CORRESPONDENCE

Authors’ response

We have read with great interest the comments by Dr Persson1 on our recent paper in Thorax, in which we showed that clinical control of asthma associated significantly with lower numbers of activated eosinophils in the bronchial wall, yet only weakly with sputum eosinophils. As the number of eosinophils in biopsies did not associate with clinical control of asthma, we speculated that activation of eosinophils (measured as eosinophil protein X (EXP) immunopositive pixels per area) in bronchial biopsies reflects the level of disease control better than the number of eosinophils itself.2 As lysis of activated eosinophils and degranulation of toxic eosinophil proteins may damage the surrounding tissue,3 Persson wondered whether EXP immunopositivity in our biopsies associated with epithelial fragility, particularly in uncontrolled asthma.

In line with Persson’s hypothesis, the percentage of intact epithelium correlated negatively with EXP immunopositivity (Spearman’s r=−0.30, p=0.016), whereas there was no significant correlation with the number of eosinophils in bronchial biopsies (Spearman’s r=−0.12, p=0.35) (figure 1). This was not due to effects of current smoking, which is associated with increased epithelial cell proliferation, goblet cell hyperplasia, as well as with reduced eosinophil numbers in bronchial biopsies in asthma,4 since we excluded current smokers from our analysis. An additional regression model adjusted for inhaled corticosteroid use and atopy confirmed that loss of epithelial integrity and higher EXP immunopositivity are significantly associated with uncontrolled asthma, yet not with numbers of airway wall eosinophils (data not shown).

Another question from Persson’s letter was whether free granules locate in close proximity of denuded epithelium. Unfortunately, this ‘geographical’ relationship is very difficult to quantify in a reliable way. Moreover, we believe this specific question could be better investigated prospectively using an allergen provocation model; collecting blood, biopsies and sputum at regular time points; similar to what has been done in the past by Aalbers et al.5 In our existing dataset, the dynamics of transepithelial migration of eosinophils6 (tissue-lumen correlations) cannot be investigated in a reliable way.

In conclusion, our statistical analysis supports Persson’s hypothesis that ongoing lysis of activated eosinophils contributes to uncontrolled asthma. Our previous publication and our current analyses support the notion that loss of epithelial integrity may serve an important role in this respect, since it is independently associated with loss of asthma control.

Fatemeh Fattahi,1,2,3 Franke Volbeda,1,3,4 Martine Broekema,2,3 Monique E Lodewijk,2,3 Machteld N Hylkema,2,3 Helen K Reddel,5 Martine Broekema,2,3 Monique E Lodewijk,2,3 Dirkje S Postma,1,3,4 Nick H T ten Hacken1,3
1Department of Pulmonology, University of Groningen, University Medical Center Groningen, The Netherlands
2Department of Pathology and Medical Biology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands
3Groningen Research Institute for Asthma and COPD (GRIAC), University of Groningen, University Medical Center Groningen, Groningen, The Netherlands
5Woolcock Institute of Medical Research and University of Sydney, Sydney, Australia

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