Lipocalin2 protects against airway inflammation and hyperresponsiveness in a murine model of allergic airway disease.

Abstract:
Background Allergen-induced bronchial asthma is a chronic airway disease that involves the interplay of various genes with environmental factors triggering different inflammatory pathways. Objective The aim of this study was to identify possible mediators of airway inflammation (AI) in a model of allergic AI via microarray comparisons and to analyse one of these mediators, Lipocalin2 (Lcn2), for its role in a murine model of allergic airway disease. Methods Gene microarrays were used to identify genes with at least a twofold increase in gene expression in the lungs of two separate mouse strains with high and low allergic susceptibility, respectively. Validation of mRNA data was obtained by Western blotting, followed by functional analysis of one of the identified genes, Lcn2, in mice with targeted disruption of specific gene expression. Epithelial cell cultures were undertaken to define induction requirements and possible mechanistic basis of the results observed in the Lcn2 knock-out mice. Results Lcn2 was up-regulated upon allergen sensitization and airway challenges in lung tissues of both mouse strains and retracted on the protein level in bronchoalveolar lavage fluids. Functional relevance was assessed in mice genetically deficient for Lcn2, which showed enhanced
airway resistance and increased AI associated with decreased apoptosis of lung inflammatory cells, compared with wild-type controls. Similarly, application of Lcn2-blocking antibodies before airway challenges resulted in increased inflammation and reduced apoptosis. Conclusion These data indicate a protective role for Lcn2 in allergic airway disease, suggesting a pro-apoptotic effect as the underlying mechanism. Cite this as: A. M. Dittrich, M. Krokowski, H.-A. Meyer, D. Quarcoo, A. Avagyan, B. Ahrens, S. M. Kube, M. Witzenrath, C. Loddenkemper, J. B. Cowland and E. Hamelmann, Clinical & Experimental Allergy, 2010 (40) 1689-1700.