P4091
Inhibition of collagen receptors: α1β1 and α2β1 integrins, has no impact on lymphocytes, but decreases eosinophil transmigration through human extracellular matrix and collagen I coated inserts
Stanisława Bazan-Socha, Joanna Zak, Cezary Marcinkiewicz, Jacek Musial. II Department of Internal Medicine, Jagiellonian University Medical College, Cracow, Poland II Department of Internal Medicine, Jagiellonian University Medical College, Cracow, Poland

Introduction: T helper lymphocytes are likely to play a pivotal role in directing disease development and progression in asthma. We recently described presence of α1 and α2 integrins on blood eosinophils and α2 on blood CD4 and CD8 T lymphocytes in chronic asthma. We hypothesize that collagen receptors: α1β1 and α2β1 integrins may play an important role in cell transmigration to the sites of asthmatic inflammation.

Methods: We studied effects of functional active, mouse anti-human monoclonal antibodies against I-domain of α1 and α2 integrin subunit (Chemicon, USA) on eosinophil and lymphocyte transmigration through human extracellular matrix and collagen I coated cell culture inserts (Beckton Dickinson Falcon Cell Culture Inserts – 3 μm pore size). In 6 atopics asthmatics lymphocytes were separated from peripheral blood by gradient centrifugation and eosinophils by gradient centrifugation and negative magnetic separation (Vario MACS, Miltenyi Biotec).

Results: None of the antibodies used influenced lymphocyte transmigration through human extracellular matrix and collagen I coated inserts. However, movement of peripheral blood eosinophils through human extracellular matrix was inhibited by both antibodies (% of inhibition: 30±26 for anti-α1, 25±24 for anti-α2 mAb). Anti-α2 mAb was also active on collagen I coated inserts (37 ± SD33); anti-α1 mAb was not effective.

Conclusion: The α2β1 integrin is present on lymphocytes, but seems to play no role in lymphocyte infiltration. However, both α1β1 and α2β1 integrins might be important in eosinophil transmigration and support airway inflammation.

P4092
Suppressive effect of a mint aqueous extract on IL-13 production
Fatemeh Hajighasemi. Department of Immunology, Faculty of Medicine, Shahed University, Tehran, Islamic Republic of Iran

Background: Medicinal plants have been broadly used in treatment of various diseases. Mints are a group of plants belonging to labiatae family have anti-inflammation, anti-tumoral and anti-inflammatory effects. Peppermint is a mint specious extensively used in therapy of several disorders such as common cold and bronchitis. The anti-bronchospasmic and anti-allergic effects of peppermint have also been untried. Elevation of interleukin-13 (IL-13) (a Th2-type cytokine) level is a well known indicator of allergy. In the present study the effect of aqueous extract of peppermint on IL-13 production in human peripheral blood mononuclear cells (PBMCs) has been assessed in vitro.

Methods: The hPBMCs were isolated from the venous blood of healthy volunteers by ficoll-hypaque-gradiente centrifugation. Then the PBMCs were cultured in complete RPMI medium. The cells at logarithmic growth phase, were incubated with different concentrations of aqueous extract of peppermint leaves (0.01-10 mg/ml) in triplicate for 24 hours. Afterward the cell culture supernates were collected and the IL-13 concentration was measured using a standard ELISA kit.

Results: Peppermint aqueous extract significantly decreased the IL-13 production in hPBMCs dose-dependently.

Conclusions: The results of this study indicate that peppermint aqueous extract down-regulates the production of IL-13 in hPBMCs. Regarding the important role of IL-13 in atopic allergy, the anti-allergic activity of peppermint and also its inhibitory effect on bronchospasm (a symptom of respiratory allergy), may be partly due to its inhibitory effects on IL-13 production.

