Reviewer's report

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

Version: 8 Date: 3 November 2009

Reviewer: Tatiana Torres

Reviewer's report:

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).

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

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).

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”.

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.

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

**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 interests