2004-2005 Annual Report

Division of Allergy and Immunology
Department of Internal Medicine
The Joy McCann Culverhouse Airway Disease Center
University of South Florida College of Medicine
and The James A. Haley Veterans' Hospital
Tampa, Florida

MISSION STATEMENT

The University of South Florida College of Medicine, Department of Internal Medicine, Division of Allergy and Immunology was founded in 1972 by Samuel C. Bukantz, M.D. 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 Center was dedicated in February, 1998. In 1998, Mrs. Mabel Simmons also 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. Hospital, 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 Division may contact Richard F. Lockey, M.D. or any faculty member at (813) 972-7631 (e- mail:rlockey@hsc.usf.edu).

DIVISION OF ALLERGY AND IMMUNOLOGY FACULTY AND STAFF

Core Faculty

Samuel C. Bukantz, M.D., Professor Emeritus of Medicine and Medical Microbiology and Immunology; Director Emeritus

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

Rama Ganguly, Ph.D., M.P.H., Professor of Medicine

Mark C. Glaum, M.D., Ph.D., Assistant Professor of Medicine and Pediatrics

Prasanna Kumar Jena, Ph.D., Research Instructor, Joy McCann Culverhouse Airway Disease Center

Monroe J. King, D.O., Affiliate Associate Professor of Medicine and Pediatrics

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

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

Shyam S. Mohapatra, Ph.D., Professor of Pediatrics and Medicine and Medical Microbiology and Immunology, Director of Basic Research, Joy McCann Culverhouse Airway Disease Center

The late, Andor Szentivanyi, M.D., D.SC., University Distinguished Professor of Medicine and Pharmacology

Joint Faculty

Stuart M. Brooks, M.D., Professor of Public Health and Medicine

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

Morna Dorsey, MD, MMSc, Assistant Professor of Pediatrics and Medicine

Sandra G. Gompf, M.D. Assistant Professor of Medicine

Gary W. Litman, Ph.D., Hines Professor of Pediatrics and Medicine

Robert Nickeson, Jr., Assistant Professor of Pediatrics and Medicine

Mandel R. Sher, M.D., Affiliate Professor of Pediatrics and Medicine

Mitchel J. Seleznick, M.D., Associate Professor of Medicine

John W. Sleasman, M.D., Professor of Pediatrics and Medicine, Robert A. Good Professor of Immunology; Chief, Division of Allergy/Immunology, Department of Pediatrics, University of South Florida, All Children's Hospital

Nutthapong Tangsinmankong, M.D., Associate Professor of Pediatrics and Medicine

Clinical Affiliate Faculty

Rosa Codina, Ph.D., Affiliate Assistant Professor of Medicine

Elliot Ellis, M.D., Affiliate Professor of Medicine

Mary L. Jelks, M.D., Affiliate Assistant Professor of Medicine

German F. LeParc, M.D., Affiliate Associate Professor of Pathology and Medicine

Brett E. Stanaland, M.D., Affiliate Assistant Professor of Medicine

G. Edward Stewart II, M.D., Affiliate Assistant Professor of Medicine

Hugh H. Windom, M.D., Affiliate Associate Professor of Medicine

Robert E. Windom, M.D., Affiliate Professor of Medicine

Fellows

Thomas Chacko, M.D., 1st year fellow

Steven L. Cole, D.O., 1st year fellow

Denise M. Kearney, M.D., 2nd year fellow

Alexander T. Vu, M.D., 2nd year fellow

Research Staff Members

Gary Hellermann, Ph.D.

Arun Kumar, Ph.D.

Dong-Won Lee, Ph.D.

Bishwabhusan Sahoo, Ph.D.

Weidong Xu, Ph.D.

Weidong Zhang, M.D.

Volunteers and Summer Interns

Elena Hernandez, M.D.

Hong Yang, M.D.

Administrative Personnel- All Children's Hospital

Linda Callahan, Training Program Assistant

Administrative Personnel-USF Airway Diseases Research Laboratory

Michelle Gonzalez, Administrative Assistant

Administrative Personnel James A. Haley Veterans' Hospital

Peggy Hales, Program Assistant

Geeta Gehi, Administrative Secretary

Sandra Rocha, Administrative Secretary

Becci Carter, Administrative Secretary

Clinical Research Unit Personnel

Michelle Grandstaff, LPN, CRC - Clinical Research Administrator and Administrative Assistant to the Director

Brooke Fimbel, B.A., CRC - Assistant Clinical Research Administrator and Lead Clinical Research Assistant

Shirley McCullough, B.S., Clinical Research Coordinator

Stephanie Merrell, Regulatory Coordinator

BASIC RESEARCH PROJECTS

I. Mucosal IFN-γ Gene Transfer, Which Attenuates Allergic Sensitization, Airway Hyperresponsiveness and Respiratory Syncytial Virus (RSV) Infection in Allergen Sensitive Mice.

