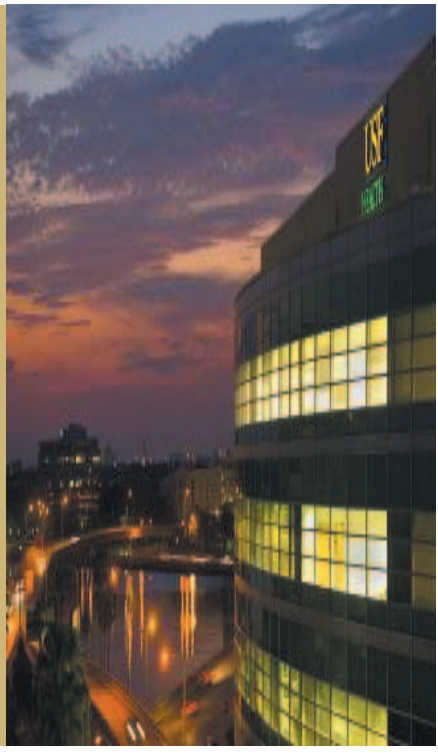
University Of South Florida

Division of Allergy and Immunology
Department of Internal Medicine
Joy McCann Culverhouse Airway Disease Research Center and The James A. Haley V.A. Medical Center
Tampa, Florida



2010 Annual Report

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UNIVERSITY OF SOUTH FLORIDA

Contents

University of South Florida College of Medicine, Department of Internal Medicine, Division of Allergy and Immunology

The late Samuel C. Bukantz, M.D., founded the University of South Florida College of Medicine, Department of Internal Medicine, Division of Allergy and Immunology in 1972. Richard F. Lockey, M.D. succeeded Dr. Bukantz in 1983 and is the current Director of the Division. Mrs. Joy McCann Culverhouse endowed the Division in 1997 and The Joy McCann Culverhouse Airway Disease Research Center was dedicated in February 1998. In 1998, Mabel and Ellsworth Simmons endowed the Division with a grant for education and research. The goals of the Division are: first, to provide care to patients with allergic and immunologic diseases at the University of South Florida College of Medicine, Tampa General Hospital, James A. Haley V.A. Medical Center, All Children's Hospital, and H. Lee Moffitt Cancer Center; second, to train students, residents, and fellows in the subspecialty of allergy and immunology; and third, to conduct basic and clinical research in allergy, asthma, and immunology.

Individuals interested in collaborating with members of the Medicine Division may contact Richard F. Lockey, M.D. or any faculty member at (813) 972- 7631 (e-mail: rlockey@health.usf.edu).

John W. Sleasman, M.D. or any other faculty member in the Pediatric Division may be contacted at 727-553-3533 or Jsleasma@health.usf.edu.

Division of Allergy and Immunology Faculty and Staff

Core Faculty

Richard F. Lockey, M.D., *University Distinguished Health Professor, Professor of Medicine, Pediatrics, and Public Health; Division Director; Joy McCann Culverhouse Chair of Allergy and Immunology*

Roger W. Fox, M.D., *Professor of Medicine, Pediatrics and Public Health*

Dennis K. Ledford, M.D., *Professor of Medicine and Pediatrics*

Shyam S. Mohapatra, Ph.D., *Mabel & Ellsworth Simmons Professor of Medicine, Director of Basic Research, Division of Allergy and Immunology-Joy McCann Culverhouse Airway Disease Research Center, Director, USF Nanomedicine Research Center.*

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Narasaiah Kolliputi, Ph.D., *Assistant Professor of Medicine*

Srinivas Nagaraj, Ph.D., *Assistant Professor of Medicine*

Michael Teng, Ph.D., *Assistant Professor of Medicine*

Arun Kumar, Ph.D., *Research Instructor, Joy McCann Culverhouse Airway Disease Research Center*

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Joint Faculty

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Noorbibi Day, Ph.D., *Professor of Pediatrics and Medicine*

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Hugh H. Windom, M.D., *Clinical Associate Professor of Medicine*

Rosa Codina, Ph.D., *Clinical Assistant Professor of Medicine*

Mary L. Jelks, M.D., *Clinical Assistant Professor of Medicine*

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Glenn Whelan, Pharm.D., *Assistant Professor of Medicine*

Nathan Tang, M.D., *Adjunct Professor of Pediatrics*

2010 Fellows-in-Training

2nd Year Fellows

Robert Pesek, M.D., Chief Fellow

Michel Alkhalil, M.D.

1st Year Fellows

Ahmed Butt, M.D.

David Fitzhugh, M.D.

Jim Parkerson, D.O.

Salman Aljubran, M.D., Research Fellow

From left to right: Michel Alkhalil, M.D., Ahmed Butt, M.D., Robert Pesek, M.D., Jim Parkerson, D.O., David Fitzhugh, M.D., Salman Aljubran, M.D.