P4093
Role of thrombin-activatable fibrinolysis inhibitor in lipopolysaccharide-induced acute lung injury
Masahiro Naito1, Osamu Taguchi1, Takehiro Takagi1, Tetsu Kobayashi1, Corina D’Alessandro-Gabazza2, Esteban Gabazza2. 1Department of Respiratory Division, Mie University School of Medicine, Tsu, Japan; 2Department of Immunology, Mie University School of Medicine, Tsu, Japan

Background: In acute lung injury, excessive coagulation induced by inflammatory responses may feedback to further increase the inflammatory response and promote fibrosis. Thrombin-activatable fibrinolysis inhibitor (TAFI) is mainly synthesized in the liver and circulates in the bloodstream as an inactive proenzyme. It can be activated by the thrombin-thrombomodulin complex to a carboxypeptidase (TAFIa), which acts as an anti-fibrinolytic factor by inhibiting the activation of plasmin through the removal of carboxy-terminal lysines from fibrin. Recent studies have shown that TAFIa can also regulate inflammatory responses by its ability to inhibit complement C3a and C5a, and osteopontin.

Objective: Our aim was to evaluate the effect of TAFI on acute lung injury in the mouse.

Methods: Acute lung injury was induced in wild type and TAFI deficient (KO) C57/BL6 mice by intratracheal instillation of lipopolysaccharide (LPS;5mg/kg). Mice treated with saline served as controls. We compared the inflammatory response to LPS in both groups. Animals were sacrificed 24 hours after LPS injection and broncho-alveolar lavage fluid (BALF) was sampled.

Results: TAFI KO mice had worse acute lung injury as their total protein, total cell count, and levels of IL-1β, IL-6 and TNF-α were increased in BALF in LPS-treated TAFI KO mice compared to wild type. The increase in cells in BALF was due to an increase in neutrophils. Complement C5a in both BALF and plasma was increased in LPS-treated TAFI KO mice compared to wild type.

Conclusions: These results suggest that TAFI protects against acute lung injury at least partially through its ability to inactive complement C5a.

420. Experimental modulation of airway inflammation
**Thematic Poster Session**

**P4094**

Critical immunoregulatory role for activin-A in human allergic asthma

Sofia Touza1, Maria Šemčitolou1, Ioanna Christopoulou1, Konstantinos Samitas2, Giannis Paraskevopoulos3, Catherine Hawrylowicz4, Vladimir Alioshkin3.

Our studies have revealed that activin-A, a cytokine increased in the sera and lungs of asthmatics, is a critical controller of experimental asthma as it suppresses allergic responses and protects against airway hyperresponsiveness and linked disease in mice. Still, the role of activin-A in human asthma remains elusive. Here, we investigated the effects of activin-A in the suppression of allergic responses of atopic and asthmatics. Peripheral blood (PB) was obtained from atopics and mild/moderate or severe asthmatics (n=12/group). Bronchoalveolar lavage (BAL) was obtained from severe asthmatics (n=5). The effects of recombinant activin-A or control on allergen-specific CD4+ and CD8+ T cell proliferation and cytokine release were investigated during stimulation with allergen ex vivo. Activin-A’s role in the generation of suppressive human regulatory T cells (Tregs) was studied. Our findings reveal that activin-A significantly suppresses allergen-driven CD4+ T cell proliferation and IL-5, IL-13, IFN-γ, IL-10 release in atopics and asthmatics. Activin-A suppresses BAL mononuclear cell responses of severe asthmatics. Importantly, activin-A enhances dexamethasone-induced suppression of allergic Th2 responses of severe, treatment refractory, asthmatic. Activin-A-mediated suppression is associated with the generation of human CD4+Foxp3+ Tregs that completely inhibit allergic Th2 responses. Our results uncover activin-A as a novel potential asthma therapy. Our findings have important clinical implications for the use of activin-A, or activin-A induced human Tregs, as novel immunotherapies for asthma.

**P4095**

Fluticasone propionate decreases MUC5AC expression on airway epithelial cells induced by rhinovirus infection in the airway

Sofia Touza1, Naoto Fueki2, Makoto Fueki2, Sohei Makino1, Hironori Sagara3.

