Conclusions: These findings demonstrate that OTC and LA can inhibit activation of NF-κB, Nrf2, and HIF and thus attenuate allergen-induced airway remodeling, suggesting that antioxidants may provide therapeutic benefit in chronic asthma and other airway disorders.

509 CCL3L1 Protein Did Not Affect IL-6 Expression, but Significantly Up-regulated IL-10 Expression in the Allergic Response
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Background: Previously, we found that the mean copy number of CCL3L1 in patients with asthma was significantly lower than that of control subjects (3.13 vs 3.75, 

Results: Treatment of THP-1 cells with various concentration of HDM extract induced marked up-regulation of the expression of cytokines IL-10 and IL-6, which indicated that allergic responses were efficiently induced. Recombinant CCL3L1 protein had no effect on cytokine expression of THP-1 Cells in absence of HDM extract stimulation. In the presence of HDM extract (10 μg/mL) stimulation, CCL3L1 protein significantly up-regulated IL-10 expression (Ratio to ng/mL CCL3L1) dose-dependently (0 μg/mL CCL3L1 + 0.3/1.24, 10 μg/mL CCL3L1; 15.8 ± 1.1, 50 μg/mL CCL3L1; 16.8 ± 0.3, 100 μg/mL CCL3L1; 18.0 ± 0.8, (P > 0.05), but did not affect IL-6 expres

Conclusion: The significantly elevated asthma risk in subjects with a low copy number of the CCL3L1 gene which may be down-regulating IL-10 expression, not IL-6 expression.

510 Caspase-9 is Involved in CD30 Activation Induced Eosinophil Apoptosis
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Background: We evaluated whether ligation of CD30 incite the apoptosis, and investigated the mechanisms of CD30 induced eosinophil apoptosis is dependent on caspase activation.

Methods: We purified eosinophils using MACS system. Expression of CD30 on eosinophils were measured and eosinophils were cultured in the wells pretreated with anti-CD30 mAb and isotype control IgG1, IL-5 and dexamethasone in RPMI 1640 media supplemented with 10% FBS, and the apoptotic rate were measured using flow cytometry. To evaluate whether caspase-9 is involved in CD30- induced eosinophil apoptosis, the apoptotic rate was evaluated with addition of caspase-9 inhibitor and the expression of procaspase-9 was also measured using Western blot.

Results: The apoptotic rates of eosinophils cultured in the presence of anti-CD30 mAb were significantly increased to 29.1 ± 6.1% and 47.3 ± 4.7% compared with 17.1 ± 6.7% and 29.4 ± 9.2% of the control at 4 and 24 hours, respectively (both P < 0.05). Caspase-9 inhibitor suppressed the mAb induced eosinophil apoptosis from 54.8 ± 6.9% and 71.5 ± 11.6% to 24.5 ± 6.0% and 47.8 ± 11.4% at 18 and 36 hours, respectively (both P < 0.001).

We also showed the expression of procaspase-9 with the mAb was diminished compared with that of the control and of IL-5.

Conclusions: This study showed CD30 activation enhances the eosinophil apoptosis and the effect is mediated by Caspase-9 activation.

511 Role of NLR (Nucleotide Oligomerization Domain (NOD)—like Receptor) on Allergic Inflammation in a Mouse Model of Allergic Rhinitis
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Background: Recently, a new set of pattern-recognition receptors, the nucleotidebinding oligomerization domain (Nod)-like receptors (NLRs), have emerged. Their activation, either by allergens or microbes, triggers an inflammatory response. Objective: To investigate whether recognition of bacterial microbial-associated molecular patterns in the nose may result in susceptibility to developing allergic reactions, and to understand the molecular mechanisms by which such triggers block natural tolerance.

Methods: Ligands of intracellular microbial-associated molecular pattern recognition receptors—the nucleotidebinding oligomerization domain (Nod)-like receptors, Nod1 and Nod2—were given intranasally with antigen, and their ability to modulate airway tolerance was analyzed. Seventy 2 mice were randomized to one of 6 groups: control (n = 12), AR (n = 12), pre NOD1 group (n = 12), pre NOD2 group (n = 12), post NOD1 group (n = 12), and post NOD2 group (n = 12). All mice except for the control group were sensitized by an intraperitoneal injection of ovalbumine (OVA) and aluminum hydroxide. Two weeks after sensitization, all sensitized mice were challenged intranasally with OVA. The control group was received phosphate buffered saline intranasally. The allergic symptom after the final challenge was recorded. Interleukin (IL)-5, interferon-γ (IFN-γ), and IL-10 levels in nasal lavage fluid (NALF), as well as serum OVA-specific IgE levels were measured. The number of eosinophils in lamina propria was evaluated. The levels of T-bet, GATA-3, and Foxp3 mRNA expression in splenic mononuclear cells were determined by real-time polymerase chain reaction.

Results & Conclusion: We show that a Nod-like receptor is a novel, previously unrecognized, pathway that adversely links innate and adaptive immunity and leads to allergic rhinitis.
Results: Histamine release after ConA challenge varied from 0% to 100% in Indian subjects. Eighteen percent subjects showed less than 5% histamine release (non-releasers). Flow-cytometric analysis revealed a significantly reduced expression of FcεRI on non-releaser basophils (P < 0.05). Total serum IgE levels were also significantly low (P < 0.05) in non-releasers. Flow-cytometric analysis revealed a significantly reduced expression of Lyn and Syk kinases in basophils (P < 0.05). Histamine release also significantly correlated with expression of Lyn and Syk kinase (P < 0.05). Non-releasers showed the presence of SNP at +79 (T>C), which leads to the one amino acid change at 8th position in the mature IL-3 from serine to proline.