Division Research and Administrative Staff

Research Staff Members

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Marcia Cubillos, B.S., Para-professional
Mahasweta Das, Ph.D., Technical and Para Professional
Julio Garay, Ph.D., Adjunct Assoc. Researcher
Gary Hellermann Sr., Ph.D., Sr. Biologist Scientist
Battula Kiran, Ph.D., Post-doc, Scholar, Researcher
Kunyu Li, Technical and Para Professional
Allison Nelson, Research Technician
Jian Qin, Ph.D., Visiting Scholar
Saniya Rangooni, M.S. Research Technician
Sowndharya Ravi, M.S., M. Phil., Research Technician
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Jia-Wang Wang, Ph.D., Research Associate

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Ruan Cox, PhD student
Yvonne Davis, PhD student
Jordan Heft, PhD student
Rhonda Wilbur, PhD student
Terianne Wong, PhD student

Administrative Personnel

Administrative Assistant to the Division Director

Michelle Singleton, LPN, Clinical Research Administrator and Administrative Assistant to the Division Director

Administrative Personnel for the Division and The James A. Haley V.A. Medical Center

Peggy Hales, Program Assistant
Becci Carter, Administrative Secretary
Geeta Gehi, Administrative Secretary

Administrative Personnel-USF Joy McCann Culverhouse Airway Disease Research Laboratory

Rebecca McCrery, Administrative Secretary

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Diana Miller, B.A., Clinical Research Coordinator
Ivonne Pena, B.S., Regulatory Coordinator

Administrative Personnel for All Children's Hospital

Amy Baldwin, Administrative Assistant to Dr. Sleasman
Marjorie Peak, , Allergy and Immunology Fellowship Coordinator (Pediatrics)

Meet Our New Faculty Members

Narasaiah Kolliputi, Ph.D.,
Assistant Professor

Srinivas Nagaraj, Ph.D.,
Assistant Professor

Michael Teng, Ph.D.,
Assistant Professor

A. Inflammatory Lung Disease

1. Inhibiting ANP signaling through its receptor, NPRA, reduces lung inflammation in an experimental asthma model.

The human body has many systems that do double duty. Kidneys filter impurities from the blood but also regulate the blood volume and levels of sodium and potassium. The heart pumps the blood but also makes hormones that regulate blood pressure. One of these heart hormones, ANP, plays an important role in regulating inflammation in the lungs. It activates several different kinds of cells by binding to a receptor called NPRA on the cell surface. Isatin is a small molecule drug that interferes with ANP signaling. Using an asthmatic mouse model, we have found that isatin inhibition of ANP signaling through NPRA reduces the inflammation in the lungs and allows the mice to breathe better. A derivative of the ANP prohormone, NP73-102, decreases the level of NPRA on the cell surface and inhibits ANP signaling. This year we have continued investigating the mechanism of NPRA action and developed new nanoparticle formulations to reduce inflammation and disease. The anti-inflammatory peptide, NP73-102, has proven to be a strong candidate for DNA-based therapy aimed at inflammatory diseases.

2. Mutations in the ANP pathway are associated with asthma.

As mentioned before, ANP is a hormone that wears several hats. It was first discovered as the hormone responsible for maintaining sodium-potassium balance in the body and normal blood pressure through regulating the volume of fluid in the blood. Our lab and others, however, have been studying its role in the immune system and have discovered that ANP signaling, through its receptor NPRA, has a major effect on inflammation in asthma, cancer and other diseases. As in all diseases, there is a genetic component along with the effects of environment. We have been studying the ANP gene to determine if mutations in the DNA affect ANP activity. Such changes are known to affect the activity of ANP in regulating blood pressure and cardiovascular disease but few studies have been done to look at the inflammatory aspects of ANP-NPRA signaling. Our results will be published soon and will show that single base changes in the ANP gene can have significant effects on its activity. This knowledge enables us to design better drugs and DNA-based therapeutics to modify the inflammatory activity of ANP in an effort to protect people from diseases such as asthma and allergy.

3. The role of microRNAs in the genesis of asthma.

MicroRNAs (miRNAs) are small ribonucleic acid molecules, 18 to 25 bases long, that have a large effect on gene expression. It is estimated that from 30 to 50% of human genes are regulated by miRNAs and one miRNA can control as many as 200 genes. Mutations in the DNA that codes for miRNAs may contribute to many human diseases such as cancer, asthma, allergy and chronic infections. We have developed a microarray detection system for miRNAs that allow us to obtain a profile on the types and amounts of a large number of miRNAs from a person's blood sample. Experiments to correlate miRNA expression with inflammation, allergy, and asthma in a mouse model are being performed as a preliminary to testing miRNA targeting in humans. We are also creating transgenic mouse models that over-express or are deficient in these miRNAs in order to study their function.

4. Mechanism of MDSC-mediated T cell tolerance in inflammation.

The objective of this study is to identify and characterize myeloid-derived suppressor cells in acute and chronic asthma and to determine the function of these cell types and their mechanistic role in enhancing or inhibiting inflammation. Inflammation reflects a well-orchestrated pattern of cytokine and cellular events from acute to chronic disease stages. Chronic airway inflammation results in impaired T cell immunity. It is known, that a heterogeneous group of myeloid cells termed myeloid-derived suppressor cells (MDSC) accumulate in almost all models of cancer, infection and other pathological conditions. The exact role played by these cells in inflammation and the function and mechanism of these cells in T cell suppression is not known.