Viral infections such as a common cold in the airway can potentially exacerbate signs and symptoms of asthma, including mucous overproduction, airway hyperresponsiveness, and airway obstruction. These signs and symptoms are associated with progression of airway remodeling. MUC5AC is related intimately to mucous hypersecretion in the airway and is localized in airway epithelial goblet cells. Fluticasone propionate and salmeterol are used to treat asthma. These drugs reduce mucus overproduction in the airway and are localized in airway epithelial goblet cells. Fluticasone propionate and salmeterol are used to treat asthma. Here, we investigated the effects of fluticasone propionate or salmeterol on rhinovirus 14 (RV14)-induced MUC5AC gene expression in a human airway epithelial cell line (NCI-H292). Fluticasone propionate significantly decreased RV14 expression in rhinovirus-infected NCI-H292 cells. Our results suggest that fluticasone propionate prevents exacerbation of asthma due to rhinovirus infection by decreasing MUC5AC expression in the airway, potentially slowing the progression of airway remodeling.

**P4096**

Standard therapy increases the sensitivity of peripheral blood lymphocytes to glucocorticoids in cystic fibrosis but not in severe asthma

Sofia Touza1, Naoto Fueki2, Makoto Fueki2, Sohei Makino1, Hironori Sagara3.

Cystic fibrosis (CF) is a genetic disease that affects the ability to control mucus in the lungs and intestines. CF patients with lung exacerbations demonstrate low cell sensitivity to glucocorticoids, while healthy subjects demonstrate high cell sensitivity to glucocorticoids. The therapy did not affect high cell sensitivity to GC. CF patients with lung exacerbations demonstrated low cell sensitivity to GC (ΔΔCt = 0.36±0.23), but after antibiotic treatment the sensitivity significantly increased (ΔΔCt = 0.54±0.24; p=0.014). On the contrary, the cell sensitivity of asthmatic patients remained extremely low. The therapy did not affect high ΔΔCt level, which averaged before and after exacerbation treatment 2.67±0.27 and 2.65±0.31, respectively. In conclusion, patients with severe asthma have stably diminished GC sensitivity of PBL, while compared with CF patients and healthy subjects. We believe that such a resistance is a consequence of GC treatment during a long period of time and may be associated with both immune cell selection and epigenetic changes of GC receptors.

**P4097**

Cultured normal human bronchial epithelial cells may produce collagen type I stimulation with TGF-β

Sofia Touza1, Naoto Fueki2, Risako Seki1, Akemi Koyama1, Takenori Okada1, Hironori Sagara3.

The clinical characteristics of asthma can be logically explained by asthma-specific airway inflammation and airway remodeling. The details of which have been recently elucidated. Airway remodeling is an important feature of chronic airway disease, but the mechanisms involved remain unclear. Since TGF-β has been implicated in the development of airway remodeling in asthma based on its strong capacity to induce extracellular matrix (ECM) production, it is possible that Smad7 may also play some roles in the regulation of the process.

**Method:** We analyzed using by real time RT-PCR and Western blotting method We thought to determine the relationships between collagen type I production in normal human bronchial epithelial cells (NHBE). Normal human bronchial epithelial cells (NHBE) cells stimulated with TGFβ type cytokine TGF-beta or regularly cytokine IL-10. Production levels of Type I collagen was expressed in cultured epithelial cells NHBE stimulation with TGF-b. Furthermore, collagen type I production in NHBE cells stimulation with TGF-b up-regulate in a dose and time dependent manner. And also we found that protein levels of collagen type I were increased from activated NHBE cells stimulating with TGF-b.

In contrast, IL-10 decreased collagen type I expression in NHBE cells. In conclusion, these findings suggested bronchial epithelial cells may produce collagen type I production and IL-10 is a key cytokine possible make an important role of airway remodeling.

