Author's response to reviews

Title: Differentially Expressed Alternatively Spliced Genes in Malignant Pleural Mesothelioma Identified Using Massively Parallel Transcriptome Sequencing

Authors:

lingsheng Dong (ldong@partners.org)
Roderick V Jensen (rvjensen@vt.edu)
Assunta De Rienzo (aderienzo@partners.org)
Gavin J Gordon (ggordon@partners.org)
Yanlong Xu (yxu11@partners.org)
David J Sugarbaker (dsugarbaker@partners.org)
Raphael Bueno (rbueno@partners.org)

Version: 9 Date: 28 November 2009

Author's response to reviews: see over
Editor’s request:

“Please also ensure that your revised manuscript conforms to the journal style. (http://www.biomedcentral.com/info/ifora/medicine_journals). It is important that your files are correctly formatted.”

Answer: Yes. We corrected the manuscript according to the requirements.

Reviewer 2:

The authors have addressed most of the points raised in my previous report. Especially, they have added key data that was missing from the first version of the manuscript. I would like to re-emphasize some points that were not fully addressed and would further improve the manuscript.

Minor Essential Revisions:
1. The confusion regarding the samples used in this investigation still remains in some parts the manuscript.

A. Methods (Page 5, 2nd paragraph) – Please indicate the subset from the former study that was used in this investigation (4 tumors and one normal).

Answer: Corrected as suggested by the reviewer.

B. Discussion (Page 12, 1st paragraph) – Please amend the statement “Using the same dataset [15]” to clarify that a subset was used.

Answer: Corrected as suggested by the reviewer.

2. Of the 10 candidate EJs analyzed with qRT-PCR, six have a level of expression in the normal lung sample that falls well within the range of expression of the 4 MPM tumors. This should be mentioned in the Results section (page 10, 2nd paragraph).

Answer: Corrected as suggested by the reviewer.

3. The authors should also include in the manuscript that they formally tested the differences between the EJEIs of the five samples (point #7 of my first report) and that they “were not able to find statistical difference between both differentially expressed exon junctions and the comparison of the results among different platforms”.

Answer: Corrected as suggested by the reviewer.

4. In response to the point #8 in my first report, the authors mentioned that “The cut-off value was quite arbitrary” and that “To confirm the test as valid diagnostic tool, more samples are needed.”. Hence, the claims that “splice variants provided reliable markers for disease” and that they “could also be used together to classify the samples with high
sensitivity and specificity” (page 13, 2nd paragraph) are overstatements. The two splice variants could be used as diagnostic markers only once the limitations of this investigation (arbitrary cut-off, few samples) are overcome. Please acknowledge this in the ms.

Answer: Corrected as suggested by the reviewer.

5. There are many typos in the supplementary files and some in the ms. Please check the files very carefully.

Answer: Corrected as suggested by the reviewer.

Discretionary Revisions
6. Some essential data in the additional file 5, such as the normalized EJEI values and the RT-PCR EJEI, would be better presented as a table in the manuscript.

Answer: Based on additional file 5, we have created a brief version table (Table 2 in the manuscript) which contained the normalized EJEI and RT-PCR results.

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests: I declare that I have no competing interest