Respiratory syncytial virus infection is associated with childhood bronchiolitis and asthma. Recurrent RSV infection in ovalbumin (OVA) allergen-sensitized mice causes an increased expression of Th2-associated inflammatory responses and subsequent development of airway hyperresponsiveness (AHR). The mucosal IFN-γ gene transfer in both allergic sensitization and protection from acute RSV infection was examined in this study by using chitosan, a naturally biodegradable cationic polysaccharide, as a gene delivery agent. Following IFN-γ gene transfer via intranasal and/or oral administration of chitosan, mice were sensitized to ovalbumin (OVA). Then the mice were infected with RSV and challenged with ovalbumin (OVA). The allergic response and RSV titers were determined. Mucosal delivery of chitosan-IFN-γ (CIN) to mice reduced both AHR and IgE synthesis. Mice receiving CIN also increased production of IFN-γ and reduced levels of produced IL-5 in ovalbumin stimulated splenocyte cultures. CIN treatment also decreased lung inflammation manifested by treated mice, which exhibited less eosinophil infiltration than untreated controls. In a separate study, mucosal vaccination also significantly reduced RSV titers in murine lungs. Together, these results suggest that mucosal delivery of IFN-γ gene is beneficial against both allergic inflammation and RSV infection.

II. Inhibition of Respiratory Syncytial Virus (RSV) Replication by Vector-derived Small Interfering RNAs Against Non-structural Protein 1 (NS1) Protein

Respiratory syncytial virus (RSV) is an important virus associated with bronchiolitis and asthma. Available antiviral treatments of RSV infections are only partially effective and nonspecific. Small interfering RNAs (siRNA) provide a novel approach to inhibit specific viral gene expression. The inhibition of virus replication by a plasmid expressing siRNAs capable of silencing the non-structural protein 1 (NS1) gene of RSV was examined in this study. Human alveolar epithelial cells (A549) were transfected with either siRSV-NS1 or siHPV_{18} E7 (control) and infected twenty-four hours later with rgRSV (recombinant RSV containing the gene encoding enhanced green fluorescence protein, EGFP) at an MOI (multiplicity of infection) of 1. The number of cells infected with rgRSV were quantified by fluorescence microscopy or by flow cytometry one day post-infection, and viral protein expression in cultured cells was detected by western blotting. The percentage of cells expressing green fluorescence protein decreased in siRSV-NS1-treated cells demonstrating that rgRSV replication was inhibited in a dose-dependent and sequence-specific manner. Expression of NS1 could not be detected in siRSV-NS1-treated cells. A cell- based plaque assay of cultured supernates from infected A549 cells indicating that SiRSV-NS1 also significantly decreased the rgRSV virus titer compared to control. The cytotoxicity of siRSV-NS1 plasmid on A549 cells tested by methyl thiazole tetrazolium (MTT) assay revealed no difference ($P>0.05$) in viability between siRSV-NS1-treated cells and controls

at the highest dose of plasmid (4 μg) used. These results demonstrate that siRSV-NS1 is capable of significantly decreasing RSV replication in human epithelial cells and provide a basis for the development of siRSV-NS1 as potential prophylaxis and therapy of RSV infection in humans.

III. Activation of PKC Isozymes in Normal Human Bronchial Epithelial Cells by Respiratory Syncytial Virus Infection

Human carcinoma-derived cell line type-II alveolar epithelial cells A549 respond to respiratory syncytial virus (RSV) by activating nuclear factor kB (NFkB), mitogen-activated protein kinase (MAPK) and protein kinase C (PKC) pathways. Since it is not known whether similar signaling mechanisms are activated in normal human bronchial epithelial (NHBE) cells the present study was designed to determine the role of PKC in the NHBE response to RSV infection. NHBE cells were exposed to sucrose-purified RSV (pRSV) for various periods of time and examined for expression of different PKC isoforms. Translocation of PKC was investigated by confocal microscopy. Western-blotting analysis of whole-cell lysates showed that NHBE cells express PKC-α, -β2, -γ, -δ, -ε, -λ, and -ζ isozymes. A time course experiment of pRSV-exposed NHBE cells indicated that by 8 hours all of the PKC isozymes, except PKC-β2, were degraded. In addition, PKC-α and –β isozymes increased in expression at 1 hour and 2 hours post-infection, respectively, whereas PKC-β2 increased by 1 hour, declined at 2 hours, and increased again at 8 hours. Western-blots of cell fractions revealed that PKC-α translocated from the membrane fraction to both the cytoplasmic and particulate fractions after 30 minutes of pRSV exposure. Confocal microscopy also showed translocation of PKC isozymes after 30 minutes. Furthermore, there is a significant reduction in the number of infected cells (more than 2 orders of magnitude), after they are pretreated with inhibitors of PKC isozymes. These results indicate that PKC activation is required for RSV to infect NHBE cells. By defining the role of a specific PKC isozyme during RSV infection will help the design of new therapies against RSV infection.

IIII. Given Intranasally, Chitosan Nanoparticle Carrying a Plasmid Encoding Novel Peptide, NP_{73-102}, Reverses Established OVA-RSV Induced Asthma in Mice

A family of natriuretic peptides (NP) with broad physiologic effects on the lung and cardiovascular system has been described. A novel peptide of pro-atrial natriuretic factor, NP_{73-102}, shows anti-inflammatory activity and causes a long-lasting bronchoprotective effect in a prophylactic model of allergic asthma (Kumar *et al*, JACI, 2002, Hellerman *et al* JACI, 2003). The immunomodulatory effects of this peptide and its potential in ameliorating established asthma were examined using a murine model of allergen ovalbumin, (OVA) respiratory syncytial virus (RSV) infection-induced asthma. Mice were sensitized and challenged with OVA and then infected with RSV prior to intranasal treatment with chitosan nanoparticles carrying a plasmid encoding NP_{73-102} (CHIpP) or directly incorporating NP_{73-102}. The extent of lung inflammation was determined by examining bronchoalveolar lavage fluid and lung sections. Airway hyperreactivity (enhanced pause, Penh) was measured by whole-body plethysmography, and cytokines were measured by intracellular cytokine staining (ICS). Therapy with CHIpP reversed OVA induced airway reactivity (% Penh, $P<0.01$), and reduced pulmonary pathology as revealed by lung histology, decreased the % of eosinophils

