Author's response to reviews

Title: Serum diagnosis of diffuse large B-cell lymphomas and further identification of response to therapy using SELDI-TOF-MS and Tree Analysis Patterning

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Author's response to reviews: see over
Dear Dr. Edmunds,

Thank you for your kind decision and the reviewer’s comments. We have accordingly revised the manuscript. The revised version has been edited by a native English speaker from International Science Editing, Compuscript Ltd, Shannon Industrial Estate West, Shannon, Co. Clare, Republic of Ireland. Following is a point to point response to the reviewer’s comments.

REVIEWER 2

Comments and answers:

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. The supplementary figures are not cited in the text and should appear in the result section. These figures must be available for readers, not only for reviewers.

Answer: We cited these supplementary figures in the result section from line 20 to line 21 of page 8, and line 1 to line 2 of page 10.

2. The abbreviation BPS should be explained in the text.

Answer: We have explained the abbreviation BPS in line 14 of page 5 in the revised manuscript.

3. Page 11, last paragraph, “spectroscopy” has been employed (instead of “spectrometry”?)

Answer: We have corrected it in line 2 of page 12 in the revised manuscript.

Discretionary Revisions (which the author can choose to ignore)

The biomarkers identified were not further used in order to discriminate the groups. It should have been interesting to know if a classification tree using the biomarkers work better or not than biomarker pattern software. This point was not assessed, even if asked by reviewer 3.
Answer: The discriminatory peaks were detected from the learning set. According to the reviewers’ suggestion we testified them in the test set. For example, nine top-scored peaks, at M/Zs of 2821, 2954, 3266, 4779, 5638, 5707, 5838, 5907, and 7975 were selected for predicting the diagnosis. The sensitivity was from 62% to 84% and specificity was from 73% to 85%.

In the potential discriminatory biomarkers for discriminating the good prognosis and poor prognosis cases, 4078, 4304, 5481 and 8608 were chosen. The sensitivity was from 61% to 80% and specificity was from 65% to 88%.

In the potential discriminatory biomarkers for discriminating relapse patients from non-relapse patients, 2954, 4304, 4320, 5069 and 16093 were chosen. The sensitivity was from 60% to 74% and specificity was from 59% to 76%.

Although these discriminatory peaks showed the highest discrepancy and significant difference between two groups, the sensitivity and specificity of any single peak are lower than those of biomarker patterns from BPS, and the combination of the discriminatory peaks didn’t enhance the sensitivity and specificity significantly. If it is reproducible in another cohort of samples, these biomarkers will be good candidates for protein identification in future study.

We added these in the result section from line 17 to line 18 of page 8, from line 28 to line 29 of page 8, and from line 4 to line 5 of page 9. We also added comments in the discussion section from line 10 to line 19 of page 13.

**REVIEWER 3**

Comments and answers:
1. There are still syntax errors and occasionally the language is hard to follow. It is therefore recommended that the authors seek the advice of a colleague proficient in the English language and revise the language accordingly prior to the publication of the manuscript.

   Answer: The revised version has been checked by a native English speaker from International Science Editing, Compuscript Ltd, Shannon Industrial Estate West, Shannon, Co. Clare, Republic of Ireland.

2. In the abstract, it should be made clear that the classification rates reported refer to the test /blinded set. (for example: the authors may write that “the proteomic patterns achieved a sensitivity of 94% and a specificity of 94% detecting DCBL in test set of 85 samples…..”).

   Answer: We are sorry that we did not describe it clear in the manuscript. In the 2nd revised manuscript we described it in detail. These mends were added in the abstract from line 10 to line 14 of page 2.
3. A couple of points that will facilitate understanding of the results particularly those dealing with the difference between the "discriminatory peaks" and the peaks selected during the decision tree analysis include: Were the discriminatory peaks detected from the whole set of samples or just from the learning set of samples? Were any combinations of the discriminatory peaks tested for sample classification efficiency? A couple of comments on these issues would be helpful for the better understanding of the manuscript.

Answer: The discriminatory peaks were detected from the learning set. According to the reviewers’ suggestion we testified them in the test set. For example, nine top-scored peaks, at M/Zs of 2821, 2954, 3266, 4779, 5638, 5707, 5838, 5907, and 7975 were selected for predicting the diagnosis. The sensitivity was from 62% to 84% and specificity was from 73% to 85%.

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We added these in the result section from line 17 to line 18 of page 8, from line 28 to line 29 of page 8, and from line 4 to line 5 of page 9. We also added comments in the discussion section from line 10 to line 19 of page 13.

We hope you will find the revised manuscript acceptable for publication in BMC Cancer.

Best regards.

Sincerely yours,

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