**P4098**

Investigation of the effect of histone deacetylase 2 function on Wegener’s granulomatosis

Dai Takagi, Yuji Nakamato, Satoshi Fukuda. Otolaryngology Head and Neck Surgery, Hokkaido University Graduate School of Medicine, Sapporo, Japan

**Backgrounds:** It has been reported that anti-neutrophil cytoplasmic antibodies (ANCA) activate neutrophils result in induction of glomerulonephritis in Wegener’s Granulomatosis (WG) by released hydrogen peroxide. Histone deacetylase (HDAC) deacetylates histone and deacetylation of histone associates with gene repression. In this study, we investigated whether HDAC2 activity decreased in WG patients, and effect of oxidative stress on expression of HDAC2.

**Results:** Levels of HDAC2 in bronchoalveolar lavage (BAL) fluid and that this reduction affects inflammation and vasculitis of WG. Oxidative stress may worsen the disease via reduction of HDAC2 function. Thus, HDAC2 may serve therapeutic targets by modulating the function, which eventually regulates the development of WG.

**P4099**

Polyphenolic compounds and experimentally induced allergic asthma

Sona Franova1, Marta Joscova1, Martina Sutovska1, Olga Pechanova2, Gabriela Nosalova3.

1Department of Pharmacology, Jessenius Faculty of Medicine, Comenius University, Martin, Slovakia (Slovak Republic); 2Department of Normal and Pathological Physiology, Slovak Academy of Sciences, Bratislava, Slovakia (Slovak Republic); 3Department of Otolaryngology, Head and Neck Surgery, University Hospital, Martin, Slovakia (Slovak Republic).

Some epidemiological studies related asthma symptoms contain data supporting the idea that health benefits associated with fruits, vegetables and red wine in the...
Cigarette smoke extract suppresses the maturation and function of bone marrow derived dendritic cells

Masoumeh Givi, Frank Redegeld, Gert Folkerts, Esmaeil Mortaz. Division of Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Utrecht, Netherlands; Chronic Respiratory Disease Research Center, National Research Institute of Tuberculosis and Lung Disease, Tehran, Islamic Republic of Iran

Chronic obstructive pulmonary disease (COPD) is characterized by chronic airway inflammation. Cigarette smoke has been considered as a major risk factor in the pathogenesis of COPD. The potential role of DCs in the respiratory tract of smokers’ lungs and COPD patients is poorly understood. In this study, we are investigating the effects of cigarette smoke extract (CSE) on the maturation, development and function of mouse bone marrow. Bone marrow derived DCs were developed by culturing isolated cells from femur and tibia of BALB/C mice in presence of GM-CSF (20 ng/ml) for 10 days. CSE was added to cells cultures for 10 days. The surface expression of maturation and co-stimulatory markers were CD11C, MHCII, CD80, CD86 expressed by control (CD86, n=10) and CSE treated DCs (CD86, n=10), respectively, as measured by FACS analysis. The functional capacity of DCs was measured by uptake of Dextran-FITC and by in vitro method; by in vivo method (used whole bodyplethysmograph). The degree of differentiation was evaluated by eosinophil calculation and by estimation of inflammatory cytokines IL-4, IL-5 in bronchoalveolar lavage fluid (BALF).

The results of our experiments showed that: Polynucleotides compounds Provilond and Flavin7 possess an efficient antiasthmatic activities. They cause bronchodilatation and also suppress asthmatic inflammation in the airways. Quercetin and resveratrol are able to induce only acute bronchodilatation without antiinflammatory effects. Our results demonstrate positive antiasthmatic effect of mixture of polynucleotides. This outcome confirm the hypothesis, that may be an additional therapy in prevention of airway hyperresponsiveness in asthma subjects.