($P<0.05$), neutrophils and lymphocytes in the BAL of CHIpP-treated mice. Thus, *de novo* expression of NP_{73-102} reverses established asthma, suggesting that this peptide may be useful in developing novel therapies for asthma.
Collaboration: In collaboration with David Vesely, M.D., Ph.D., Professor of Internal Medicine, Division of Endocrinology, and Dr. William Gower, Ph.D., Department of Molecular Biology at USF.

IV. Evaluation of the Effects of Corticosteroid and/or Long-acting Beta Agonist Therapy on a Murine Model of Asthma with Respiratory Syncytial Virus (RSV) Infection and on Airway Cell Cultures

Infections, usually viral infections, are the most common triggers of severe asthma exacerbations. Studies in progress are investigating the effects of corticosteroid and/or long-acting beta agonist therapy on a murine model of asthma with RSV infection on airway cell culture. Allergen sensitized and challenged mice were pre-treated with placebo vs. fluticasone, salmeterol or the combination. Results of these experiments suggest that there appears to be anti-inflammatory effects of the salmeterol in this model. Studies are investigating the effects of these same therapies on the ability of cultured airway epithelial cells to be infected with RSV. Further study of anti-inflammatory properties of these drugs may lead to novel therapeutic approaches to prevent or treat RSV infection in humans.

CLINICAL RESEARCH PROJECTS

A. Pollen and Mold Counts and Immunochemical Quantification of Outdoor Allergens

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, located on the roof of the James A. Haley V.A. Hospital. Pollen counts are performed twice weekly, disseminated to local media once weekly and to the Internet twice weekly.

B. Skin Aging Study

This study compared skin tests performed on both sun-exposed and non-sun-exposed areas in 120 allergic individuals in two age groups, 20-50 years of age, and 60 years and older. Tests also included nasal challenge to dust mite (*D. pter.*) and measurement of total and specific IgE to 5 common allergens. Approximately 120 subjects have been skin tested. Findings to date indicate that: 1) older subjects have positive skin tests; 2) older men had more skin changes on their upper back than do younger and older women and younger men; 3) histamine responses were smallest in the upper back of older men; 4) specific IgE responses were positive in older and younger subjects (no statistical difference); 5) older individuals had smaller skin tests than younger individuals. All tests have been completed and the data is being analyzed.

C. Indoor Levels of Fungal Spores were Determined in Central Florida Homes Without Obvious Moisture Problems by a Non-culturable Sampling Method

Interest in measuring levels of airborne fungal spores has evolved because of increasing concern about indoor air quality. Mold spores were collected from twenty single-family homes in central Florida by utilizing a battery operated pump with cassettes containing a microscope slide. Total spores and spore types were analyzed by means of light microscopy. Descriptive statistics will be calculated for two outdoor and three indoor samples from different locations. The results of this study will allow for better interpretation of fungal laboratory results.

D. Efficacy of Using Oxymetazoline Hydrochloride Combined with Nasal Glucocorticosteroid to Treat Perennial Allergic and Non –Allergic Rhinitis in Subjects with Persistent Nasal Congestion.

The 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 non- allergic 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.

E. Efficacy of an Educational Program on Children at an Asthma Camp

This project evaluated the effectiveness of an educational program on children's asthma knowledge at an asthma camp. The hypothesis is that educated camp participants will be better educated about asthma and therefore correctly use their inhalers and peak flow meters at the end of camp vs. the beginning of camp. The outcome measures included: total test score of an asthma pre- and post-test (AT), peak flow usage score (PFS), inhaler usage score (IS), and spirometry. The results and conclusions: there was improvement in the participants' knowledge of asthma at the end of camp and an improvement in the proper use of inhaler and peak flow meter with greatest improvement in the proper use of the peak flow meter and females having greater improvement in proper inhaler use. Improvement in asthma testing and use of the peak flow meter as the same in both genders; returning campers scored higher on the AT, PFS, and IS pre- and post-test than did first time campers, but the difference was not as wide as expected.

F. Does Addition of a Topical Antibiotic to Treat Chronic Rhinosinusitis Improve Efficacy?

Chronic rhinosinusitis is a pervasive and costly disease. Estimates describe the costs of treating over 20 million Americans suffering from this diagnosis exceeds $4.3 billion per year. Primary therapy consists of oral antibiotics and nasal steroid sprays with some studies advocating nasal irrigation. Intravenous antibiotics and surgery were used for severe or recalcitrant cases. Several studies have investigated the use of topical antibiotics in rhinosinusitis, but no prospective blinded controlled study has been done. The purpose of this prospective, randomized, double-blinded, placebo-controlled clinical study is to establish whether the addition of a topical antibiotic to a conventional regimen of oral antibiotics and topical nasal steroids results in a significant improvement in radiographic findings and quality of life when compared to oral antibiotics, nasal steroids, and saline placebo irrigation.

