Reviewer's report

Title: Increased IL-4 mRNA Expression and Poly-aromatic Hydrocarbon Concentrations from Children with Asthma

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Reviewer: Dominique MA Bullens

Reviewer's report:

In this manuscript the authors study blood cytokine production at the mRNA level in circulating leukocytes and compare the results in healthy and asthmatic children. They correlate this cytokine production with the level of serum PAH (sum of 12) in these children and found a positive correlation in asthmatics. In a rat model exposed to one PAH (benzopyrene) they observe similar findings on blood leukocyte cytokine production as in asthmatic children with high serum PAH concentration.

The manuscript is well-written.

However, some major concerns remain:

1) Asthma is diagnosed on questionnaires only; no individual data on lung function, reversibility on Salbutamol, medication use... are given.
2) in the rat model, asthma was not induced

It is important that the authors stress the correlation between leukocyte cytokine production and PAH levels, which differ between the two groups they studied, of whom one group also had features of asthma. They should have included a control group with identical exposure levels without asthma, in order to attribute their findings to the asthma features of group 2. Now they can only hypothesize that the serum PAH levels are linked with their asthmatic characteristics.

Other minor concerns:

1) introduction: last paragraph: I would also include a disadvantage of blood, namely that by using blood no data of the area of interest (eg the lungs) can be obtained. I would include induced sputum besides BAL and biopsies.
2) Can the authors explain the difference in HDL cholesterol levels between asthmatics and healthy subjects?
3) Do the authors have an idea about individual importance of the different PAH they studied and summed up. Is any of these of specific importance or can the sum also be mimicked by one or two of these PAH? If yes, is benzopyrene one of these most important ones?
4) is there any reason why benzopyrene in the rat model has been chosen?
5) there is now substantial evidence that in sputum and BAL from severe asthmatics IFN-gamma is also overexpressed. This means that not only the blood data can be correlating with the human data but also the data at the area...
of interest. In that way, it is a pity that the authors have no idea about the cytokine expression in the lungs/bronchi of their study subjects. I would at least add some of the manuscripts studying IFN-gamma in sputum/BAL of severe asthmatics to the discussion section.

6) the legend of figure 2B is not correct: non-asthamtic should be non-asthmatic (X2)

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I have no competing interests