5. Role of extracellular ATP in hyperoxia-induced lung inflammation.

Extracellular ATP (eATP) serves as a danger signal to alert the immune system of tissue damage by acting on P2X or P2Y receptors. Patients with chronic lung pathology such as allergic asthma or chronic obstructive pulmonary disease were reported to present enhanced ATP levels in the bronchoalveolar lavage fluid (BALF). However, whether increased eATP is a danger signal during pulmonary oxidative stress is not known. We hypothesized that increased eATP from damaged cells in the lungs could trigger in hyperoxic lung injury. To test this hypothesis ATP was quantified in BALF of control room air mice and mice that were exposed to 100% oxygen for 72 hours. The contribution of eATP as a danger signal was assessed in a hyperoxia-induced acute lung injury murine model to study human acute lung injury. We administered the stable, nonhydrolyzable ATP analog, ATPγ into the lung and exposed mice to 100%O2. Mice treated with vehicle were used as controls. Hyperoxic mice have elevated ATP content in BALF in comparison with control mice. Mice treated with eATP had enhanced lung injury survival in 100% oxygen showed compared to control mice indicated by higher lung wet/dry weight, alveolar−capillary protein leakage and enhanced infiltration of inflammatory cells in bronchoalveolar lavage fluid, and increased content of thiobarbituric acid−reactive substances in lung homogenate. Our results also indicate that modulation of eATP levels with ATP-degrading enzyme apyrase significantly reduced hyperoxia induced inflammation. Together these findings suggest that increased eATP released from hyperoxia-injured lung cells constitutes a major endogenous danger signal in acute lung injury. This work was submitted as an abstract to American Thoracic Society 2011 annual meeting, which will be held 2011, May 13-18 in Denver Colorado.

6. Isolation and characterization of a new human mast cell line (USF-1) as a model for inflammatory disease research.

A stable human mast cell line derived from human cord blood stem cells has been established. Compared to the standard NIH mast cell lines, HMC-1 and LAD-2, this line shows greater stability with respect to the markers FeR1 and CD117, grows faster and requires a much simpler growth medium; hence, it is significantly less expensive to use. USF-1 is not a tumor cell line like the other cell lines, so retains all of its natural physiological functions. Currently we are incorporating the SV40 large T gene into USF-1 to immortalize it. One interesting preliminary result involves the plant compound, resveratrol, which is the active anti-inflammatory principle in grape skins and red wine. Resveratrol has been tested on the new human mast cell line, USF-1. It was found to cause increased production of an anti-inflammatory protein, SirT-1, and to inhibit degranulation and release of histamine from the cells.

B. Biology of host-virus interactions: DNA-based antiviral therapeutics.

Respiratory syncytial virus (RSV) encodes two small nonstructural proteins, NS1 and NS2, that play important roles in viral pathogenesis. Both NS proteins have been shown to antagonize host cellular interferon responses. In addition, the NS proteins affect viral RNA synthesis, virion morphogenesis, and additional cellular innate immune responses. We are currently defining the mechanisms by which the NS proteins alter these processes and identifying the structural requirements for these activities.

1. Respiratory syncytial virus (RSV) subverts the innate antiviral immune response.

Respiratory syncytial virus kills a substantial number of infants each year and has been associated with pneumonia in the elderly. Vaccination against this virus is largely unsuccessful because RSV is able to inhibit the immune system's antiviral surveillance program. The first protein made by the virus after it infects a cell is called NS1 (nonstructural protein 1). This protein inhibits the activity of interferon which is an antiviral compound critical for the body to mount an effective antiviral defense. We have made substantial progress in understanding how NS1 does this and how to counteract the viral subversion of the immune system. These research findings may be extremely beneficial in preventing death and severe illness in babies and young children.

The mitochondria of the cells are targets of the NS1 protein. Mitochondria are primarily known as the producers of ATP, the cell's energy supply, but they also are involved in antiviral defense. Two mitochondrial proteins, MAVS (mitochondrial antiviral signaling gene) and the adaptor protein, RIG-I, have to get together to trigger expression of antiviral genes and it is here that RSV's tactical weapon, NS1, acts. Using a combination of *in vitro* and *in vivo* experiments, we showed that NS1 blocks interaction of MAVS with RIG-I, thereby short-circuiting the antiviral system and prolonging survival of the virus. By preventing the virus from making NS1, we hope to stop RSV infections before they start.

2. Respiratory syncytial virus NS1 protein is localized to the nucleus.

The activity of the RSV protein, NS1, is quite complex. RSV infects lung cells and makes copies of itself, eventually resulting in damage to the lung that can be lethal. The NS1 protein blocks the antiviral interferon response of the cells allowing the virus to grow. How does NS1 do this? As described above, one way is by interfering with the interaction of mitochondrial proteins; however, NS1 does other things. Our data shows that NS1 localizes to the cell's nucleus but in doing so, blocks the entry of a protein called STAT-1 that is necessary for expression of antiviral genes. NS1 binds preferentially to *importin-α5*, a nuclear transport protein, and keeps it from binding to STAT-1. Hence, STAT-1 is prevented from entering the nucleus and cannot switch on the antiviral program. Antiviral therapeutics that block production of NS1 should be effective in restoring a good immune response.

3. Akt as a therapeutic target for respiratory syncytial virus.

We are examining the role of cellular signal transduction in respiratory syncytial virus (RSV) infection. We have found that RSV infection activates signaling through the Akt pathway and that inhibition of Akt decreases RSV replication and gene expression. We are currently determining the molecular mechanisms of Akt activation by RSV and defining how Akt inhibition reduces RSV infection.

In collaboration with Drs. David Jans and Reena Ghildyal at Monash University in Australia, we are examining the role of the matrix (M) protein in virion maturation of RSV. We have previously found that M traffics to the nucleus early in infection and is found predominantly in the cytoplasm later in infection. Recently, we have identified specific residues of M that regulate this process and are determining the effect of altering M trafficking on viral replication.

C. Nanomedicine

1. Nanocomplexes of DNA encoding N-terminal natriuretic peptides as vaccine or adjuvants against asthma.

NP73-102 is not the only peptide derived from the ANP prohormone that has anti-inflammatory properties. Vessel dilator (VD), which is located in the same part of the hormone as NP73-102, also prevents lung damage in mice from an allergic asthma attack. VD's mechanism of action is unknown, but we are actively studying it. These therapeutic peptides have a great advantage over conventional drugs. They can be targeted to specific cells by using nanoparticle carriers and produced on location from DNA plasmids encoding the peptides. This increases their pharmacological effectiveness and reduces side effects.