PHARMACEUTICAL SPONSORED STUDIES

Studies funded by pharmaceutical companies are conducted at the Clinical Research Unit (CRU). The funds from these studies also support the Division's research and clinical training program. Sixteen such studies were completed in 2004 and 14 more in 2005; there are 9 additional studies, which will continue into 2006. To date, the CRU has agreements for 12 new studies in 2005-2006. The Clinical Research Unit also includes the American Lung Association Asthma Clinical Research Center, one of 20 such centers throughout the United States. The American Lung Association Clinical Research Center completed 2 studies in 2004 and has 2 additional studies currently in progress.

RESEARCH SUPPORT

Basic and Clinical Research

Endowments

Joy McCann Culverhouse Endowment

Mabel and Ellsworth Simmons Endowment

Extramural Funding

National Institute of Health, National Heart Lung and Blood Institute, (three current, one pending and one submitted)

Veteran Affairs Merit Review Award

Asthma and Allergy Foundation of Florida

American Lung Association of Florida
- Career Development Award
- Asthma Clinical Research Center Award

American Heart Association of Florida

Paterson Foundation

Genetics Institute Inc, Andover, MA

Merck Medical School Grants, Merck Inc, PA

GlaxoSmithKline Medical Research Grants

Pharmaceutical Sponsors

Abbott Laboratories

AstraZeneca

Altana/Byk Gulden

Aventis Pharmaceuticals

Bayer Pharmaceuticals

Baxter Healthcare

Bristol-Myers Squibb

Covance

Clintrials

Dura Pharmaceuticals

Dyax Pharmaceuticals

Forest Laboratories

Genentech

Glaxo Wellcome

Hoffman LaRoche Pharmaceuticals

King Pharmaceuticals

Merck and Co., Inc.

Novartis Pharmaceuticals

Ono Pharmaceuticals

Otsuka Pharmaceuticals

Pharmacia & Upjohn

Primary Immune

Schering-Plough

Sepracor

Whitehall Robbins

3M

GlaxoSmithKline Primary Immune / Pharming Inc.

Greer Laboratories

- A USF associated "spin-out" biotech company was formed under the direction of Shyam Mohapatra, PhD, 2004.

- Shyam Mohapatra, PhD, Gary Hellerman PhD, and staff formed an on-line journal, *Genetic Vaccines and Therapy* in 2004.

PUBLICATIONS

Books or Monographs published or in press: 2003 – 2005

Lockey; RF, Bukantz SC, Bousquet J (eds). Allergens and Allergen Immunotherapy for Allergic Diseases, 3rd edition. Marcel Dekker Inc., New York, NY, 2004 (800 pages).

Levine M, Lockey RF (eds.). Insect Allergy. American Academy of Allergy Asthma and Immunology, 2003 (280 pages).

Book Chapters published or in press: 2004 – 2005

Arias J, Ledford DK: Nonallergic Rhinitis. *In:* Conn's Current Therapy, 56th edition. W. B. Saunders, PA, Rakel RE, Bope ET (eds) 2004.

Bukantz SC, Lockey RF: Adverse Effects and Fatalities Associated with Subcutaneous Allergen Immunotherapy. *In:* Allergens and Allergen Immunotherapy, 3rd. Lockey RF, Bukantz SC, Bousquet J (eds). Marcel Dekker, Inc., New York, NY, Chap 39, p-711, March 2004.

Codina R, Ramey J, Lockey RF: Allergen Immunotherapy, *In*: Atlas of Allergic Diseases, 2nd ed, chapter 17,pp163-9, Lieberman P.L., Blaiss M.S. eds Current Medicine Inc., Philadelphia 2005.

Cox L, Lockey RF: Instructions and Consent Forms for Allergen Immunotherapy. *In*: Allergens and Allergen Immunotherapy 3rd ed. Lockey RF, Bukantz SC, Bousquet J (eds). Marcel Dekker, Inc., New York, NY. Chap 41, p-755, March 2004.

Fernandez-Caldas E, Puerta L, Caraballo L, Lockey RF: Mite Allergens, *In*: Allergens and Allergen Immunotherapy, 3rd ed. Lockey RF, Bukantz SC, Bousquet J (eds). Marcel Dekker, Inc., New York, NY. Chap 14, p-251, March 2004.

Fox RW, Lockey RF: Allergen Immunotherapy. *In*: Allergic Diseases- Diagnosis and Treatment, second edition, Lieberman P and Anderson JA (eds), Humana Press, Totowa, NJ 2000 pp 421-436. 3rd edition to be published in 2005.

Fox RW: Allergic Diseases of the Skin-Urticaria. *In*: Atlas of Allergic Diseases, Lieberman P and Blais M (eds), Current Medicine, Inc., Philadelphia, PA, 2002. 2nd edition. pp 73-83. 2005.

Larche, M. Mohapatra, S.S. And Ferreira, F: Novel Approaches for Immunotherapy for Inhalant Allergens. *In*: Allergens and Allergen Immunotherapy for Allergic Diseases, 3rd edition. Marcel Dekker, Inc., New York, NY, in press.

Ledford DK: Anaphylaxis and Serum Sickness. *In:* Conn's Current Therapy, 56th edition. Rakel RE, Bope ET, (eds), W. B. Saunders, PA., 2004.

