allergic asthma (Moore WC, et al AJRCCM, 2010). We hypothesized that common and potentially deleterious rare variation in this pathway would be associated with severe asthma based on SARP cluster designation.

**Methods:** To evaluate common variants (minor allele frequency or MAF >5%), 419 SARP non-Hispanic white participants with a cluster assignment were genotyped for 182 single nucleotide polymorphisms (SNPs) in Th2 pathway genes using whole-genome SNP data. Individual SNPs and a cumulative model of significant SNPs were evaluated using contingency tables with a chi-square test for trend and ordinal regression models adjusted for age, sex, and principal components. Rare (MAF <5%) amino acid changes and splice site alterations in this pathway were tested for association with asthma severity outcomes in 20 SARP subjects with whole exome sequence data.

**Results:** Individual Th2 pathway variants were associated with overall SARP cluster assignment, and allergic clusters of increasing severity (1, 2, and 4), including GATA3 polymorphism rs1244186 (P = 0.005). In an 18-SNP additive model, an increasing number of Th2 pathway risk genotypes were highly associated with severe allergic asthma (P = 3.9 × 10^{-6}). For example, in cluster 4, the percentage of subjects with at least 9 risk genotypes was 83% compared to 35% in cluster 1. Additionally, there was evidence that subjects with rare variants in this pathway were more likely to report allergy symptoms (P = 0.006), especially in the fall (P = 0.003), compared to subjects with no rare variants.

**Conclusions:** Common Th2 pathway variants predict an increased likelihood of severe allergic asthma and rare variants were associated with increased seasonal allergy symptoms.

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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-flowcytometry 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 had significant increased 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.

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**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.

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**27 Serine Protease Inhibitor Attenuates Ova Induced Inflammation in Mouse Model of Allergic Airway Disease**

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**Background:** Serine proteases promote inflammation and tissue remodeling by activating proteinase-activated receptors, urokinase, metalloproteinases and angiotensin. In the present study, AEBSF (4-(2-Aminoethyl) benzene-sulfonyl fluoride) a serine protease inhibitor, was evaluated for prophylactic and therapeutic treatment in mouse model of airway allergy.

**Methods:** BALB/c mice were sensitized by i.p route on 0 and 14 day and challenged with OVA (25, 26 and 27 day) by i.n. route. Mice were treated i.n. with AEBSF, 1 hour before/after challenge and sacrificed on day 29 to collect BALF, blood and lungs. OVA specific immunoglobulins were measured in serum. Proteolytic activity, total cell eosinophil count, eosinophil peroxidase activity (EPO), IL-4, IL-5, IL-10, cytokine leukotrienes and 8-isoprostane (oxidative stress marker) were determined in BALF. Haematoxylin and eosin stained lung sections were examined for cellular inflammation and airway inflammation.

**Results:** Mice exposed to OVA and treated with PBS showed significantly high levels of IgE, IgG1 and IgG2a as compared to sham mice. Both prophylactic and symptomatic AEBSF treatment reduced serum IgE and IgG1 significantly (P ≤ 0.05) than control, however there was little increment
in IgG2a level. AEBSF could effectively reduce the proteolytic activity in BALF. IL-4 and IL-5 decreased significantly (P ≤ 0.05) after AEBSF treatment while a significant (P ≤ 0.05) increase was observed in IL-10 in BALF. Airway inflammation reduced significantly as revealed by lung histopathology, EPO activity and cysteinyl leukotrienes in BALF after treatment. AEBSF also suppressed oxidative stress in terms of 8-isoprostan in BALF. Among the treatment doses, 10 and 50 μg of AEBSF were most effective in reducing majority of the inflammatory parameters.

**Conclusions:** Prophylactic and therapeutic treatment of AEBSF attenuates the airway inflammation in mouse model of airway allergy and have potential for the treatment of inflammatory allergic diseases.

**28 Potential Role of Scavenger Receptors in Human Mast Cell Cytokine Response to Oxidized LDL**

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**Background:** Human atherosclerotic lesions contain mast cells and oxidatively modified low-density lipoprotein particles (oxLDL). Scavenger receptors are cell surface receptors that bind and internalize oxLDL, and they play an important role in macrophage foam cell development, a key event in the initiation and development of atherosclerotic lesions. The purpose of the study was to analyze expression of the most common scavenger receptors in mast cells, and determine whether oxLDL particles can induce them to secrete pro-inflammatory cytokines that are potentially capable of inducing and amplifying atherogenic processes.

**Methods:** Mast cells were differentiated from human cord blood-derived CD34+ progenitor cells in vitro (CBMC), and their expression of scavenger receptors was analyzed by conventional RT-PCR, flow cytometry and Western blot techniques. Fluorescently-labeled oxLDL was used to investigate LDL internalization by mast cells. Secretion of pro-inflammatory cytokines into the incubation medium and degranulation of the mast cells in response to oxLDL were assayed by ELISA and a colorimetric-enzymatic test for beta-hexosaminidase, respectively.

**Results:** CBMC expressed mRNA and protein for LOX-1, SR-AI and CD68, but not for CD36, and the expression of LOX-1 and SR-AI was upregulated by incubation of the cells with oxLDL. CBMC internalized oxLDL more efficiently than native LDL, while simultaneous neutralization of CD68, SR-AI and LOX-1 with monoclonal antibodies resulted in reduced oxLDL uptake. Moreover, in response to oxLDL, CBMC showed increased release of β-hexosaminidase, and a dose-dependent secretion of the pro-inflammatory cytokines IL-8 and MCP-1.

**Conclusion:** Our results reveal that cultured human mast cells express scavenger receptors that are upregulated by oxLDL. In atherosclerotic lesions, oxLDL may activate MC to secrete pro-inflammatory cytokines, and so they cause mast cells to act as a cellular link between oxLDL and the inflammatory response in atherosclerosis.

**30 Ragweed Allergy – What Role Does It Play in Bavaria?**

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**Background:** Ragweed (Ambrosia artemisiifolia), is increasingly spreading in Southern Germany and Central Europe. Little is yet known about the sensitization and allergy rates in Bavaria.

**Methods:** In 2008 to 2010 patients from a Bavarian university allergy unit were enrolled into the study. The patient’s history was recorded by a standardised questionnaire concerning allergies. Sensitization rates were measured by skin prick test (SPT) for seasonal aeroallergens including ragweed. Patients sensitized to ragweed were further characterized by measuring specific serum immunoglobulin E (IgE) for ragweed specific allergens (by ImmunoCAP and ELISA). To determine the clinical relevance challenge tests (nasal/conjunctival) with ragweed were performed.

**Results:** 1022 patients were enrolled in the study (665 female, 357 male). 289 patients were sensitized to ragweed (SPT positive). In ragweed sensitized patients the sensitization rate to mugwort was 61.8% whilst in patients not sensitized to ragweed it was 7.4%. The sensitization to birch was 78.1% resp. 36.4%. In 120 ragweed sensitized patients challenge tests with ragweed extract were performed (nasal n = 110; conjunctival n = 60) with positive results in 29 (26%) resp. 12 (20%) patients. In 232 ragweed sensitized patients specific IgE to nArt v 1 was observed significantly more frequently than to nAmb a 1.2

**Conclusions:** The results of this 3-year study show that in a Bavarian allergy unit sensitization to ragweed is frequent. Often ragweed-sensitized patients have sensitivities to multiple seasonal aeroallergens. There is a coexistence of ragweed and mugwort specific allergens. One fourth of the challenged...