2. Nanotherapeutic approach for differentiation of MDSCs

The objective of this study is to develop and apply multifunctional targeted nanoparticles to effectively promote the differentiation of MDSCs as an anticancer strategy. [and to synergize multifunctional nanoparticle with… Take out the preceding phrase. It makes no sense by itself.] One of the major mechanisms of tumor progression is the inability of the host system to develop an effective antitumor immune response. Indeed, accumulating evidence has now shown that a population of cells with suppressive activity, known as myeloid-derived suppressor cells contributes to the failure of the immune system to tackle the tumor cells and also towards the low efficacy of cancer vaccines. Cancer therapy involving either the differentiation or elimination of suppressive cells may be a successful treatment strategy compared to direct cancer therapy to eliminate tumor cells which has often proved futile. MDSCs are a heterogeneous mixture of precursors of dendritic cells, macrophages and monocytes. One of the most plausible ideas for boosting the antitumor immune response will be differentiating these cells into their mature counterparts which lack suppressive function. Based on our recent work in cancer and nanotherapy we hypothesize that the development and application of multifunctional nanoparticles to target and effectively promote the differentiation of MDSCs will prove an effective anticancer strategy. This project has been submitted to NIH and American Cancer Society.

3. Curcumin nanoparticles alter dendritic cell activity and reduces inflammation.

Plant extracts and other natural compounds offer a huge area for discovery of novel anti-inflammatory agents. A study of the activity of curcumin, an ingredient in curry powder, was completed this year with extremely interesting findings. Curcumin, which is isolated from the turmeric plant, has been used for years as an alternative medicinal compound in the treatment of a wide variety of inflammatory diseases. We have discovered a link between the anti-inflammatory properties of curcumin and the innate immune system. Dendritic cells are the cells of the immune system that look for pathogens, cancer cells and foreign substances, digest them and 'present' them to the T lymphocytes which then mount an immune response. Our results showed that incubation of dendritic cells with curcumin caused them to undergo changes that reduced their inflammatory activity. While this may sound contrary to what was stated above, a reduction in dendritic cell activity is sometimes beneficial because they sometimes go overboard and cause more damage through an excessive inflammatory response, such as may be seen in asthma and allergy. It is this over-reaction that curcumin is inhibiting.

D. Other Research

1. Immunomodulation by CD4 T cells in cancer

The objective of this study was to investigate the role played by MDSCs in the inhibition of CD4+ T cell function, and to determine if activated antigen-specific CD4+ T cells can modulate the function of MDSCs as a possible negative feedback mechanism.

T-cell tolerance is one of the major mechanisms of tumor escape. Myeloid-derived suppressor cells (MDSCs) suppress CD8+ T-cell responses and this effect is universally accepted, albeit the exact mechanism is a subject of debate. However, the effect of MDSCs on CD4+ T cells remains controversial. The question remains as to whether MDSCs can suppress CD4+ T cells and whether this suppression is antigen-specific. Using an experimental system employing the adoptive transfer of transgenic CD4+ T cells into naïve recipients, we demonstrated that MDSCs could induce antigen-specific tolerance of CD4+T cells. MDSCs isolated from mice bearing different types of tumors vary greatly in their level of MHC class II expression. Cells with a low level of MHC class II expression failed to induce CD4+ T cell tolerance. Our hypothesis is that activated CD4+ T cells but not CD8+ T cells are able to convert MDSCs from antigen-specific suppressor cells to cells able to inhibit nonspecific T-cell responses. We are exploring the role played by retrograde MHC class II signaling on MDSC function.

2. The effect of pine cone extract (PCE) on OVA-sensitized mice.

Pine cone extract has been previously shown to reduce levels of IgE and Th2 cytokines including IL-4 as well as to enhance production of IFN-gamma and IL-12 in C57BL/6 and Balb/c mice. The purpose of this study was to analyze the effect of PCE on Th2 cytokines and IgE levels in Balb/cJ mice that have undergone sensitization to ovalbumin. This study is complete and the abstract has been accepted by the American Academy of Asthma, Allergy and Immunology 2011 meeting in San Francisco, CA.

3. Role of forkhead transcription factor FOXO3a in acute lung injury

Acute lung injury (ALI) is a devastating clinical problem involving the key events of inflammation and alveolar epithelial cell death. The fundamental mechanism of this serious condition evolves from an imbalance between pro- and anti-inflammatory cytokines ultimately resulting in oxidative stress-induced cell death. FOXO transcription factors are important regulators of cell survival in response to a variety of stress stimuli, among which are oxidative stress, DNA damage, and nutrient deprivation, however, the role of FOXO3a in acute lung injury and epithelial cell death is not known. It was hypothesized that FOXO3a protects alveolar epithelial cells from H2O2 (peroxide)-induced cell death. To test this hypothesis, the effects of H2O2 on subconfluent human alveolar epithelial cell (A549) cultures were tested. A549 cells were transfected with vector containing wild type FOXO3a cDNA (FOXO3a-WT) or vector containing mutant FOXO3a cDNA (FOXO3a-M) and treated with or without H2O2 for one hour to induce oxidative stress. The results showed that H2O2 induced significant alveolar epithelial cell necrosis and apoptosis. In contrast epithelial cells transfected with FOXO3a-WT inhibited H2O2-induced cell necrosis and apoptosis. However cells transfected with the mutant FOXO3a-M did not alter H2O2-mediated epithelial cell apoptosis and necrosis. Together these results suggest that FOXO3a protects alveolar epithelial cells from oxidative stress-induced cell death. *This work was submitted as an abstract to Experimental Biology 2011 annual meeting, which will be held 2011, April 9-13 in Washington DC.*