Ledford DK: Allergic Rhinitis. *In:* Allergy and Asthma 3rd edition Lieberman P, Anderson J (eds) in press.

Mohapatra SS, Lockey RF, Polo F: Weed Pollen Allergens, *In*: Allergens and Allergen Immunotherapy, 3rd ed. Lockey RF, Bukantz SC, Bousquet J (eds). Marcel Dekker, Inc., New York, NY. Chap 12, p-207, March 2004.

Mohapatra SS, Modifying Allergens and Using Adjuvants for Specific Immunology. *In:* Allergen Immunotherapy Larche M. Mohapatra SS, Ferreira F, Novel Approaches for Immunotherapy for Inhalant Allergens. *In:* Allergen Immunotherapy. Lockey RF, Bukantz SC, Bousquet J (eds). Marcel Dekker, Inc., New York, NY., pp 641-661, 2004.

Müller U, Golden DBK, DeMarco PJ, Lockey RF: Immunotherapy for Hymenoptera Venom and Biting Insect Hypersensitivity. *In:* Allergens and Allergen Immunotherapy, 3rd ed. Lockey RF, Bukantz SC, Bousquet J (eds). Marcel Dekker, Inc., New York, NY, Chap 29, p-541, March 2004.

Nelson RP, Lockey RF: *In:* Atlas of Allergic Diseases, 2nd ed, pp220-226, Lieberman P.L., Blaiss M.S. eds Current Medicine Inc., Philadelphia 2005.

Internet Publications

Kaliner MA, Lockey RF. 22 September 2004. Acute Asthma (online). World Allergy Organization Allergic Diseases Resource Center. Available from: Http://www.worldallergy.org/professional/allergic_diseases_center/asthma/index.shtml

Ledford DK. Anaphylaxis and Immune Complex Disease, UpToDate, 2004.

Lockey RF, Kaplan A, co-eds: "Global Allergy Information Network", official web-site of the World Allergy Organization (WAO), www.worldallergy.org, 2000-2004.

Lockey RF, Editor: Manuscripts by Medical Professionals in the Field of Allergy/Immunology for www.eMedicine.com, 2000-present.

Lockey RF, Editor-in-Chief: World Allergy Organization (WAO Web-site), www.worldallergy.org, 2004-present.

Lockey RF. 19 July 2004. Anaphylaxis (online). World Allergy Organization Allergic Diseases Resource Center. Available from: http://www.worldallergy.org/professional/allergic_diseases_center/anaphylaxis/anaphylaxissynopsis.shtml

Zhang W, Yang H, Kong X, Mohapatra S, San Juan H, Hellermann G, Behera S, Singam R, Lockey RF, Mohapatra SS: 26 December 2004. Inhibition of respiratory syncytial virus infection with intranasal siRNA nanoparticles targeting the viral NS1 gene. (on-Line). *Nature Medicine* www.nature.com/naturemedicine

Manuscripts published or in press: 2004 – 2005

Bousquet J (ed) Lockey RF (one of 18 contributors): Area in the Pharmacy: Management of Allergic Rhinitis Symptoms in the Pharmacy. Allergic Rhinitis and its Impact on Asthma, 59, 373-387, 2004.

Dolan CM, Fraher KE, Bleecker ER et al, (Lockey RF, contributor): Design and Baseline Characteristics of the Epidemiology and Natural History of Asthma: Outcomes and Treatment

Regimens (TENOR) Study: A large cohort of patients with severe or difficult-to-treat asthma. *Annals of Allergy, Asthma & Immunology,* 92(1), 2004.

Fernandez-Caldas E, Lockey RF: *Blomia tropicalis,* A Mite Whose Time Has Come. *Allergy* Nov; 59(11):753-7, 2004.

Fish JE, Szefler SJ, Frieri M, Lang D, Lazarus SC, Ledford D. et al. Quick reference guide for clinicians: systematic review of the evidence regarding potential complications of inhaled steroid use in asthma. *Annals Allergy Asthma Immunology*; 92: 294-304, 2004.

Fox RW. The Fungal Phenomenon. *Current Allergy and Asthma Reports* 2004; 4:415-416 Practice Parameters, Anaphylaxis: Assessment and Management, *Journal of Allergy and Clinical Immunol,* 115(3)Supplement 2: S483-523 Feb 2005.

Hellermann, G, Kong X, Gunnarsdottir J, San Juan H, Singam R, Behera S, Zhang W, Lockey RF, Mohapatra SS: Mechanism of Bronchoprotective Effects of a Novel Natriuretic Horomone Peptide. *Journal of Allergy and Clin Immunol*, 113: 79-85, 2004.

Hellermann, G. Kong, X., Gunnarsdottir, J., San Juan, H., Singam, R., Behera, S., Zhang, W., Lockey, RF., Mohapatra, SS. Mechanism of Bronchoprotective Effects of a Novel Natriuretic Hormone Peptide. *Journal of Allergy and Clinical Immunology*. 113(2): S221, 79-85, 2004.

Johansson SGO, Bieber T, Dahl R, Friedmann PS, Lanier B, Lockey RF, et al: A Revised Nomenclature for Allergy for Global Use (2003). World Allergy Organization (WAO) Position Statement. *Journal of Allergy and Clinical Immunol*, 113(5): 832-6, 2004.