LSC 2011 Abstract: The effect of endothelin-1 on human basophil function in vitro

Katharina Cima, Silvia Blunder, Susanna Desole, Julia Günther, Judith Löffler-Ragg, Christian M. Kähler. Pneumologie, Internal Medicine, Medical University of Innsbruck, Innbruck, AT Internal Medicine, Laboratory of Immunology, Innsbruck, AT

Endothelin-1 (ET-1) has proinflammatory properties and contributes to allergic late-phase responses. As basophils play a key role in allergic rhinitis or asthma, we investigated the effect of ET-1 on basophils. Cells were isolated from venous blood of healthy donors via magnetic cell sorting.

To show ETA or ETB receptor expression RT-PCR was performed. The chemotactic effect of ET-1 [10-6 - 10-16M] was analysed in modified Boyden chambers (positive control MCP-1 [10-7M]). To show ETA or ETB receptor expression RT-PCR was performed. The chemotactic effect of ET-1 [10-6 - 10-16M] was analysed in modified Boyden chambers (positive control MCP-1 [10-7M]). To show ETA or ETB receptor expression RT-PCR was performed. The chemotactic effect of ET-1 [10-6 - 10-16M] was analysed in modified Boyden chambers (positive control MCP-1 [10-7M]). To show ETA or ETB receptor expression RT-PCR was performed. The chemotactic effect of ET-1 [10-6 - 10-16M] was analysed in modified Boyden chambers (positive control MCP-1 [10-7M]).

The RT-PCR revealed basophils to express both, ETAR and ETBR. ET-1 [10-6 - 10-8M] further proved to be a strong chemoattractant for human basophils in a concentration range between 10-6 - 10-10M. The cytokine production did not differ between the experimental groups. However, restimulation with CSE resulted in significant less cytokine production (each p<0.05). The cytokine production did not differ between the experimental groups. However, restimulation with CSE resulted in significant less cytokine production (each p<0.05). The cytokine production did not differ between the experimental groups. However, restimulation with CSE resulted in significant less cytokine production (each p<0.05). The cytokine production did not differ between the experimental groups. However, restimulation with CSE resulted in significant less cytokine production (each p<0.05). The cytokine production did not differ between the experimental groups. However, restimulation with CSE resulted in significant less cytokine production (each p<0.05). The cytokine production did not differ between the experimental groups. However, restimulation with CSE resulted in significant less cytokine production (each p<0.05). The cytokine production did not differ between the experimental groups. However, restimulation with CSE resulted in significant less cytokine production (each p<0.05). The cytokine production did not differ between the experimental groups. However, restimulation with CSE resulted in significant less cytokine production (each p<0.05). The cytokine production did not differ between the experimental groups. However, restimulation with CSE resulted in significant less cytokine production (each p<0.05). The cytokine production did not differ between the experimental groups. However, restimulation with CSE resulted in significant less cytokine production (each p<0.05). The cytokine production did not differ between the experimental groups. However, restimulation with CSE resulted in significant less cytokine production (each p<0.05). The cytokine production did not differ between the experimental groups. However, restimulation with CSE resulted in significant less cytokine production (each p<0.05). The cytokine production did not differ between the experimental groups. However, restimulation with CSE resulted in significant less cytokine production (each p<0.05). The cytokine production did not differ between the experimental groups. However, restimulation with CSE resulted in significant less cytokine production (each p<0.05).
Methods: Bronchial asthma was induced by sensitization and challenge with ovalbumin (OVA). Littermates treated with saline were used as controls. The effect of inhaled different dose of thrombin was assessed by administering prior to OVA airway inflammation which was evaluated by measuring the number of inflammatory cells and the level of cytokine in bronchoalveolar lavage fluid (BAL). Airway hyperresponsiveness was measured using a plethysmograph.

Results: The levels of IL-5, the number of eosinophils in BAL were decreased in low dose of thrombin treated mice compared to saline treated mice. The degree of airway hyperresponsiveness was significantly decreased in low dose of thrombin treated compared to saline treated mice.

Conclusion: These results suggest thrombin exerts a differential effect in bronchial asthma depending on its concentration.