Clinical Research Projects Conducted at the Division's Clinical Research Unit

1. Repeated nasal challenge in skin prick-puncture negative, intradermal positive dust mite allergic rhinitis patients

Skin prick-puncture testing is a specific test to determine whether or not an individual is allergic. The primary goal of this study is to evaluate the clinical usefulness of intradermal skin testing when prick-puncture tests are negative. Intradermal skin testing is more sensitive but less specific than prick-puncture testing. There is little evidence-based data to support the clinical relevance of a negative prick-puncture test with a positive intradermal test result. This study's hypothesis is that subjects who have a clinical history of perennial rhinitis symptoms associated with dust exposure or not associated with other perennial allergens, will have a positive challenge with *Dermatophagoides pteronyssinus* when they have a positive intradermal test and a negative prick-puncture test. Subjects who are prick-puncture negative and intradermal skin test positive to *Dermatophagoides pteronyssinus* will be challenged with nasal sprays containing either placebo or *Dermatophagoides pteronyssinus* extract solution seven separate days under observation in the research office (no more than three days between visits). This will be followed by a one month washout period, then patients will cross over and return to the research office for the administration of the other nasal spray under observation, again on seven separate days. Both subjects and investigators will be blinded to the spray being used. Recruitment for this project is ongoing at this time.

2. Pollen and mold counts

Particles, other than pollen, which transport aeroallergens, have been described. The Division, which houses the Pollen and Mold Counting Station for Tampa, has two collectors adapted to collect both pollen and pollen aeroallergens. The collectors are located on the roof of the James A. Haley V.A. Medical Center Research Building. Pollen counts are performed twice weekly, disseminated to local media once weekly, and to the Internet twice weekly. Dr. Mary Jelks reads and interprets the slides.

3. Effect of supplemental oral curcumin on patients with atopic asthma

Curcumin, a naturally occurring polyphenolic molecule derived from the root of the *Curcuma Ionga* plant, has been shown in animal models to have intracellular molecular targets such as transcription factors AP-1 and NF-κB. It prevents the secretion of both pro-inflammatory (TNF-α, IL-6) and anti-inflammatory (IL-10) cytokines. Curcumin given in vitro to *Dermatophagoides farinae*-stimulated lymphocyte cell cultures demonstrated a decreased production of IL-2, IL-4, IL-5, and GM-CSF. The purpose of this pilot study is to evaluate the effect of oral supplementation with curcumin on patients with persistent atopic asthma in a randomized, double-blinded, placebo-controlled trial. Twenty nine subjects have been screened for this project, 17 have been randomized and 15 have completed this study. A paper is in press for this project.

4. Measurement of natriuretic hormone peptides in exacerbation of asthma

Evidence exists that atrial natriuretic peptide is a regulator of smooth muscle airway tone. In animal models, atrial natriuretic peptide is a potent bronchodilator. Natriuretic hormone peptides include atrial natriuretic peptide, vessel dilator, kaliuretic peptide, long-acting natriuretic peptide, cardiac natriuretic peptide and brain natriuretic peptide. For these reasons, we wish to measure atrial natriuretic peptide and 4 other natriuretic hormone peptides (vessel dilator, kaliuretic peptide, long-acting natriuretic peptide, and brain natriuretic peptide).

We hypothesize that there is a statistically significant decrease in natriuretic hormone peptides in subjects with asthma exacerbation compared to levels following treatment of an exacerbation of asthma. Measurement of natriuretic hormone peptides in a patient suffering an asthma exacerbation may be useful to the clinician. If our hypothesis is correct, and natriuretic hormone peptides are decreased, such information may be valuable to evaluate patients with an exacerbation of asthma. Although asthma presents with shortness of breath, coughing and wheezing, other conditions can also present similarly (congestive heart failure, myocardial infarctions, vocal cord dysfunction, interstitial lung diseases). Studying the relationship of natriuretic hormone peptide levels to asthma exacerbation may help to better understand the physiology and pathogenesis of asthma. Since the study began, 29 subjects have been screened and 24 have completed the study. Screening and enrollment for this study continues.

5. Procalcitonin as an aid in the diagnosis of acute bacterial sinusitis

The purpose of this pilot study is to determine if clinical bacterial sinusitis is associated with elevated procalcitonin. Sinus infection is one of the most commonly diagnosed diseases in the United States, affecting nearly 16% of the population annually. Although viral upper respiratory infection is relatively straightforward in terms of diagnosis and management, the diagnosis of acute bacterial sinusitis is difficult and is often incorrectly made, resulting in a high rate of inappropriate use of antibiotic therapy for viral infections. Current recommendations advise that acute bacterial sinusitis should be suspected when upper respiratory infection symptoms last greater than 10-14 days. Procalcitonin is a 116 amino acid protein that is a precursor of calcitonin. Although confined mainly to the thyroid C-cells in health, procalcitonin can be induced in multiple cells lines[types??] in inflammatory conditions and is elevated in bacterial infections. Procalcitonin levels have been shown to be elevated in bacterial but not in viral infections. We hypothesis that elevated procalcitonin level predicts the presence of bacterial sinusitis in patients presenting with sinus complaints. We have screened 12 subjects and 10 have completed the study. All recruitment and subject visits are complete and the study data is being analyzed at this time.