Kearney DM, Lockey RF (ed), Introduction: From Allergen to Asthma: Points for Intervention, Symptomatic Relief, and Effective Therapy, *Allergy & Immunology Report*, (Selected reports from the 2004 Annual Scientific Meeting of the American College of Allergy, Asthma & Immunology; 1(2): 12-19, 2005.

King MJ, Bukantz SC, Phillips S, Mohapatra SS, Tamulis T, Lockey RF: Serum total IgE and specific IgE to *Dermatophagoides pteronyssinus*, but not eosinophil cationic protein, are more likely to be elevated in elderly asthmatic patients. *Allergy Asthma Proc.* 25(5):321-5, Oct. 2004.

Kong X, Hellermann GR, Patton G, Kumar M, Behera A, Randall TS, Zhang J, Lockey RF, Mohapatra SS: An immunocompormised BALB/c mouse model for respiratory syncytial virus infection. *Journal of Virology*, 2: 3, 2005.

Kong X, San Juan H, Behera A, Lockey RF, Mohapatra SS: ERK ½ is Required for RSV Injection, *FEBS Lett* 559:33-38, 2004.

Kumar RMNV, Sameti M, Mohapatra SS, Kong X, Lockey RF, Bakowsky U, Lindenblatt G, Schmidt H, Lehr CM: Cationic Silica Nanoparticles as Gene Carriers: Synthesis, Characterization and Transfection Efficiency *in vitro* and *in vivo*. *J Nanosci. Nanotech*, 4: 876-881, 2004.

Kumar RMNV, Hellermann G, Lockey RF, Mohapatra SS: Nanoparticle-mediated Gene Therapy: State of the Art. Expert Opinion *Biol Ther*. 4(8):1213-24, Aug. 2004.

Ledford DK: Oral Immunotherapy: Too Good to be True? (editorial). *Annals Allergy Asthma Immunol*. 92: 1-2, 2004.

Lieberman P, Fineman S, Bielory L, Ledford DK, Skoner D, Storms W: AAAAI/ACAAI Conjoint Position Statement on Over the Counter Status of Nasal Fluticasone. *Journal of Allergy and Clin Immunol*, (in press).

Lockey RF: News from EAACI, Baena-Cagnani Named New WAO President, *Academy News*, 10(1): 26, January, 2004.

Lockey RF: News from EAACI, Amsterdam Hosts EAACI Congress, *Academy News*, 10(3), April, 2004.

Lockey RF, et al: News from Societies, AAAAI Helps Allergists/Immunologists Certify and Recertify, *EAACI Newsletter*, 7(1): 15, 2004.

Lockey RF: News from Societies, New AAAAI President – Michael Schatz, *EAACI Newsletter*, 7(2), 2004.

Lockey RF: News from EAACI, GA²LEN: Global Allergy and Asthma European Network, *Academy News*, 10(5), June, 2004.

Lockey RF: Allergen Immunotherapy, Its Origin and Future. *Allergy & Clinical Immunology International,* Journal of the World Allergy Organization; 16:107-111, 2004.

Lockey RF, (Commentary), on "Outcomes of Allergy to Insect Stings in Children, with and Without Venom Immunotherapy", *N Engl J Med.* 351(7): 668-74, 2004, Aug 12. Commentary, The *Journal of Pediatrics*; 146: 145-146, 2005.

Lockey RF, et al: Mechanism of Bronchoprotective Effects of a Novel Natriuretic Hormone Peptide, *Journal of Allergy and Clinical Immunology.* 113(1):79-85 Jan 2004.

Mohapatra SS, Lockey RF, Vesely DL, Gower W: Natriuretic Peptides and Genesis of Asthma: An Emerging Paradigm? *Journal of Allergy and Clin Immunol*;114(3):520-526, 2004.

San-Juan-Vergara H, Peeples ME, Lockey RF, Mohapatra SS.Protein kinase C-alpha activity is required for respiratory syncytial virus fusion to human bronchial epithelial cells. *J Virology.*78(24):13717-26, 2004 Dec.

Vu, AT, Lockey RF: Exercise-induced anaphylaxis, Allergy, *Clinical Immunology Intl. –J World Allergy Org.* (in press 2005)

Zhang W, Singam R, Hellermann G, Kong X, san Juan H, Lockey RF, Wu SJ, Mohapatra SS: Attenuation of Dengue Virus Infection by Adeno-associated Virus-mediated siRNA Delivery. *Gene Vaccines Ther.* 9;2(1):8, 2004 Aug.

Zhang W, Yang H, Kong X, Mohapatra S, San Juan-Vergara H, Hellermann G, Behera S, Singam R, Lockey RF, Mohapatra SS: Inhibition of respiratory syncytial virus infection with intranasal siRNA nanopartiacles targeting the viral NS1 gene. *Nature Medicine*; 11:56-62, 2005.

Abstracts presented in 2004 – 2005

Bagg AS, Ledford DK, Lockey RF: Progesterone associated angioedema and vasculitis. American Academy of Allergy, Asthma and Immunology Annual Meeting, San Antonio, TX, March 2005. *J Allergy Clin Immuno.* 115(2): S105,(#420) Feb 2005.

DeMarco PJ, Codina R, Bagg AS, Fox RW, Lockey RF: Indoor levels of fungal spores in central Florida homes without obvious moisture problems. American Academy of Allergy, Asthma & Immunology Annual Meeting, San Antonio, TX, March 2005. *Journal Allergy Clin Immun.* 115;(2):520,(#81) Feb.2005.