Conclusions: About 18% of the Indian subjects studied showed non-releaser phenotype and also had reduced serum IgE levels and FcεRI expression. Non-releasers have shown the presence of less potent isoform of IL-3/p8, which is suspected to be common factor responsible for the non-releaser phenotype. This needs to be extended to a larger sample size and could be a potential target for the development of therapeutics for allergic patients.

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IL-17 Role in the Regulatory Function of B Cells
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Background: B lymphocytes are known to be important cytokine sources in inflammation and play a pathogenic role by producing autoantibodies in a number of chronic inflammatory diseases. However, B cell depletion therapy induced an exacerbation of symptoms in some patients with autoimmune disorders, revealing that B cells play a critical anti-inflammatory role mediated by IL-10 release. We therefore investigated the human B cell regulatory subset producing IL-10 in response to stimulation.

Methods: Highly purified B cells were obtained from tonsils by using a multiple-step separation procedure which included rosette depletion, adherence depletion, CD3− cell magnetic-activated depletion and CD19+, magnetic-activated positive cell selection. CD20+ purity was verified by flow cytometry. The CD19+CD20+ B cells were stimulated with CpG oligonucleotide, IL-4, IFN-gamma, anti-CD40, IL-17A and IL-17F, either alone or in combination. The expression of both IL-6 and IL-10 mRNA was analyzed by quantitative RT-PCR and by ELISA. B regulatory cell subsets expressing IL-10 and the markers CD5 and CD1d were quantified by FACS analysis. B cell proliferation was determined by 3H thymidine incorporation or CFSE labeling.

Results: Expression of IL-10 mRNA and protein in purified B cells from tonsils was weakly stimulated by anti-CD40 antibody, CpG oligonucleotide or with IL-17. When B cells were simultaneously stimulated with IL-17, anti-CD40 antibody and CpG oligonucleotide, the mRNA and protein expression of IL-10 was strongly increased (n = 3; P ≤ 0.001). B cells proliferation was also significantly increased. In contrast, stimulation with IL-4 alone or in combination with anti-CD40 antibody, decreased the expression of IL-10 (n = 3; P ≤ 0.001).

Conclusions: TLR9 receptor stimulation synergizes with CD40 and IL-17 receptors stimulation in the induced proliferation and potent release of IL-10 cytokine while decreasing IL-6 production in B cells. These novel findings provide evidence that B lymphocytes might be an important source of the anti-inflammatory IL-10 cytokine, and provide novel evidence that stimulation of B lymphocytes with IL-17 cytokine could be an important regulatory mechanism in immune responses.

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Role of TH-17 Cytokines in Steroid Insensitivity in Peripheral Blood Mononuclear Cells. Relationship to GR-alpha and GR-beta Expression
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Background: Inhaled corticosteroids represent the most common treatment for asthma. Although most asthmatic patients respond well, a significant proportion of severe asthmatics require higher doses or even fail to respond to oral or inhaled corticosteroids. We previously reported that glucocorticoid receptor-beta is associated with corticosteroid resistance in airway epithelial cells from asthmatic patients and that Th-17 cytokines increase steroid insensitivity via a mechanism involving GR-beta upregulation. We aim to investigate whether IL-17A and F cytokines enhance steroid unresponsiveness in PBMCs from normal subjects and severe asthmatics via the upregulation of GR-beta isoform.

Methods: PBMCs were cultured for 48 hours in the presence or absence of IL-2, IL-4, IL-17A, IL-17F or IL-23 cytokines. Expression of GR-alpha, GR-beta, IL17F and IL-6 was determined using Q-RT-PCR and/or Western blotting. Response to Dexamethasone was determined on the inhibition of PHA-induced proliferation by Dexamethasone (IC50) using either 1H-thymidine or CFSE-labelled cells. Response of the cells to Dexamethasone-induced apoptosis was determined by Annexin-V staining.

Results: Treatment of PBMCs with IL-17A+IL-17F combined significantly decreased the mRNA expression of GR-alpha while that of GR-beta was significantly upregulated. IL-2+IL-4 in combination significantly decreased GR-alpha expression but had no effect on GR-beta receptor expression. IL17A+IL17F+IL-23 combined induced the highest ratio of GR-beta/GR-alpha in PBMC from normal subjects. Either IL-17A+F or IL-2+IL-4 combinations significantly decreased the inhibitory effect of Dexamethasone on PBMC proliferation (IL-17A+F IC50 = 190 nM Dex; IL-2+4 IC50 = 1060 nM Dex), when compared to the control without cytokine stimulation. In the presence of Dexamethasone, IL-2+IL-4 but not IL-17A+IL-17F, inhibited the expression of the glucocorticoid-inducible leucine zipper gene (GILZ) in PBMCs from both normal (60%) and asthmatics (45–50%), which was correlated with significantly higher apoptosis in cells stimulated with IL-2+IL-4.

Conclusions: IL-17A, IL-17F, IL-2, and IL-4, which are known to be upregulated in the blood and lung tissue of asthmatics, contribute to steroid insensitivity of severe asthmatic patients by modulating the expression of GR-alpha and GR-beta receptors on peripheral blood PBMCs. GR-beta could protect PBMCs from Dex-induced apoptosis. Furthermore, the increased GR-beta/GR-alpha ratios by both IL-17A+F and IL-2+4 cytokines correlates with the decreased inhibitory effect of Dexamethasone on PHA-induced PBMC proliferation.

OCCUPATIONAL ALLERGIES

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Prevalence of Latex Sensitization Between Medicine and Dentistry Students from Nuevo Leon University
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