6. Effects of pine cone extract (PCE) on IgE levels in patients with allergic rhinitis

Pine cones and their aqueous extracts have been known to have medicinal properties in Japanese populations as far back as 2000 years ago. Anecdotal reports have suggested that use of PCE improves allergic rhinitis symptoms and in the mouse model has been shown to significantly reduce serum IgE levels. The purpose of this study was to determine if oral PCE extract administered in a double-blind fashion significantly reduced IgE levels in patients with evidence of perennial allergies. We are currently enrolling subjects.

7. Efficacy of using oxymetazoline hydrochloride combined with nasal glucocorticosteroid to treat perennial allergic and nonallergic rhinitis in subjects with persistent nasal congestion.

This study hypothesizes that treatment with oxymetazoline, in addition to a nasal glucocorticosteroid for fourteen days, will decrease the nasal congestion persisting in subjects with allergic or nonallergic rhinitis despite maximum recommended dosages of a nasal glucocorticosteroid. It is also hypothesized that nasal glucocorticosteroid therapy will prevent the development of rhinitis medicamentosa secondary to therapy with oxymetazoline. The primary endpoint will be the change in Average Daily Nasal Congestion Scores from baseline to the end of treatment with oxymetazoline. The secondary endpoint will compare quality of life scores at the baseline visit to visits on day 7, day 14, and day 28. The results of this study have been accepted for publication in the *World Allergy Journal.*

8. To determine the prevalence of food allergy in adult patients with eosinophilic esophagitis

Food allergies are known to play a significant role in children with eosinophilic esophagitis; but little is known about the prevalence of food allergies in adult patients with eosinophilic esophagitis. The purpose of this study is to determine the prevalence of food allergies in a cohort of adult patients with eosinophilic esophagitis. These results will be compared to findings in adult patients with gastroesophageal reflux disease. This study is in the start up phase.

9. Myeloid suppressors in inflammation

The purpose of this study is to identify and characterize specific cell types (human dendritic cells, myeloid-derived suppressor cells and T lymphocytes) that are present in acute and chronic asthma, and to determine the function of these cell types and their mechanistic role in enhancing or inhibiting inflammation. Twenty healthy donor blood samples will be obtained from Florida Blood Services, twenty patient blood samples will be obtained from patients experiencing an acute asthma exacerbation and twenty human samples will be obtained from chronic asthmatics. From each sample arm, human monocyte-derived dendritic cells, MDSC, and T cells will be isolated to determine population concentrations for each cell type and also to determine if T cells are inhibited in their ability to produce IFN-g following stimulation with and without LPS. We have collected 6 samples thus far. We are actively recruiting subjects for this project.

10. Effect of oxymetazoline hydrochloride in combination with nasal glucocorticoid on the apnea hypopnea index (AHI), nocturnal oxyhemoglobin saturation, snoring, and sleep quality in subjects with persistent nasal congestion. A double blinded, placebo control, cross over prospective trial.

The goal of the trial is to evaluate the effectiveness of the addition of oxymetazoline to intranasal ICS (mometasone) on the apnea/hypopnea index (AHI), and on other sleep parameters in subjects with persistant nasal congestion secondary to allergic or nonallergic rhinitis despite treatment with the highest recommended doses of intranasal ICS, mometasone. This project has been submitted to the University of South Florida Instutional Review Board.

Clinical Research Unit

The University of South Florida, Asthma, Allergy and Immunology Clinical Research Unit was established in 1977 to improve the treatment of patients who suffer from asthma, allergic and immunologic diseases. The Clinical Research Unit is a segment of the Division of Allergy and Immunology, Department of Internal Medicine at the University of South Florida College of Medicine. The Division is affiliated with the H. Lee Moffitt Cancer Center, James A. Haley Veterans Administration Hospital and the University of South Florida Medical Clinics in Tampa. The Unit is also affiliated with All Children's Hospital and Bay Pines Veterans Hospital, both in St. Petersburg.

The Unit provides quality research in a variety of clinical areas which include the following: allergic conjunctivitis; allergen immunotherapy; allergen skin testing; allergic rhinitis; asthma; atopic eczema; bronchitis, acute and chronic; contact dermatitis; chronic obstructive pulmonary disease; exercise induced asthma; headache (migraine and tension); hereditary angioedema; HIV disease and any of its complications; immunodeficiency diseases; insect allergy; intravenous immunoglobulin; osteoporosis; rheumatoid arthritis; sinusitis, acute and chronic; temporomandibular joint disease; urticaria and vasomotor rhinitis.

Studies funded by pharmaceutical companies are conducted at the Division's Clinical Research Unit (CRU). Funds from these studies support the Division's research and clinical training program. Seven studies were completed in 2009, ten in 2010 and ten additional studies will continue into 2011. To date, the CRU has agreements for six new studies in 2011.

The CRU is a member of the American Lung Association's Asthma Clinical Research Center network, one of 20 centers throughout the United States. The American Lung Association Clinical Research Center completed two studies in 2009, and one in 2010, four are still in progress. The American Lung Association has several new protocols pending approval.

