Reviewer's report

Title: Profile of Blood Cells and Inflammatory Mediators in Periodic Fever, Aphthous Stomatitis, Pharyngitis and Adenitis (PFAPA) syndrome

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Reviewer: Marco Gattorno

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The paper by Brown et al analyze the a number of laboratory parameters and cytokine serum levels in PFAPA patients either during fever episodes and in the inter-critical periods in comparison to age-matched healthy controls.

The paper is generally well written and results are clearly presented. However a number of points should be raised:

Results

1) The first paragraph is not completely clear and could be deleted or incorporated to the second one. In fact, the laboratory parameters reported in this paragraph cannot be considered as markers of a “typical PFAPA”. This definition is mainly done on the clinical ground (see patients and methods).

2) Data shown on additional Figures 2 and 3 are much more convincing than Table 3 and give a clearer idea or the statistical differences among the three groups. I would leave Table 3 as a supplemental file.

3) It is rather surprising to find low levels of WBCs in two febrile PFAPA patients. How the Authors can be sure that the febrile episodes was not related to a viral infection? At least Authors should comment on it.

4) Data on cytokine serum levels are quite interesting. However, even is statistically significant, it is rather difficult to draw a conclusion based on 3 points for each group only. Indeed, is not clear to me why only three patients for group were analyzed for each cytokine, whereas IP-10 serum levels are available from an higher number of patients and controls. How did the Authors selected the patients for the cytokine assay? Maybe it would be better to use a multiple cytokine kit as a screening method to identify the more relevant features. After this screening phase a dedicated kit should be used on a larger number of patients to verify the hypothesis arising from the first screening procedure (as correctly done for IP-10)

5) The experiment on monocytes is rather interesting. However it is really a pity that the Authors did not chose to add also a stimulation to the assay (LPS? PMA + inomycine?). This would add further interesting insights on the function of circulating PBMC from PFAPA patients.

Level of interest: An article whose findings are important to those with closely
related research interests

**Quality of written English:** Needs some language corrections before being published

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