Glaum, M.C., LaRosa, D.F., Apter, A.J., Levinson, A.I.: Longstanding Common Variable Immunodeficiency (CVID) Sans Recurrent Sinopulmonary Infection. *J Allergy Clin Immunol* 113(2):81, 2004.Conference of the American Academy of Allergy Asthma & Immunology: San Francisco, California, 3/2004.

Glaum, M.C., Levinson, A.I.: Signaling of Human Naïve and Memory B cells via Toll-like Receptor 7 Modulates Their Immunoglobulin Production. *Clin Invest Med*, 27 (4): 3066, 2004.Meeting of the 12th International Congress of Immunology and 4th Annual Conference of the Federation of Clinical Immunology Societies (FOCIS). Montreal, Canada, 7/2004.

Hellermann GR, Lockey RF, Mohapatra SS: Oral Administration of a Chitosan/Ovalbumin Peptide Complex Reduces the OVA-Specific Allergic Response in BALB/c Mice. ATS 2005 International Conference May 20-25, San Diego, CA, *Proceedings of the American Thoracic Society*, Official publication of the American Thoracic Society (ATS), 2: p. A83, 2005.

Hellermann G, Gunnarsdottir J, Kong X, San Juan H, Singam R, Behera S, Zhang W, Lockey RF, Mohapatra SS: Mechanism of bronchoprotective effects of a novel natriuretic horomone peptide.60th American Academy of Allergy Asthma & Immunology Meeting, San Francisco. CA, March 19-23, 2004. *J Allergy Clin Immun.*2004, 113(2):S221.(#781) 2004.

Kong X, Zhang W, Lockey R, Auais A, Piedimonte G, Mohapatra S: Intranasal Delivery of Chitosan RNAi Nanoparticles for RSV-NS1 Gene Attenuates Pulmonary Infection and Inflammation in Fischer 344 Rats and BALB/c Neonates. ATS 2005 International Conference May 20-25, San Diego, CA, *Proceedings of the American Thoracic Society*, Official publication of the American Thoracic Society (ATS), 2: p. A453, 2005.

Kong X, San Juan H, Behera A, Lockey RF, Mohapatra SS:
Cross-talk between ERK-1/2 and STAT-1 alpha pathways in respiratory syncytial virus-induced early gene expression in human epithelial cells.
60th American Academy of Allergy Asthma & Immunology Meeting, San Francisco, CA, March 19-23, 2004. *J Allergy Clin Immunol* 2004; 113(2) 5265. (#955)

Kong X, Zhang W, Lockey R, Auais A, Piedemonte G, Mohapatra SS: Short interference RNA for RSV-NS1 Gene attenuates virus infection in Fischer 344 Rats. For American

Academy of Allergy, Asthma and Immunology Annual Meeting, San Antonio, TX, March 2005, *J Allergy Clin Immun* 115(2) S141,(#563) Feb. 2005

Lynn, J., Glaum, M.C., Levinson, A.I.: Signaling of Human B cells via Toll-like Receptors 7 and 8 Modulates Immunoglobulin Production. *J Allergy Clin Immunol* 113(2):114, 2004.Conference of the American Academy of Allergy Asthma & Immunology: San Francisco, California, 3/2004.

Mohapatra SS, Singam R, Kong X, Behera S, Hellermann G, Mohapatra S, San Juan H, Jena P, Yang H, Zhang W, Lockey RF: Chitosan lipid nanoparticles (CLNs) augment gene delivery and expression in mice. Controlled Release Society 31st Annual Meeting Transactions. (#234), 2004.

Mohapatra S, Lockey RF, Kong X, Singham R, Behera S, Jena P, Hellermann G, Zhang W: Modulation of asthma by natriuretic peptide nanoparticles: Role of treg cells. XIXth World Allergy Organization Congress, XXIVth Congress of the European Academy of Allergology and Clinical Immunology, Munich, Germany, June 26-July 1, 2005.*Journal of the World Allergy Organization*, (suppl 1) p561, 2005.

Ramey J. Lockey RF: Preseptal cellulitis secondary to a dental abscess, in press.

Ramey J., Lockey RF: Possible allergic reaction to sublingual transdermal nitroglycerin. The American Academy of Allergy, Asthma and Immunology Annual Meeting, San Antonio, TX, March 2005.*Allergy Clin Immunol Int-J World Allergy Org.* (upcoming issue)

San Juan Vergara HG, Lockey RF, Mohapatra SS: Inhibition of PKC-alpha activity blocks respiratory syncytial virus infection. 60th American Academy of Allergy Asthma & Immunology Meeting, San Francisco, CA, March 19-23, 2004. *J Allergy Clin Immun.* 115(2):S141, Feb 2005. (#681)

San Juan Vergara H, Cuevas J, Lockey RF, Mohapatra SS: Role of calcium in PKC-α activation and RSV infection of normal human bronchial epithelial (NHBE) cells. 61st American Academy of Allergy, Asthma and Immunology Annual Meeting, San Antonio, TX, March 18-22, 2005.*J Allergy Clin Immunol* 2005:115(2): S141.(#564).