2009 – 2010 Pharmaceutical Sponsors

Almirall Pharmaceuticals	Dyax Corporation
Forest Laboratories	Genentech Inc.
GlaxoSmithKline	Jerini, US
Merck and Co., Inc.	MedImmune
Novartis Pharmaceuticals	Pharming Inc.
Pfizer	Sanofi-Aventis Pharmaceuticals
Schering-Plough Corporation	Viropharma

Basic and Clinical Research Support

Endowments

The Joy McCann Culverhouse Endowment
The Mabel and Ellsworth Simmons Endowment

Extramural funding

American Lung Association Asthma Clinical Research Center Award
American Heart Association
Bankhead Coley Research Program
Florida Biomedical Research Foundation
Florida Hi Tech Corridor Grant
James & Esther King Biomedical Research Program
National Institute of Health
Office of Naval Research
Pfizer Visiting Professor Grant
TransGenex Nanobiotech, Inc.
Universidad del Norte, Baranquilla, Colombia
Veteran Affairs Merit Review Award
Veterans Affairs Career Scientist Award

Division's open-access online journal

Genetic Vaccines and Therapy, BioMed Central Publishing, London, UK. Shyam Mohapatra, Ph.D., Editor-in-Chief and Gary Hellermann, Ph.D., Managing Editor, 2004 to present. http://www.gvt-journal.com

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Rael, E.L., Ramey, J.T., Lockey, R.F. Oxymetazoline (OXY) hydrochloride combined with mometasone nasal spray (MNS) for persistent nasal congestion (NC). 66th Annual American Academy of Allergy, Asthma & Immunology Meeting, New Orleans, LA, February 26 – March 2, 2010. *J Allergy Clin Immunol* 2010; 125(2): AB173. (#680).

Reddy, S., Chandrakasan, S., Butt, A., Secord, E. Autosomal recessive chronic granulomatous disease (CGD) presenting with liver abscesses. Poster presentation at American College of Allergy, Asthma and Immunology National Meeting, Miami, FL, November 5-10, 2009. Accepted for publication in the *Annals of Allergy, Asthma & Immunology*.

Shin, B., Cole, S.L., Park, S., Ledford, D.K., Lockey, R.F. A new symptom based questionnaire for predicting asthma. 65th Annual American Academy of Allergy, Asthma & Immunology Meeting, Washington, DC, March 13 – 17, 2009. *J Allergy Clin Immunol* 2009; 123(2): S5. (#4).

Wang, J., Zhang, W., Li, K., Chen, D., Liu, G., Lockey, R.F., Mohapatra, S.S. Npr1 deficiency upregulates regulatory T cells (Tregs) through impaired dendritic cell (DC) development. 65th Annual American Academy of Allergy, Asthma & Immunology Meeting, Washington, DC, March 13 – 17, 2009. *J Allergy Clin Immunol* 2009; 123(2): S93. (#350).

Wang, J., Li, K., Zhang, W., Lockey, R.F., Mohapatra, S., Mohapatra S.S. Over-expression of MiRRA2 in vivo impairs T lymphocyte activation. 66th Annual American Academy of Allergy, Asthma & Immunology Meeting, New Orleans, LA, February 26 – March 2, 2010. *J Allergy Clin Immunol* 2010; 125(2): AB76. (#301).

Wong, T., Boyapalle, S., San Juan-Vergara, H., Cha, B., Garay, J., Teng, M., Mohapatra, S. A novel fluorescent labeling approach to detect early events in RSV-infected living cells. 67th Annual American Academy of Allergy, Asthma, and Immunology Meeting, San Francisco, CA Mar. 18 - 22, 2011. Pending.

Wong, T., Zhang, W., Boyapalle, S., Mohapatra, S. An inducible expression system for respiratory syncytial virus NS1. James A. Haley Veteran's Hospital Research Day, Tampa, FL, April 29, 2010.

Zeballos-Chavez, R., Butt, A., Reddy, S., Secord, E. HIV first STI for most infected teens: Majority asymptomatic at diagnosis. Poster presentation at the American Academy of Allergy, Asthma, and Immunology National Meeting, New Orleans, LA, Feb. 2010. *Journal of Allergy & Clinical Immunology* 2010; 125(2) Suppl 1:AB78 (#308).

Zhang, W., Cao, X., Chen, D., Wang, J., Yang, H., Mohapatra, S., Hellermann, G., Kong, X., Lockey, R.F., Mohapatra, S.S. Atrial natriuretic peptide receptor signaling plays a critical role in induction of tolerogenic dendritic cells. 66th Annual American Academy of Allergy, Asthma & Immunology Meeting, New Orleans, LA, February 26 – March 2, 2010. *J Allergy Clin Immunol* 2010; 125(2): AB227 (# 891).

Zhang, W., Boyapalle, S., Cao, X., Wang, J., Lockey, R.F., Mohapatra, S.S. RSV NS1 protein blocks the IFN response by blocking RIG-I interaction with the mitochondrial antiviral signaling protein. MAVS. 65th Annual American Academy of Allergy, Asthma & Immunology Meeting, Washington, DC, March 13 – 17, 2009. *J Allergy Clin Immunol* 2009; 123(2): S208. (#801).

Faculty and staff awards: 2009-2010

Roger W. Fox, M.D., Selected as one of *"The Best Doctors in America"* Guide 2008- 2009.

Roger W. Fox, M.D., 30 years Department of Veterans Affairs Service Award, 2009.

Mark C. Glaum, M.D., Ph.D., Selected as one of *"The Best Doctors in America"* Guide 2008-2009.

Mark C. Glaum, M.D., Ph.D., promoted to Associate Professor, August 2010.

Mark C. Glaum, M.D., Ph.D., Platinum Dean's Recognition Award for achievements and leadership in education and research /scholarly activity, December 2010.

Sandra G. Gomph, M.D., Re-elected by Infectious Disease Subspecialty peers for inclusion in "Best Doctors in America®" from 2011 to 2012

Sandra G. Gomph, M.D., Elected by Infectious Disease Subspecialty peers for inclusion in "Best Doctors in America®" from 2009 to 2010

Narasaiah Kolliputi, Ph.D., Society for Experimental Biology and Medicine, Young Investigator Award, Maywood, New Jersey 2009

Dennis K. Ledford, M.D., President of the American Academy of Allergy, Asthma and Immunology, 2011 to 2012.

