Author’s response to reviews

Title: Unique Immunologic Patterns in Fibromyalgia

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Christna Chap, Ph.D.
Senior Executive Editor
The BioMed Central Editorial Team

RE: MS: 2020487049761183 Unique Immunologic Patterns in Fibromyalgia

Dear Dr. Chap:

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

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

In reference to Reviewer #3, Fumiharu Togo, it was explained that the revision we provided “substantially addressed the deficiencies” that had previously been cited. Consequently, there is no need or basis 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.” Though you, Dr. Chap, did not ask us to specifically respond to the revision requested by this individual, we are providing this response. Specifically, we were asked to compare our results and abnormalities as it concerned patients with chronic fatigue syndrome (CFS) and determine if there was a substantial overlap with patients with fibromyalgia.

However, at no time did our article ever make mention of patients with chronic fatigue syndrome nor did any of our studied patients provide us with confirmed diagnoses that they had a chronic fatigue syndrome. Therefore, the requested revision cannot be considered pertinent as it relates to a subject that at no time was ever part of our study. Additionally, and according to the definition of chronic...
fatigue syndrome as outlined by the United States Centers for Disease Control, the chronic fatigue syndrome is a distinct disorder that is different from fibromyalgia. And as have we have explained, since none of our patient population had been given a confirmed diagnosis of a chronic fatigue syndrome, we cannot do the requested comparative analysis.

Regarding, Reviewer #4, Nurcan Uceyler, the following comments are germane.

When Dr. Uceyler did her initial review of our article, she made ten different major compulsory revision demands. We responded to each and everyone of them. In particular, she criticized us for making specific cytokine level measurements and she inaccurately claimed that we only did one type of such measurement.

In Dr. Uceyler’s comments of October 17, 2012, a whole different set of criticisms were made. In other words, we feel we have a constant “moving target” in reference to her remarks.

There also appears to be misunderstandings on Dr. Uceyler’s part. In particular, we have never done a single method. Secondly, we did not rely on just general plasma measurements of cytokines.

According to numerous publications by Dr. Uceyler and her associates, they relied on comments concerning the role of cytokines in fibromyalgia based solely upon a single methodology, which was merely to measure levels of cytokines in the plasma. As we have explained in our manuscript, there have been numerous published researches on changes in serum cytokine levels in fibromyalgia patients and they have all revealed conflicting results. We do not subscribe to the claim made by Dr. Uceyler and others that purely by measuring serum cytokine levels valuable information of a diagnostic purpose can result. It is therefore obvious that our research undermines the basis for Dr. Uceyler’s publications and perspective and we feel that having done so has engendered possible unfounded animus.

In particular, the methods we relied upon included more than just the “single” approach of Dr. Uceyler, which is to measure serum cytokine levels. Besides obtaining that data, via a separate methodology, we also 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 goes far beyond what Dr. Uceyler claimed was only a single study methodology.

Dr. Uceyler’s demand that we also change our title for a second time is unfounded. It was Dr. Uceyler, herself, who relied on a specific title, “A Systematic Review on the Effectiveness of Treatment with Anti-Depressants in Fibromyalgia Syndrome” regarding her personal research. This appeared in the journal, Arthritis and Rheumatism, Volume 59. And in that publication, these authors said that they only, in fact, selected 26 of 167 available and potentially pertinent studies.
In an earlier publication by Uceyler, et al., in this same journal, Volume 54, it was implied that Th2 was a factor in the potential pathogenesis of chronic widespread pain. In point of fact, we just as others who have studied cytokines in fibromyalgia were not able to reproduce Dr. Uceyler’s claims.

We find it interesting that in a publication by Uceyler and Sommer in Volume 2 of the journal, Current Pain and Headache Reports, conceded that there was a need for “understanding pathophysiology” of how cytokines act. It was exactly that approach that we relied upon.

Our results were based upon objective tests regarding our study population. Dr. Uceyler and her associates, such as in the journal, Neuropsychiatric Disease and Treatment, Volume 4, conceded that there findings were based instead on subjective patient responses, a factor which we specifically criticized in our report.

So too did we criticize the concept that fibromyalgia is by definition a neurologic disorder. Dr. Uceyler has in her multiple publications implied otherwise. Hence, we do feel that there is unequivocal evidence of competing interests on Dr. Uceyler’s part, particularly in light of the comments of the other reviewers.

We have made what we believe to be appropriate modifications to our article. This modified article has been appended.

We trust that we will receive a prompt, fair and unbiased analysis of this latest submission and in a timely fashion. We specifically chose to use a BMC Central publication because of its open access. We have recent experience with a sister journal, BMC Genomics, where we recently had another manuscript accepted and published (BMC Genomics, 2012, 13:344 (27 July 2012), Analyses of Lead Toxicity in Human Cells.

Sincerely yours,

Frederick G. Behm, M.D.
Francis B. Geever Professor and Head

cc: Bruce S. Gillis, M.D., M.P.H.