concern could be bypassed.

A minor issue relates to few parts of the text where syntactical langue issues are present.

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

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Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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