Author's response to reviews

Title: Unique Immunologic Patterns in Fibromyalgia

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Dr. Diana Marshall  
Senior Managing Editor  
The BioMed Central Editorial Team

RE: MS: 2020487049761183  
Unique Immunologic Patterns in Fibromyalgia

Dear Dr. Marshall:

In regard to the peer reviews that came from Reviewers 1, 3 and 4, the following responses are being provided.

Reviewer #1, Mario D. Cordero, stated that the revisions we provided “substantially addressed the deficiencies” that had previously been cited. Consequently, there is no need or basis for us to make any changes in regard to this reviewer’s conclusions.

In reference to Reviewer #3, Fumiharu Togo, it was explained that our manuscript had “improved” since we made modifications to it. Though we were not specifically asked to respond to the latest revision request by this individual, we are providing this response. Specifically, Dr. Togo asked us to compare our results and abnormalities as it concerned patients with chronic fatigue syndrome (CFS) and to determine if there was a substantial overlap with patients with fibromyalgia.

Our article does not make mention of patients with chronic fatigue syndrome because none of our studied patients provided us with confirmed diagnoses that they had a chronic fatigue syndrome. Therefore, while we appreciate this reviewer’s perspective, we have no data available that can address it. We do recognize that in the future, studies should be done to address patients who may have overlapping symptoms.

Regarding, Reviewer #4, Nurcan Uceyler, the following comments are germane.
There appears to be misunderstandings on Dr. Uceyler’s part. This includes an alleged need to include a “second method” regarding cytokine analyses. However, we have never done a single method of measurement. Secondly, we did not rely on just general plasma results of cytokines.

According to publications by Dr. Uceyler and her co-authors, including “Reduced levels of anti-inflammatory cytokines in patients with chronic widespread pain,” Arthritis and Rheumatism, 2006 Aug;54(8):2656-64, they subscribed to a methodology concerning the role of cytokines in fibromyalgia based solely upon a single methodology, which was to measure levels of cytokines in the plasma. As we have explained in our manuscript, there has been numerous published research on serum cytokine levels in fibromyalgia patients and they have yielded conflicting results. We do not agree with the opinion that purely by measuring serum cytokine levels valuable diagnostic information regarding fibromyalgia will result.

The methods we relied upon included more than just the “single” approach of measuring serum cytokine levels. Besides obtaining that data, via a separate, second methodology, we stimulated peripheral blood mononuclear cells and we relied on multiple mitogens to do so. Hence, our approach to obtaining a diagnostic methodology in fibromyalgia was clearly different and it goes far beyond a single methodology. The significance of our second methodology as reported is striking. There was a statistically significant difference in supernatant cytokine levels between controls and patients with fibromyalgia which was observed following the stimulation of isolated and cultured mononuclear cells.

We believe that our title is appropriate. There is no question that the immunologic patterns that we detected in fibromyalgia patients have never been reported before. We also strongly believe that these findings constitute a strong diagnostic basis in reference to fibromyalgia. We have been able to uncover distinct peripheral blood mononuclear cell responses which when analyzed on a statistically comparative basis reveals a very strong, novel and authentic set of findings. They define a new and unprecedented approach to understanding the etiologic pathways in fibromyalgia.

Prior publications on the subjects of cytokine and fibromyalgia have implied that there were certain other cytokine abnormalities on which to account for the pathogenesis of the chronic widespread pain that afflicts fibromyalgia patients. However, we were not able to duplicate those findings. Additionally, we do not think that an appropriate methodology for uncovering etiologic pathways in fibromyalgia can rely on subjective patient responses. That approach is open to wide patient variability. Hence, we find it necessary to instead rely on objective criteria.
As stated in our manuscript, we find that fibromyalgia has as its foundation the immunologic processes which we were able to uncover. There may be conflicting perspectives which may lead to competing interpretations of our data. However, as has been explained, our results were based upon a more careful analysis of fibromyalgia patients and a larger population of fibromyalgia patients then has ever been previously achieved.

Sincerely yours,

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