Reviewer’s report

Title: Anti-TNF Inhibits The Airways Neutrophilic Inflammation Induced By Inhaled Endotoxin in Human.

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Reviewer: Stefan Zielen

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Anti-TNF inhibits the airways neutrophilic inflammation induced by inhaled endotoxin in human.

Olivier Michel, et al:

This is an excellent paper which targets an important field of down regulation of neutrophilic inflammation in chronic lung disease.

Treatment of neutrophilic inflammation is a demanding challenge for many chronic respiratory diseases like COPD, Bronchiolitis obliterans and neutrophilic asthma.

At present no effective therapy is available. The LPS inhalation model is an excellent tool to study neutrophilic inflammation and new drugs in prove of concept studies.

Nevertheless I have several comments to make:

It is unclear why initially 49 volunteers were enrolled but only 30 volunteers were randomized. The authors should explain why so many volunteers were excluded. Did some volunteers not responded to 20 µg LPS, if so, the authors should explain why this was the case.

Unfortunately the authors did not show any clinical symptoms after LPS inhalation in the volunteers.

Inhaled endotoxin provocation may induce influenza-like symptoms associated with an inflammatory immune response and a constrictive feeling of the airway in the chest. The safety of the method in healthy adults was recently investigated by Kitz et al. (Kitz R et al. Endotoxemia 2008). If endotoxin provocations are performed by experienced investigators, they are very safe and they do not lead to worsening of asthma or changes in lung function and very few symptoms. However in almost all studies of LPS inhalation an increase in body temperature was recorded.

Please report all clinical complaints after LPS challenge and include a section on increase of body temperature.

If you induced sputum protocol is excellent you will find a similar picture of lung resident cells comparable to BAL. After induced sputum you expectorate
macrophages 80-90 % lymphocytes and neutrophils, in normal controls not monocytes, Please change monocytes to macrophages this in the text and all figures.

Although effectiveness of steroids on lymphocytes is not the major focus of the paper the authors should discuss that oral steroids reduce the lymphocyte count significantly.

Please give some suggestions why this not the case for Anti-TNF.

Minor comments: Fig. 3 and Fig. 4: The colours for anti TNF, prednisolone and controls should be similar in all Fig.

**Level of interest:** An article of outstanding merit and interest in its field

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

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

**Declaration of competing interests:**

'I declare that I have no competing interests'