Title: Nasal and bronchial levels of Th2 cytokines correlate during a virus induced asthma exacerbation

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Body: Asthma is a heterogeneous condition and it is vital to accurately predict responders to targeted therapies. However, difficulties in measuring IL5 and IL13 have forced reliance on indirect markers of Th2 inflammation with limited success. Using the human model of experimental rhinovirus (RV) induced asthma exacerbation (AE) and new techniques to absorb nasal (nasosorption) and bronchial (bronchosorption) mucosal lining fluid (MLF), we explored Th2 inflammation during a RV-induced AE. Methods: 32 mild-to-moderate asthmatics and 14 healthy subjects were inoculated with RV-16. Bronchoscopies were performed 2 weeks prior to inoculation and on d4 post-inoculation. Cytokines were measured in both bronchial and nasal samples at baseline and on d4 with further nasal sampling on days 2,3,5,7,10 and 42. Results: Nasal IL5 and IL13 were significantly increased in asthma during infection compared to baseline (p<0.001) and increased compared to healthy subjects (p<0.01). In the lung, there were relationships between bronchial IL13 (p<0.05) and IL5 (p=0.059) and total chest symptom score in asthma. Nasal IL5 and IL13 correlated with bronchial levels during infection (p<0.01) whilst baseline levels in the nose correlated strongly with infection levels (p<0.001). Conclusion: RV induced Th2 inflammation correlated with AE severity. Nasal Th2 inflammation correlated with bronchial levels whilst baseline Th2 levels predicted the magnitude of Th2 induction during the AE. Nasosorption is a non-invasive, rapid technique capable of measuring Th2 inflammation directly. It may be possible to use this technique as a biomarker to guide therapy with anti-IL5 and anti-IL13 mAb treatments.