Singam RV, Kong X, Hellermann G, San Juan H, Behera S, Zhang W, Jena PK, Lockey RF, Mohapatra SS:Inhibition of respiratory syncytial virus replication by vector-derived small interfering RNAs against NS1 protein. 60th American Academy of Allergy Asthma & Immunology Meeting, San Francisco, CA, March 19-23, 2004. *J Allergy Clin Immunol.* 2004: 113(2) 5330 (#1225).

Singam RV, Kong X, Hellermann G, San Juan H, Behera S, Zhang W, Jena PK, Lockey RF, Mohapatra SS: Chitosan Nanoparticle-mediated de novo synthesis of a novel natriuretic hormone peptide reverses established asthma in mice. 60th American Academy of Allergy Asthma & Immunology Meeting, San Francisco, CA, March 19-23, 2004. *J Allergy Clinical Immunol.* 2004:113(2): S325.(#1201).

Singam R, Ledford D, Lockey RF, Mohapatra SS: The use of fluticasone propionate (FP with salmeterol (S) is a more effective treatment than FP alone for respiratory syncytial virus (RSV) infection-induced airway inflammation in the presence or absence of allergen sensitization. ATS 2004 International Conference, May 21-26, Orlando, Fl.. *Amer Journal of Resp & Critical Care Med*, official Journal of American Thoracic Society (ATS), 169(7) p. A126, April, 2004.

Singam R, Jena PK, Behera S, Ledford D, Lockey RF, Mohapatra SS: Combined Therapy of Fluticasone Propionate (FP) with Salmeterol (S) in a Murine Model of Allergen and Respiratory Syncytial Virus-Induced Asthma. ATS 2005 International Conference May 20-25, San Diego, CA, *Proceedings of the American Thoracic Society*, Official publication of the *American Thoracic Society* (ATS), 2: p. A603, 2005.

Zhang W, Yang H, Behera S, Kong X, Lockey RF, Mohapatra SS: Prophylaxis of respiratory syncytial virus infection with intranasal siRNA-Nanoparticles of the NS1 gene *in vivo*. For American Academy of Allergy, Asthma & Immunology Annual Meeting, San Antonio, TX, March 2005. *J Allergy & Clin Immun.*115(2):S135(#540).

2004-2005 VISITING PROFESSOR GUESTS LECTURERS

Thomas J. Grier, Ph.D., Senior Research Scientist Director, Allergen Development, Greer Laboratories, Inc., Lenoir, North Carolina, "Allergenic cross-reactivity: Concepts, patterns and clinical implications", April 27, 2004

Robert P. Nelson, Jr., M.D., Associate Professor of Medicine Indiana University School of Medicine, Division of Hematology/Oncology, Bone Marrow Transplant Service, Indiana University Hospital/Riley Children's Hospital, "Living with two immune systems as a result of hematopoietic and solid organ transplantation", June 15, 2004.

Giovanni Piedimonte, M.D., Professor of Pediatrics and Medicine, University of Miami Director, Division of Pulmonology, Pediatric Lung Transplant Program, Cystic Fibrosis, and Asthma Center, "Pathophysiology of allergic rhinitis: From inflammatory mediators to symptoms", August 18, 2004.

Søren Pedersen, M.D., Ph.D., D.M.Sc, Professor of Pediatric Respiratory Medicine at the University of Southern Demark and Adjunct Professor at McMaster University, Ontario, Canada. Consulting Pediatric Chest Physician and Allergist at the Department of Pediatrics at Kolding Hospital in Denmark, "Use of inhaled corticosteroids in asthma-children and adults", October 11, 2004.

David P. Huston, M.D., Cullen Chair of Immunology, Department of Medicine and Immunology; Director, Biology of Inflammation Center; Chief, Immunology, Allergy & Rheumatology Methodist Hospital, Houston, Texas, "Autoimmunity & Urticaria", "T-32 Application", January 18-19, 2005.

Michael E. Wechsler, M.D., Associate Physician, Pulmonary and Critical Care Medicine Asthma Research center Brigham and women's Hospital Boston, Massachusetts, "Pharmacogenetics and Asthma Therapy: Are We There Yet?", Pharmacogenetics (update in asthma research), February 22-23, 2005.

Jan Nuijens, M.D., Senior Director of Clinical Development Pharming Technologies BV, Netherlands, "Recombinant Human C1 Inhibitor and Hereditary Angioedema", Discuss study protocol, May 3-4, 2005.

John Latall, M.D., University of Chicago, Allergic Bronchopulmonary Aspergillosis , May 18, 2005.

Pravin Muniyappa, M.D., University if Chicago, Rhinosinusitis, May 19, 2005.

Gerald J. Gleich, MD, Professor of Dermatology, University of Utah School of Medicine, "Serendipity Happens: Discovery of a Novel Glucocorticomimetic Agent", "Eosinophil Associated Syndromes: New Insights and New Treatments", "Eosinophil Associated Syndromes: New Insights and New Treatments", "Eosinophil Granule Major Basic Protein Homolog (MBP2): Specific Eosinophil Marker" September 21-22, 2005.

James E. Fish, MD, Senior Medical Director, Genentech Specialty Biotherapeutics Adjunct Professor of Medicine, Jefferson Medical College, Thomas Jefferson University Phil, PA, "IgE, Its Receptor and Role in Asthma", "Airway Remodeling: Fact or Fiction" October 11-12, 2005.

Dr. John Lima, PhD, Nemours Children's Clinic, Jacksonville, FL 12/13, "Pharmacogenetics of Asthma" December 13-14, 2005.