Conclusions: In this animal model, both corticosteroid and montelukast treatments were more effective reducing the number of eotaxin and NF-kB positive cells compared to OV A group. The higher efficacy of this therapeutic approach is contributed to the control of the inflammatory response in distal lung parenchyma along the vessel wall in 30 sec (saline: 12.4±2.1 vs Cpn60.1: 2.8±0.5) significantly lower in lung parenchyma when mice were treated by the IL-13 neutralizing antibody. In conclusion, our data generated in a rodent model suggest that inhaled anti-IL-13 Fab’ could represent a novel and effective therapy for the treatment of asthma.

Efficacy of inhaled anti-IL-13 mAb in a mouse model of asthma

Jonathan Hacha1, Maud Guiderd1, Kate Tomlinson2, Genevieve Paulissen3, Natacha Rocks1, Agrès Noël1, Roger Palfraiman2, Didier Cataldo3, Laboratory of Tumor & Development Biology (GIGA-Research), University of Liege, Liege, Belgium; 4Immunology Research, UCB, Slough, United Kingdom

Interleukin-13 (IL-13) is a prototypic Th2 cytokine and a potential cornerstone of asthma pathology. IL-13 is involved in IgE synthesis, bronchial hyperresponsiveness, mucus hypersecretion, subepithelial fibrosis and eosinophil infiltration. We assessed the potential efficacy of an inhaled high affinity monoclonal antibody (mAb) Fab’ fragment neutralizing IL-13 against allergen-induced inflammation and hyperresponsiveness. BALB/c mice were subjected to ovalbumin (OVA) exposure for 1, 5, and 10 weeks referred to as short term (ST), intermediate term (IT) and long term (LT) protocols respectively. The antibody was administered as an aerosol (75 μg/ml) in a tower airflow exposure with a face only exposure of 7 min.

In a one-week OVA-exposure model (ST), we assessed the effectiveness of different doses of anti-IL-13 (0.5 to 5 mg/ml). We report a dose-dependent increase of the anti-inflammatory effect reaching a maximum at a 5 mg/ml. Airway responsiveness to methacholine became by using the flexVent system. In the different protocols used in this study, administration of the anti-IL-13 Fab’ by inhalation significantly decreased bronchial responsiveness to methacholine, BALF eosinophils and mucus cell infiltration in lungs, mucus cell hyperplasia, peribronchial collagen deposition and smooth muscle hyperplasia. After 1 and 5 weeks of allergic exposure (ST and IT), levels of pro-inflammatory mediators IL-13, IL-4, IL-5, CCL-11, MIP-2 and MDC were lower in C group compared to M animals (p < 0.05).

In conclusion, we data generated in a rodent model suggest that inhaled anti-IL-13 Fab’ could represent a novel and effective therapy for the treatment of asthma.

Efficacy of corticosteroid and montelukast treatment on distal lung parenchyma and airway walls in inflammation in guinea pigs with chronic allergic inflammation

Nathalia B. Gobbato1, Clécie Pinto1, Carla Máximo Prado2, Mílton Arruda Martins1, 1Comprehensive Pneumology Center, 2Department of Allergy and Clinical Immunology, Asan Institute for Life Science, Asan Institute for Life Science, Seoul, 2Department of Allergy and Clinical Immunology, Asan Institute for Life Science, Asan Institute for Life Science, Seoul, Korea

Rationale: The effects of montelukast or dexamethasone in asthma pathophysiology are barely understood.

Aims and methods: To evaluate the inflammation in distal lung parenchyma and airway walls in guinea pigs (PG) with chronic allergic inflammation. PG were sensitized and challenged with ovalbumin (OVA) exposure for 1, 5, and 10 weeks referred to as short term (ST), intermediate term (IT) and long term (LT) protocols respectively. The antibody was administered as an aerosol (75 μg/ml) in a tower airflow exposure with a face only exposure of 7 min.

In conclusion, our data generated in a rodent model suggest that inhaled anti-IL-13 Fab’ could represent a novel and effective therapy for the treatment of asthma.

