

April 19, 2013

**Re: ESPS Manuscript NO 2030: Serum proteomic in chronic hepatitis B patients treated with PEG-interferon alfa-2b**

Dear Editor of World Journal of Gastroenterology:

On behalf of the authors, I would like to thank the reviewers and the editor for their comments. We have modified the manuscript accordingly and the edited parts are highlighted in yellow. We hope the revised manuscript will be deemed satisfactory for publication in the World Journal of Gastroenterology.

**Reviewer 1:**

Please copy, cut, paste the exact comments from this reviewer here

**Answer: We have revised the format of the table according to the reviewer's comment. We have separated the figures. We utilized the language editing services offered by the Faculty of Medicine, Chulalongkorn University, to improve the readability of the manuscript while preserving its contents.**

**Reviewer 2:**

1. The authors did not discuss the significant difference in the age of virological responder and non-responder patients (Table 1,  $p < 0.047$ ). Since the age of patients was different between virological responders and non-responders, and the age of patients may influence the response to the treatment, this point should be discussed.

**Answer: We thank the reviewer for pointing this out and have added the following sentences to the M&M and result sections of the manuscript: Since the sustained responders and non-responders have significant age differences, Pearson Correlation was performed between age and each protein expression value. No significant correlation between age and any protein expression was observed; therefore, it is unlikely that age will affect protein expression in this study.**

1. In results, page 10, second paragraph: the authors state that the age virological responders and non-responders patients is not significantly different; however, Table 2 showed a significant difference with  $p < 0.023$ .

**Answer: Similar to above, Pearson Correlation between age and each protein expression value in the validation phase. No significant correlation between age and any protein expression was observed.**

2. In results, page 10, last paragraph: "At the end of treatment.." but in Material and Methods, in Serum samples, say: "All patients received PEG-Interferon alfa-2b (...)..... for 48 weeks ..." Then, 24 weeks is not end of treatment.

**Answer: Thank you for noting this. We have amended the sentence from "end of treatment" to "by 24 weeks after treatment".**

3. After 24 weeks of treatment, why were included only 6 patients (3 patients per group of) for comparison between virological responders and non-responders?

**Answer: This is due to the number of limited samples we were able to obtain after treatment from a subset of patients.**

4. Table 5 should be not divided in sustained virological responders and non-responders, instead it should be presented as a single table.

**Answer: It is difficult to combine all of the information into one table because each protein was identified from a different spot using various other parameters for sustained responders and non-responders. In our manuscript, we presented each protein identified from each spot separately because there is a possibility that it may be a different isoform.**

5. Since albumin was depleted from the serum (Figure 1), why it is included in the analysis in Tables 3 and 5?

**Answer: The depletion kit cannot completely eliminate albumin. We have also mentioned this in the discussion section of the manuscript.**

6. Table 5, why in sustained virological responders, the protein CD5 antigen-like precursor is considered absent at baseline when Table 3 and Figure 1C showed relative intensity?

**Answer: CD5 antigen-like precursor from Table 3 and Table 5 were identified from different spot/position. Spot 202 in Table 5 was absent at baseline, while spot 145 in Table 3 could be detected at baseline.**

7. Page 11, last paragraph, "...suppress the expression of the low abundant proteins.." I suggest change by "suppress the detection of the low abundant proteins"

**Answer: Thank you for this suggestion. We have modified the sentence as per your recommendation.**

I hope that you will find our manuscript worthy of publication in the World Journal of Gastroenterology. I look forward to your reply.

Sincerely yours,

Nattiya Hirankarn, MD, PhD