

## INVERSE EXPRESSION OF FAS LIGAND AND ASTHMA-RELATED CYTOKINES IN AN ASPERGILLUS CHALLENGE MURINE MODEL OF ASTHMA

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### Introduction

Resolution of inflammation in asthma is typically thought of as a passive phenomenon in which proinflammatory Th2-type cytokines wane after the initial trigger. We hypothesized that active mechanisms, including anti-inflammatory cytokines and proapoptotic factors, contribute to this process. Fas Ligand (FasL) expression was particularly interesting since important effector cells in asthma (e.g. eosinophils and T helper cells) are Fas-sensitive.

### Methods

BALB/c mice were sensitized and challenged with an *Aspergillus fumigatus* extract, and sacrificed 1, 7 and 10 days later to capture events during initiation of the inflammatory response and its resolution. Endpoints included bronchoalveolar lavage (BAL) cell counts, protein array analysis of BAL fluid, and cytokine gene array of total lung RNA. Results: BAL eosinophilia peaked on day 1 and was associated with a marked increase in both Th1 and

Th2 type cytokines including IL-12, IFN $\gamma$ , IL-4, IL-5, IL-6, and IL-10 and eosinophil-active chemotactic factors. In contrast, FasL protein and gene expression was suppressed at this time point compared to baseline. Resolving eosinophilia was coincident with a marked increase in FasL expression and the return of most cytokines towards baseline although residual chemokine levels were noted 10 days after allergen challenge.

### Conclusion

We observed an inverse relationship between expression of FasL and asthma-related cytokines in an experimental asthma model. These data are consistent with a regulatory role for FasL during resolution. While Th2 cytokines are thought to orchestrate the initial response to antigen, multiple classically anti-inflammatory cytokines appear to be involved as well. ■

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*Rickshawing in  
New Delhi, India*

*Photo courtesy of  
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