24 Common and Rare Variation in the T Helper 2 Gene Pathway Predicts Allergic Asthma Phenotypes

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Results: EXPB1, an Arabidopsis protein (belonging to the beta expansin multi gene family), showed significant sequence and structural similarity to Cyn d 1. This protein was expressed in E. coli and the recombinant protein did not react with serum IgE from grass pollen allergic patients, suggesting that EXPB1 represented a non-allergenic homologue of grass group 1 allergens. It is proposed that differences in the amino acid sequence are responsible for the difference in the allergenicity profile of the Arabidopsis and grass pollen proteins.

Conclusions: Our study provides valuable data for further investigations of the molecular basis of allergenicity and cross-reactivity of grass group 1 allergens.

22 Protein-Protein Interactions Determine IgE Reactivity to Polygalacturonase From Cupressus sempervirens Pollen
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Methods: Chimeras of Bet v 1.0101 and its homologue Api g 1.0101 were and the recombinant protein was expressed in E. coli and purified by chromatographic methods. Secondary structures were checked by CD-spectroscopy. IgE ELISA with Bet v 1.0101, Api g 1.0101 and the chimeras were performed with sera of 63 Bet v 1-sensitized birch pollen allergic patients. For inhibition ELISAs, chimeras were coated and inhibition was performed with the chimeras or Api g 1.0101.

Results: IgE binding to Api g 1.0101, Api-Bet-1, -2, -3 and -4 was observed for 22, 81, 79, 70 and 38% of the sera, respectively. To assess the relevance of the grafted regions for IgE binding to Bet v 1, the amounts of IgE binding to the chimeras were compared with those to Api g 1.0101. Most of the sera recognised either 3 chimeras (39%) or all 4 chimeras (21%) better than Api g 1.0101. Only a minority of the sera showed increased binding to a single chimera. Inhibition ELISAs confirmed the presence of IgE specific for the grafted regions.

Conclusions: Our study indicates that the epitope recognition profile of Bet v 1-specific IgE is highly patient specific. Due to the different IgE binding patterns to Bet v 1, determined by binding of IgE to different chimeras, the existence of a single major IgE epitope on Bet v 1 can be excluded. Moreover, the Bet v 1-specific IgE repertoire is polyclonal and the IgE epitopes are distributed over the whole surface of Bet v 1.

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23 Grafting of BET V 1 Epitopes onto its Homologue API G 1 Reveals Patient-Specific IgE Recognition Profiles
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Methods: Chimeras of Bet v 1.0101 and its homologue Api g 1.0101 were constructed. In each of the 4 chimeras, roughly one fourth of the surface residues of Api g 1.0101 were replaced by corresponding residues of Bet v 1.0101. The proteins were expressed in Escherichia coli and purified by chromatographic methods. Secondary structures were checked by CD-spectroscopy. IgE ELISA with Bet v 1.0101, Api g 1.0101 and the chimeras were performed with sera of 63 Bet v 1-sensitized birch pollen allergic patients. For inhibition ELISAs, chimeras were coated and inhibition was performed with the chimeras or Api g 1.0101.

Results: IgE binding to Api g 1.0101, Api-Bet-1, -2, -3 and -4 was observed for 22, 81, 79, 70 and 38% of the sera, respectively. To assess the relevance of the grafted regions for IgE binding to Bet v 1, the amounts of IgE binding to the chimeras were compared with those to Api g 1.0101. Most of the sera recognised either 3 chimeras (39%) or all 4 chimeras (21%) better than Api g 1.0101. Only a minority of the sera showed increased binding to a single chimera. Inhibition ELISAs confirmed the presence of IgE specific for the grafted regions.

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25 Role of Myeloid Derived Suppressor Cells in Asthma

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Background: We know that a heterogeneous group of myeloid cells termed myeloid derived suppressor cells (MDSC) accumulate in almost all pathological conditions, which elicit an inflammatory signal. The exact role played by these cells in asthma is not known. In this study we investigated the function and role of these cells in asthma.

Methods: Accumulation of MDSC and other subsets of myeloid cells were analyzed from peripheral blood mononuclear cells from patients with non-severe asthma (FEV1 >60) and severe asthma (FEV1 <60) by multicolor-flow cytometry and compared to healthy controls. Allergic mouse models were used to determine the role of microRNA-142 (miR-142) in regulation and expansion of MDSC.

Results: There is a significant increase in the proportion of MDSC in severe versus non-severe asthmatics and controls, corresponding to a decrease in myeloid dendritic cells. Allergic mice showed a significant increase levels of MDSC expansion which were associated with increased levels of IL-6 and downregulation of miR-142. miR-142 overexpression induced MDSC differentiation.

Conclusions: An accumulation of MDSC is associated with severe asthma in humans and mice. In an allergic mouse model, IL-6 levels increase. miR-142 may play an important role in regulation and differentiation of MDSC, leading to altered immunity.

26 MIR-150 Suppresses Lung Inflammation in a Mouse Model of Experimental Asthma

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Background: Asthma is a complex disorder of the immune system caused by a combination of genetic predisposition with environmental exposures. The environmental factors play a predominant role in the etiology of asthma. It is hypothesized that epigenetic changes in miRNAs play a critical role in pathogenesis of asthma as an interface between genetic makeup and environmental exposures. (Wang, Jia-wang; Li, Kunyu; Hellermann, Gary; Lockey, Richard F.; Mohapatra, Subhra; and Mohapatra, Shyam. Regulating the Regulators: microRNA and Asthma. World Allergy Organization Journal. June 2011, Volume 4, Issue 6).

Methods: In the present study, we used miRNA array profiling in a mouse model of ovalbumin-induced asthma to identify differentially regulated miRNAs and characterized miR-150 in terms of cellular and humoral involvement and analysis of lung inflammation markers.

Results: We found that miR-150 was downregulated in CD4 T lymphocytes during asthmatic inflammation and Th1 and Th2 induction. Over-expression of miR-150 delivered by chitosan nanoparticles inhibited lung inflammation and decreased Th1 and Th2 cytokine levels. miR-150 suppressed Akt3, Cbl1 and ELK1 oncogenes, which are involved in inflammation and cytokine production. Transgenic mice overexpressing miR-150 are resistant to asthma induction, demonstrated by reduced AHR and cytokine inflammation production.

Conclusions: These results suggest that deregulation of miRNAs may be involved in the pathogenesis of asthma and miR-150 may suppress inflammation in asthma by inhibiting cytokine production by downregulating critical genes such as Akt, ELK1 and Cbl1. miR-150 may be an attractive candidate for asthma gene therapy.