Dennis K. Ledford, M.D., Selected as one of *"The Best Doctors in America"* Guide 2008- 2009.

Richard F. Lockey, M.D., President of the World Allergy Organization, 2010 to 2012.

Richard F. Lockey, M.D., Recognition Award, WAO WISC, Dubai. December 6th -8th , 2010

Richard F. Lockey, M.D., 40 years Department of Veterans Affairs Service Award, 2011.

Richard F. Lockey, M.D., Florida Super Doctors 2009, special advertising supplement to the Tampa Tribune, Gulf Coast Edition, January 17, 2009.

Richard F. Lockey, M.D., Selected as one of *"The Best Doctors in America"* Guide 2008- 2009.

Robert Pesek, M.D., ACAAI Travel Grant, 2009

Robert Pesek, M.D., Florida Allergy, Asthma, and Immunology Society Travel Grant, 2010

Robert Pesek, M.D., Chief Fellow, University of South Florida, Division of Allergy and Immunology 2010

Jia-Wang Wang, Ph.D., LPS-Responsive CHS1/Beige-Like Anchor Gene and Therapeutic Applications. Patent#: US7704963B2.

Visiting professor educational program

2010

Mario Sánchez-Borges, M.D., Professor of Allergy and Clinical Immunology Faculty of Medicine Central University of Venezuela, Director of Allergy and Clinical Immunology Department, Centro Médico-Docente La Trinidad, Caracas, Venezuela "Atopy, aspirin, and mites". December 20, 2010

Mingnan Chen, Ph.D., Center for Biologically Inspired Materials & Material Systems, Department of Biomedical Engineering, Duke University, Durham, North Carolina. "Engineering polypeptide-based vaccines and drug carriers for cancer therapy" November 19, 2010.

Robert Naclerio, M.D., Professor of Surgery, Section Chief, Otolaryngology – Head and Neck Surgery, University of Chicago, Pritzker School of Medicine, Chicago, Illinois. "Informal roundtable discussion on state of the science and pathophysiology of allergic rhinitis" and "Treatment of nonallergic rhinitis" October 27, 2010.

David B. Weiner, Ph.D., Professor, Department of Pathology & Laboratory Medicine, Chair, Gene Therapy & Vaccine Program, University of Pennsylvania School of Medicine, Philadelphia, PA SIPAIID Distinguished Lecture Series, "DNA Vaccines: Rise of the phoenix", June 15, 2010.

Georgio Walter Canonica, M.D., Professor of Allergy and Respiratory Diseases Chairman of the Allergy and Respiratory Diseases Clinic, Director of the Specialty School of Pulmonary Diseases, Genoa University, Genoa, Italy. "Sublingual immunotherapy 2010", May 14, 2010.

Chen Dong, Ph.D., Professor, Immunology, MD Anderson Cancer Center, Houston, Texas SIPAIID Distinguished Lecture Series. "Molecular pathways leading to allergic diseases". April 15, 2010.

Giovanni Piedimonte, M.D., Wyeth Research Scholar, Professor & Chairman in the Department of Pediatrics, West Virginia University School of Medicine, Physician-in-Chief, West Virginia University Children's Hospital. "State of the science: Emerging issues in basic asthma research" March 5, 2010.

2009

Rosa Codina, Ph.D., Senior Scientist Greer Laboratories. "An overview of a few miscellaneous topics for discussion, part I", November 12, 2009.

Anthony Register, Pharm.D., Sr. Regional Medical Scientist-Respiratory/G.I., Clinical Development and Medical Affairs N.A., GlaxoSmithKline, Inc.. "Use of Advair in asthma" and "Veramyst for allergic rhinitis", September 23-24, 2009.

Narasaiah Kolliputi, Ph.D., Massachusetts General Hospital. "Exogenous administration of SOCS-1 by gene transfer provides protection against hyperoxia-induced lung injury", September 4, 2009.

Michael N. Teng, Ph.D., Assistant Professor, Department of Biochemistry and Molecular Biology, Penn State University. "Multiple functions of the human respiratory syncytial virus nonstructural proteins in viral pathogenesis", June 22, 2009. "Multiple functions of the human respiratory syncytial virus nonstructural proteins in viral pathogenesis"; August 18, 2009.

Sailen Barik, Ph.D., Department of Biochemistry and Molecular Biology, University of South Alabama College of Medicine**.** "Viral counter-attack on cellular RNA interference: A novel mechanism targeting argonaute", August 13, 2009.

Ken Linsky, Pharm.D., Sr. Regional Medical Scientist, Respiratory GlaxoSmithKline. "GlaxoSmithKline respiratory sponsored and supported research update and opportunities", July 16, 2009.

Tom Taylor-Clark, Ph.D., Johns Hopkins University. "The role of the ion channel TRPA1 in the activation of airway sensory nerves by oxidative stress", July 23, 2009.

Donald D. Stevenson, M.D., Senior Consultant, Division of Allergy, Asthma & Immunology Scripps Clinic, La Jolla, California. "Aspirin desensitization"; "Pathogeneses of aspirin exacerbated respiratory disease and reactions to NSAIDS."

Mandip Singh Sachdeva, Ph.D., Professor and Section Leader Pharmaceutics, Florida A & M University College of Pharmacy, Editor-in-Chief CRC Critical Reviews in Therapeutic Drug Carrier Systems. "Formulation approaches to treat lung cancer", June 29, 2009.

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