Conclusions: In this animal model, both corticosteroid and montelukast treatments contribute to the control of the inflammatory response in distal lung parenchyma and airway walls. Dexamethasone treatment induced a greater reduction of NF-κB expression in airway walls which suggests one of the mechanisms that explains the higher efficacy of this therapeutic approach.

Supported by: FAPESP, CNPq, LIM-20-4H-FMUSP.

Efficacy of corticosteroid and montelukast treatment on distal lung parenchyma and airway walls in inflammation in guinea pigs with chronic allergic inflammation

Nathalia B. Gobbato1, Clécie Pinto1, Carla Máximo Prado2, Mílton Arruda Martins1, 1Comprehensive Pneumology Center, 2Department of Allergy and Clinical Immunology, Asan Institute for Life Science, Asan Institute for Life Science, Seoul, 2Department of Allergy and Clinical Immunology, Asan Institute for Life Science, Asan Institute for Life Science, Seoul, Korea

Rationale: The effects of montelukast or dexamethasone in asthma pathophysiology are barely understood.

Aims and methods: To evaluate the inflammation in distal lung parenchyma and airway walls in guinea pigs (PG) with chronic allergic inflammation. PG were sensitized and challenged with ovalbumin (OVA) exposure for 1, 5, and 10 weeks referred to as short term (ST), intermediate term (IT) and long term (LT) protocols respectively. The antibody was administered as an aerosol (75 μg/ml) in a tower airflow exposure with a face only exposure of 7 min.

In conclusion, our data generated in a rodent model suggest that inhaled anti-IL-13 Fab’ could represent a novel and effective therapy for the treatment of asthma.

Conclusions: In this animal model, both corticosteroid and montelukast treatments contribute to the control of the inflammatory response in distal lung parenchyma and airway walls. Dexamethasone treatment induced a greater reduction of NF-κB expression in airway walls which suggests one of the mechanisms that explains the higher efficacy of this therapeutic approach.

Supported by: FAPESP, CNPq, LIM-20-4H-FMUSP.
Results: The levels of Prx-SO3/Prx in PBMCs of asthma patients were significantly higher compared to those in normal subjects and were also related with asthma severity. Furthermore, the intracellular ROS after hydrogen peroxide treatment were remarkably enhanced and prolonged in PBMCs from asthmatics, while transiently increased intracellular ROS levels were observed in control subjects.

Conclusions: The hyperoxidation of Prx may be related with increases susceptibility to oxidative stress and possibly play a role in the pathogenesis of severe asthma.

P4110
LSC 2011 Abstract: P2Y2 receptor regulates VCAM-1 membrane and soluble forms and eosinophil accumulation during lung inflammation

ATP has been defined as a key mediator of asthma. In this study, we evaluated lung inflammation in mice deficient for the P2Y2 purinergic receptor. We observed that eosinophil accumulation, a distinctive feature of lung allergic inflammation, was defective in OVA-treated P2Y2-deficient mice compared with OVA-treated wild type animals. Interestingly, the upregulation of VCAM-1 was lower on lung endothelial cells of OVA-treated P2Y2-/- mice compared with OVA-treated wild type animals. Adhesion assays demonstrated that the action of UTP on leukocyte adhesion through the regulation of endothelial VCAM-1 was abolished in P2Y2-deficient lung endothelial cells. Additionally, the level of soluble VCAM-1, reported as an inducer of eosinophil chemotaxis, was strongly reduced in the bronchoalveolar lavage fluid (BALF) of P2Y2-deficient mice. In contrast, we observed comparable infiltration of macrophages and neutrophils in the BALF of LPS-aerosolized P2Y2+/+ and P2Y2-/- mice. This difference could be related to the much lower level of ATP in the BALF of LPS-treated mice compared with OVA-treated mice.

Our data define P2Y2 as a regulator of membrane and soluble forms of VCAM-1 and eosinophil accumulation during lung inflammation.