Reviewer’s report

Title: The identification of patients with the clinical diagnosis of fibromyalgia using a multiplex cytokine assay

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Reviewer: Nurcan Üçeyler

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Major Compulsory Revisions

The authors have investigated plasma and PBMC of patients with fibromyalgia syndrome (FMS) for cytokine protein expression using multiplex bead based arrays and have compared the expression of selected cytokines without and after cell stimulation. They report on higher cytokine levels after stimulation of PBMC of controls compared to patients.

The strength of this study are the high numbers of samples (FMS: 110, controls: 91), however, there are several major problems with the manuscript in its current version. One major point is, that the hypothesis of the study is not clear and also what the presented data mean:

1) Quantitative data should already be given in the Abstract.

2) As an aim the authors state at the end of the introduction: ".. to gain further insight regarding the role of Cytokines in FM...". The study design however, is not appropriate for functional analysis of a "role". The authors only measure current cytokine levels which does not allow any speculation on pathophysiological roles. This should be changed accordingly.

3) The title seems inappropriate as well: "The identification of patients with ...fibromyalgia" implies that the article will give the reader e.g. new diagnostic tools or criteria to help making the diagnosis of FMS. This is not the case. Only data of one single cytokine measurement is given. We do not know, what the given data on these selected cytokines mean in FMS. Therefore the title needs to be changed.

4) The Methods section is not sufficient. To just give some examples: No information is given about the diagnostic criteria used for making the diagnosis of FMS; detailed clinical data on the patient population is missing (e.g. pain since when? pain where? which additional symptoms? etc); the control population is not characterized at all; when was blood withdrawn? This is especially important because different time points of blood withdrawal can change blood cytokine levels dramatically. How were other possible confounding factors (e.g. current infection) controlled for? Which inclusion and exclusion criteria were used for FMS and controls?
The methods used are not described adequately:
The array is not described detailed enough: which sensitivity limits for the measured cytokines? Were negative and positive controls measured? Were the assessments performed in a blinded manner?

5) Why were these cytokines measured? What was the hypothesis behind this selection?

6) Data illustration should be changed from Tables to graphs, at least for those cytokines showing intergroup differences.

7) Information on the statistics used are incomplete. Which statistics software was used? Why t-test? Which test used to confirm normal data distribution?

8) The discussion is a mere repetition of the finding. There is no discussion on what the data may mean. What does it mean that in this study cytokines were less inducible in PBMC of FMS patients compared to controls? The authors explain why these data can not be compared with previous studies, however, this does not help to better understand what was found. To state that these findings "correlate well" with selected other previous studies is not appropriate in this context: in the cited two studies other methods etc. were used as well and a direct comparison is not possible.

9) Abbreviations should be used consistently (e.g. always PBMC or PBMCS)

10) Table 2 should be eliminated; Table 3 contains the data of Table 2.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests