

A fluorescence micrograph of lung tissue. The image shows a complex network of branching structures, likely alveoli and bronchioles, stained with two different dyes. The primary color is a bright green, which outlines the structures and fills some of the internal spaces. A secondary color, red, is also present, appearing as smaller, more granular spots within the green-stained areas. The background is black, making the green and red structures stand out prominently.

Pulmonary and Critical Care Medicine

Edward D. Crandall, Ph.D., M.D.
Professor and Chief

Zea Borok, M.D.
Professor and Co-Chief

Halina Biel-Milunovic
Administrator

Pulmonary and Critical Care Medicine

The Division of Pulmonary and Critical Care Medicine (PCCM) provides a vigorous and creative basic and clinical science core, an active clinical service and a high-quality teaching program. The Division provides service to all three Health Sciences Campus teaching hospitals—LAC+USC Medical Center, USC University Hospital and USC/Norris Cancer Hospital—through more than 20 full-time faculty members with national and international reputations sharing the combined research, clinical and teaching missions.

The Division administers Intensive Care Units at LAC+USC Medical Center and USC University Hospital. Consultative services to inpatients are provided at all three Health Sciences Campus hospitals. A weekly Chest Clinic at LAC+USC Medical Center renders care to over 5,100 patients annually. Over 4,100 private outpatient visits are conducted at the Ambulatory Healthcare Center. This year, more than 1,200 bronchoscopic examinations and other diagnostic procedures were performed by the Division. The Pulmonary Physiology Laboratories of all USC Health Sciences Campus hospitals processed about 12,000 arterial blood gases, 10,000 complete lung function tests and 2,000 sleep studies. The Division prides itself on the quality, depth and breadth of its clinical services. Patient and colleague satisfaction, along with state-of-the-art pulmonary and critical care medicine services, remain our primary clinical objectives.

Basic and applied research are the cornerstones of the Division, long known for cutting edge studies in mechanisms and regulation of function and biology of the pulmonary alveolar epithelium. Applied research areas include genetic markers and gene regulation in lung injury, immunology in lung transplantation and AIDS, therapeutic interventions in interstitial pulmonary fibrosis and sarcoidosis, and mechanisms of disease in the chronically ill. Division faculty and fellows published 12 peer-reviewed research papers and received nearly \$1 million in research funds in 2007-2008.

The Division remains strongly committed to providing the best possible educational environment and learning opportunities for USC medical students, housestaff, fellowship trainees and practicing physicians. Daily formal attending rounds are conducted on all our services and in all our hospitals for medical students, residents and fellows. These rounds take place at the bedside and culminate in a multidisciplinary discussion involving pulmonary physiology, radiology and pathology. An extensive daily conference schedule emphasizes case discussions and grand rounds conducted in cooperation with other specialties, including infectious diseases, pathology, radiology, immunology and genetics. In-depth lectures in clinical science and basic research are held regularly. Our well-rounded teaching program provides outstanding educational experiences for fellows, residents and medical students throughout the Health Sciences Campus.

Overall, the Division of Pulmonary and Critical Care Medicine continues to build on a tradition of excellence in its tripartite mission. We strive to be the best in teaching, research and clinical care delivery. We look forward to continued growth in partnership with our colleagues in the Department of Medicine and the entire Health Sciences Campus community.

Faculty

Richard G. Barbers, M.D.

Professor of Clinical Medicine
Medical Director, Asthma and Allergy Center
Medical Director, Cough Disorders Center
Medical Director, Lung Transplantation Program

Ahmet Baydur, M.D.

Professor of Clinical Medicine
Director, Year II Medical Student Teaching Program
Medical Director, Pulmonary Rehabilitation Program
Medical Director, Respiratory Therapy Services

Zea Borok, M.D.

Professor of Medicine
Co-Chief, Pulmonary and Critical Care Medicine
Co-Director, Will Rogers Institute Pulmonary Research Center
Director, Fellowship Training Program

C. Thomas Boylen, M.D.

Associate Professor of Clinical Medicine
Medical Director, Chest Clinic, LAC+USC Medical Center
Medical Director, Pulmonary Consult Service, LAC+USC Medical Center

Edward D. Crandall, Ph.D., M.D.

Hastings Professor of Medicine
Norris Chair of Medicine
Chief, Pulmonary and Critical Care Medicine
Director, Will Rogers Institute Pulmonary Research Center

Patricio Escalante, M.D.

Assistant Professor of Clinical Medicine
Associate Medical Director, Sleep Center

**In Memory of:
Henry Gong, Jr., M.D.
1947-2007**

Professor of Medicine and Preventive Medicine
Chair, Department of Medicine, Rancho Los Amigos National Rehabilitation Center (RLANRC)
Chief, Environmental Health Service, RLANRC
Medical Director, Respiratory Care Services, RLANRC

Ricardo H. Juarez, M.D.

Assistant Professor of Clinical Medicine
Medical Director, ICU Services, University Hospital
Medical Director, Pulmonary Exercise Center
Medical Director, High-Altitude Evaluation Test Center
Medical Director, Sleep Center

Kwang-Jin Kim, Ph.D.

Professor of Medicine
Director, Research Seminar Series

Janice M. Liebler, M.D.

Professor of Clinical Medicine
Executive Chair, PCCM Alumni Conference

Richard L. Lubman, M.D.

Associate Professor of Medicine

Albert H. Niden, M.D.

Professor of Clinical Medicine
Associate Chair for County Affairs

Renli Qiao, M.D., Ph.D.

Associate Professor of Clinical Medicine

Adupa P. Rao, M.D.

Assistant Professor of Clinical Medicine
Associate Director, Fellowship Training Program
Medical Director, Adult Cystic Fibrosis Program

Bertrand J. Shapiro, M.D.

Professor of Clinical Medicine

Om P. Sharma, M.D.

Professor of Medicine
Medical Director, Emphysema Management and Surgery Program
Medical Director, Saracoidosis and Interstitial Lung Disease Center

Hidenobu Shigemitsu, M.D.

Assistant Professor of Clinical Medicine
Medical Director, MICU/CMA, LAC+USC Medical Center
Medical Director, Saracoidosis and Interstitial Lung Disease Center

Graciela J. Soto, M.D.

Assistant Professor of Clinical Medicine

Robert S. Swinney, M.D.

Assistant Professor of Clinical Medicine
Director, MICU Data Management System, LAC+USC Medical Center

NEW FACULTY

Ching-Fei Chang, M.D.

Assistant Professor of Clinical Medicine
Medical Director, Bronchoscopy Services, LAC+USC Medical Center

Sivagini Ganesh, M.D.

Assistant Professor of Clinical Medicine

Pulmonary and Critical Care Medicine

Faculty Honors

MEMBERSHIP IN DISTINGUISHED SOCIETIES

Zea Borok, M.D.

Western Society for Clinical Investigation

Edward D. Crandall, Ph.D., M.D.

American Society for Clinical Investigation

Western Association of Physicians

Western Society for Clinical Investigation

Henry Gong, Jr., M.D.

Western Society for Clinical Investigation

Ricardo H. Juarez, M.D.

Alpha Omega Alpha

Janice M. Liebler, M.D.

Western Society for Clinical Investigation

Richard L. Lubman, M.D.

Western Society for Clinical Investigation

Om P. Sharma, M.D.

Royal College of Physicians, London, UK

Graciela J. Soto, M.D.

Golden Key National Honor Society

MEMBERSHIP IN PROFESSIONAL SOCIETIES

Richard G. Barbers, M.D.

American Academy of Allergy and Immunology

American College of Chest Physicians

American Thoracic Society

Asthma and Allergy Foundation of America, Los Angeles Chapter

Los Angeles Academy of Medicine

Los Angeles County Medical Society

Los Angeles Society of Allergy, Asthma and Clinical Immunology

Trudeau Society of Los Angeles

Ahmet Baydur, M.D.

American College of Chest Physicians

American College of Physicians

American Thoracic Society

California Thoracic Society

Society of Critical Care Medicine

Zea Borok, M.D.

American College of Chest Physicians, Fellow

American College of Physicians, Fellow

American Federation for Medical Research

American Society for Cell Biology

American Thoracic Society

Society of Critical Care Medicine

C. Thomas Boylen, M.D.

American Thoracic Society

New York Academy of Sciences

Trudeau Society

Ching-Fei Chang, M.D.

American College of Chest Physicians

Edward D. Crandall, Ph.D., M.D.

American Association for the Advancement of Science

American Chemical Society

American College of Chest Physicians

American College of Physicians

American Federation for Medical Research

American Heart Association

American Institute of Chemical Engineers

American Medical Association

American Physiological Society

American Society for Cell Biology

American Thoracic Society

Association of Professors of Medicine

Biophysical Society

California Thoracic Society

Red Cell Club

Sigma Xi

Society of General Physiologists

Tau Beta Pi

Trudeau Society

Patricio Escalante, M.D.

American Academy of Sleep Medicine

American College of Chest Physicians

American Thoracic Society

California Thoracic Society

Society of Critical Care Medicine

Sivagini Ganesh, M.D.

American College of Chest Physicians

American Society of Transplantation

American Thoracic Society

Henry Gong, Jr., M.D.

American College of Chest Physicians

American College of Clinical Pharmacology

American Federation for Medical Research

American Thoracic Society

California Thoracic Society

Ricardo H. Juarez, M.D.

American Academy of Sleep Medicine

American College of Chest Physicians

American College of Physicians

Kwang-Jin Kim, Ph.D.

American Association for the Advancement of Sciences

American Physiological Society

West Coast Salt and Water Club

Janice M. Liebler, M.D.

American College of Chest Physicians, Fellow
American Thoracic Society
California Thoracic Society
Society for Critical Care Medicine

Richard L. Lubman, M.D.

American College of Chest Physicians, Fellow
American College of Physicians-American Society of Internal
Medicine, Fellow
American Heart Association
American Physiological Society
American Society for Matrix Biology
American Thoracic Society

Albert H. Niden, M.D.

American College of Chest Physicians
American Lung Association of California
American Lung Association of Los Angeles County
American Physiological Society
American Thoracic Society
Trudeau Society
Western Society for Medical Research

Renli Qiao, M.D., Ph.D.

American College of Chest Physicians
American College of Physicians
American Lung Association
American Medical Association
American Thoracic Society

Adupa P. Rao, M.D.

American College of Chest Physicians
American Medical Association
Society of Critical Care Medicine

Bertrand J. Shapiro, M.D.

American Association for the Advancement of Science
American College of Chest Physicians
American College of Physicians
American Federation for Medical Research
American Thoracic Society
California Medical Review
California Thoracic Society
Los Angeles County Heart Association
Lung Association of Los Angeles County
Trudeau Society

Om P. Sharma, M.D.

American Academy of Allergy and Immunology
American College of Chest Physicians
American College of Physicians
American Federation of Medical Research
American Osler Society
American Thoracic Society
New York Academy of Medicine
Trudeau Society

Hidenobu Shigemitsu, M.D.

American College of Chest Physicians, Fellow
American Thoracic Society
California Thoracic Society

Graciela J. Soto, M.D.

American College of Chest Physicians
American College of Physicians
American Medical Association
American Medical Student Association
American Psychological Association
American Thoracic Society
Society of Critical Care Medicine

Robert S. Swinney, M.D.

American College of Physicians, Associate
American Medical Informatics Association
American Society of Internal Medicine
Association for Computing Machinery
Association for the Advancement of Medical Instrumentation
California Society of Internal Medicine
Society of Critical Care Medicine
Society of Graduate Internists

EDITORSHIPS/EDITORIAL BOARDS

Richard G. Barbers, M.D.

Current Opinion in Pulmonary Medicine, Asthma Section Editor
International Journal of Biomedical Sciences, Editor

Zea Borok, M.D.

American Journal of Physiology: Lung Cellular and Molecular
Physiology

Edward D. Crandall, Ph.D., M.D.

Clinical and Translational Science
Experimental Lung Research

Henry Gong, Jr., M.D.

Archives of Environmental Health
Inhalation Toxicology

Om P. Sharma, M.D.

Current Opinion in Pulmonary Medicine, Editor
Sarcoidosis, Vasculitis, and Diffuse Lung Diseases

MAJOR LECTURES

Richard G. Barbers, M.D.

Asthma intervention. Annual Meeting, Beijing Respiratory Society,
Beijing, China, 4/18/2008.

Living lobar lung transplantation. Annual Meeting, Shanghai
Respiratory Society, Shanghai, China, 4/26/2008.

Zea Borok, M.D.

Alveolar epithelial cell plasticity in lung injury, repair and fibrosis.
Lung Science Conference, European Respiratory Society, Estoril,
Portugal, 3/2008.

Pulmonary and Critical Care Medicine

Edward D. Crandall, Ph.D., M.D.

Peking Union Medical College, Beijing, China, 4/19/2008.

Kwang-Jin Kim, Ph.D.

Nanomaterials and lung alveolar epithelium: interactions and trafficking. Research Seminar, Trinity College, Dublin, Ireland, 7/27/2007.

Protein absorption across the alveolar epithelial barrier. Research Seminar, University College Cork, Cork, Ireland, 7/30/2007.

Nanomaterials and lung alveolar epithelium: interactions and trafficking. Research Seminar, University of London, London, UK, 8/3/2007.

Transport of water to ions to peptides/proteins to nanoparticles across lung alveolar epithelial barrier. Research Seminar, Keio University, Tokyo, Japan, 11/12/2007.

Interaction and trafficking of nanoparticles in lung alveolar epithelium. Research Seminar, Meijo University, Nagoya, Japan, 11/14/2007.

Expression and function of amino acid transporter B0,+ in lung alveolar epithelium. Research Seminar, Seoul National University, Seoul, Korea, 11/19/2007.

Nanoparticle interaction and trafficking in the lung alveolar epithelium. Research Seminar, Jeon-Book National University, Jeonju, Korea, 11/22/2007.

Lung alveolar epithelial transport of cationic and neutral amino acids. Research Seminar, Won-Kwang University, Iri, Korea, 11/22/2007.

Lung and nanomaterials: interaction with and trafficking across the lung alveolar epithelium. Research Seminar, Pohang Institute of Science and Technology, Pohang, Korea, 11/23/2007.

Nanoparticles and the lung: interactions with and trafficking across alveolar epithelium. Research Seminar, Centre for NanoBio Integration, University of Tokyo, Tokyo, Japan, 6/12/2008.

Pulmonary delivery: protein/peptides to nanoparticles. Research Seminar, Keio University, Tokyo, Japan, 6/13/2008.

Richard L. Lubman, M.D.

Clinical targets for stem cell therapy. Stem/Progenitor Cells and Lung Repair, Transatlantic Airway Conference, Lucerne, Switzerland, 1/25/2008.

Renli Qiao, M.D., Ph.D.

Ventilator setting: selection based on clinical scenarios. Summit Conference in Respiratory Diseases, Beijing PUMC, Beijing, China, 4/2008.

Massive pulmonary embolism. Annual Conference, Shanghai Medical Association, Shanghai, China, 4/2008.

The American healthcare systems: 1) specialty training; 2) ICU administration; 3) residency training; 4) ECFMG; 5) academic career. Chaoyang Hospital and Department of Medicine, The Capital Medical University, Beijing, China, 5/8-9/2008.

INVITED LECTURES

Richard G. Barbers, M.D.

Management of asthma. Citrus Valley Medical Center, Covina, CA, 9/25/2007.

Management of asthma. Twin Tower Correctional Facilities, L.A. County Sheriff's Department, Los Angeles, CA, 10/16/2007.

Asthma, atopy and ABPA. Annual Meeting, American College of Chest Physicians, Chicago, IL, 10/22/2007.

Review of top five asthma literature. Annual Meeting, American College of Chest Physicians, Chicago, IL, 10/24/2007.

New innovations in asthma management. Pulmonary Grand Rounds, Harbor-General/UCLA Medical Center, Torrance, CA, 10/31/2007.

Management of asthma. Glendale Adventist Medical Center, Glendale, CA, 11/28/2007.

Zea Borok, M.D.

Yale University, New Haven, CT, 8/3/2007.

Loma Linda University, Loma Linda, CA, 9/19/2007.

Emory University, Atlanta, GA, 2/14/2008

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Edward D. Crandall, Ph.D., M.D.

Biomedical Engineering Society, Los Angeles, CA, 9/29/2007.

University of California, Los Angeles, CA, 4/10/08.

Kwang-Jin Kim, Ph.D.

Nanomaterial interaction with and trafficking across lung alveolar epithelium. Research Seminar, Section of Pulmonary and Critical Care Medicine, School of Medicine, Yale University, New Haven, CT, 5/23/2008.

Hidenobu Shigemitsu, M.D

Catheter-related infections. Medical Staff Grand Rounds, Verdugo Hills Hospital, Los Angeles, CA, 7/12/2007.

Deep vein thrombosis prophylaxis. Medical Staff Grand Rounds, Promise Hospital of East Los Angeles/Suburban Medical Center, Los Angeles, CA, 10/4/2007.

Pulmonary hypertension and sarcoidosis. Medical Staff Grand Rounds, National Jewish Medical and Research Center, Division of Occupational and Environmental Medicine, University of Colorado, Denver, CO, 1/24/2008.

Update on pulmonary fibrosis. 6th Annual Alumni Conference, University of Southern California, Los Angeles, CA, 2/23/2008.

Sarcoidosis and pulmonary hypertension. Medical Staff Grand Rounds, Olympia Medical Center, Los Angeles, CA, 3/5/2008.

Update on pulmonary fibrosis. Medical Staff Grand Rounds, Verdugo Hills Hospital, Los Angeles, CA, 3/6/2008.

Deep vein thrombosis prophylaxis. Medical Staff Grand Rounds, Promise Hospital of East Los Angeles/Suburban Medical Center, Los Angeles, CA, 3/13/2008.

Genetics of sarcoidosis. 16th Annual Sarcoidosis Awareness and Education Conference, Sarcoidosis Network Foundation, Cerritos, CA, 3/29/2008.

Idiopathic pulmonary fibrosis. Promise Hospital of East Los Angeles/Suburban Medical Center, Los Angeles, CA, 5/8/2008.

Pulmonary hypertension in sarcoidosis. Division of Pulmonary/Critical Care Medicine Grand Rounds, University of California at Los Angeles/Harbor View Medical Center, Torrance, CA, 5/11/2008.

OFFICES/COMMITTEE MEMBERSHIPS HELD IN NATIONAL/REGIONAL PROFESSIONAL & OTHER SOCIETIES

Richard G. Barbers, M.D.

American Academy of Allergy, Asthma and Clinical Immunology
Allergic Bronchopulmonary Aspergillosis Committee
American College of Chest Physicians
Airways Network Steering Committee
Annual Meeting Abstract Reviewer
Membership Committee
Breathe of California, Los Angeles Chapter
Research Committee Board Member
Executive Board, Secretary
California Society of Allergy, Asthma and Immunology
Secretary/Treasurer
Medical Board of California
Expert Reviewer

Zea Borok, M.D.

American Thoracic Society
Assembly on Respiratory Cell and Molecular Biology,
Chair
Nominating Committee
Western Society for Clinical Investigation
Abstract Reviewer

Edward D. Crandall, Ph.D., M.D.

American Heart Association
Cardiopulmonary and Critical Care Council

Patricio Escalante, M.D.

American College of Chest Physicians
Chest Infections NetWork, Vice Chair
Steering Committee
Council of NetWorks
National Tuberculosis Curriculum Consortium
Publications Committee
Steering Committee

Janice M. Liebler, M.D.

Society of Critical Care Medicine
Annual Congress
Abstract Reviewer

Richard L. Lubman, M.D.

American Heart Association
Cardiopulmonary Council
American Lung Association of California
Research Fellowship Training Review Committee, Chair
Research Administrative Committee

Albert H. Niden, M.D.

Pulmonary Fibrosis Foundation
Board of Directors
Tuberculosis Advisory Council for Los Angeles County

**NATIONAL INSTITUTES OF HEALTH STUDY SECTIONS/
NOTEWORTHY GOVERNMENT ACTIVITIES**

Zea Borok, M.D.

National Institutes of Health
Lung Cellular Molecular and Immunobiology Study
Section

Patricio Escalante, M.D.

Centers for Disease Control and Prevention
Advisory Council for the Elimination of Tuberculosis

SPECIAL/INTERNATIONAL ACTIVITIES

Richard G. Barbers, M.D.

International Society for Heart and Lung Transplantation

Edward D. Crandall, Ph.D., M.D.

International Society of Aerosols in Medicine

Patricio Escalante, M.D.

International Union against Tuberculosis and Lung Diseases
Peruvian College of Physicians
Sociedad Peruana de Neumología

Kwang-Jin Kim, Ph.D.

International Journal of Epidemiology

Janice M. Liebler, M.D.

International Society for Heart and Lung Transplantation

Richard L. Lubman, M.D.

British Columbia Health Research Foundation, Reviewer
Imperial College, London, Visiting Professor
International Union against Tuberculosis and Lung Disease
Israel Science Foundation, Reviewer

Renli Qiao, M.D., Ph.D.

Beijing Olympics Medical Committee
Group for English-Chinese Manual of Medical Dialogue,
Leader
Chinese Association of Physiological Sciences
Chinese PUMC International Conference in Respiratory Medicine,
Co-Chair

Pulmonary and Critical Care Medicine

Om P. Sharma, M.D.

Indian Chest Society
Japan Sarcoidosis Society, Honorary Member
Japan Osler Society, Honorary Member
Osler Club of London
Royal Society of Medicine
Thoracic Society of Great Britain
World Association of Sarcoidosis and Other Granulomatous Disorders, President
Yugoslav Association of Sarcoidosis, Honorary Member

Hidenobu Shigemitsu, M.D.

European Respiratory Society

Graciela J. Soto, M.D.

European Society of Intensive Care Medicine
Latin American Student Association

AWARDS/HONORS

Richard G. Barbers, M.D.

America's Top Doctors

Zea Borok, M.D.

Western Society for Clinical Investigation
Outstanding Investigator Award

Ching-Fei Chang, M.D.

CHEST Best Case Report Presentation in Category of ICU Dilemmas

Kwang-Jin Kim, Ph.D.

Who's Who in America

Om P. Sharma, M.D.

American College of Chest Physicians
Master FCCP

SERVICE ON UNIVERSITY, SCHOOL, HOSPITAL AND DEPARTMENTAL COMMITTEES

Richard G. Barbers, M.D.

Keck School of Medicine
Compliance Committee
PCCM Alumni Conference Committee
USC/Norris Comprehensive Cancer Hospital
Pharmacy and Therapeutics Committee
USC University Hospital
Critical Care Committee
Endoscopy Committee, Vice-Chair
Organ Procurement/Donation Committee

Ahmet Baydur, M.D.

Keck School of Medicine
Years I and II Student Performance Evaluation Committee,
Respiratory Section
Years I and II Undergraduate Curriculum Committee

Zea Borok, M.D.

Department of Medicine
Residency Program Interviewer
Research Committee, PCCM Division
Keck School of Medicine
Dean's Ad Hoc Committee on Space and Budget
Faculty Research Council
M.D., Ph.D. Executive Committee
Medical School Admissions Committee, Interviewer

Patricio Escalante, M.D.

Department of Medicine
Practice Operations and Development Committee
Operations Subcommittee, Chair
Keck School of Medicine
Task Force on Recruitment and Retention of Women and Minorities
USC University Hospital
Pharmacy and Therapeutics Committee

Ricardo H. Juarez, M.D.

Department of Medicine
PCCM Physiology Conference, Coordinator
PCCM Quarterly Research in Progress Conference,
Coordinator

Kwang-Jin Kim, Ph.D.

Department of Chemical Engineering and Materials Science
Doctoral Dissertation Committee
Faculty Search Interviewer
Department of Molecular Pharmacology and Toxicology
Doctoral Dissertation Committee
Faculty Search Interviewer
Department of Pharmaceutical Sciences
Doctoral Dissertation Committee
Faculty Search Interviewer
Keck School of Medicine
Transport Journal Club
Will Rogers Institute Pulmonary Research Center
Radiation and Laboratory Safety Officer

Janice M. Liebler, M.D.

Keck School of Medicine
Endoscopy Committee
Lung Transplant Recipient Candidate Selection Committee

Richard L. Lubman, M.D.

Department of Medicine
Residency Program Interviewer
Keck School of Medicine
Medical Student Research Committee
GCRC Advisory Committee

Albert H. Niden, M.D.

Department of Medicine
Clinical Council
Operations Committee, Co-Chair
Peer Review Committee
LAC+USC Medical Center
Department of Medicine Oversight Committee
Home Care Service Professional Advisory Committee
Hospital Census Committee

Renli Qiao, M.D., Ph.D.
Keck School of Medicine
Residency Program Interviewer

Om P. Sharma, M.D.
Department of Medicine
Appointments and Promotions Committee
Residency Program Interviewer

Hidenobu Shigemitsu, M.D.
LAC+USC Medical Center
Central Line Infection Reduction Committee
Critical Care Committee
Infection Control Committee

Graciela J. Soto, M.D.
Department of Medicine
Residency Advisory Committee
LAC+USC Medical Center
Central Line Infection Prevention Committee
Critical Care Committee

Robert S. Swinney, M.D.
USC University Hospital
Computer Committee

Clinical Activities

LAC+USC MEDICAL CENTER

The Division of Pulmonary and Critical Care Medicine runs the Medical Intensive Care Units at the LAC+USC Medical Center. The Division, in addition, provides consultative services to inpatient and intensive care units of other divisions and departments, including internal medicine, surgery, neurology, neurosurgery, burns, emergency medicine and cardiology. The Division conducts a weekly Chest Clinic, at which residents and fellows follow new and follow-up patients, and a weekly Sarcoidosis Clinic. Each year, the Division has approximately 5,100 outpatient visits, sees approximately 650 consultations, and performs about 400 bronchoscopic examinations and numerous other procedures, including bronchoalveolar lavage, transbronchial and percutaneous needle biopsy and Wang needle biopsy. The Pulmonary Physiology Laboratory is under the direction of the Division of Pulmonary and Critical Care Medicine. PCCM performs on average 3,000 arterial blood gas studies, 1,000 lung function tests and 200 sleep studies every month.

USC UNIVERSITY HOSPITAL

The Division of Pulmonary and Critical Care Medicine administers the Intensive Care Units of the USC University Hospital (USCUH). We are involved in direct care of inpatients with a wide spectrum of lung and critical illnesses. The Pulmonary and Critical Care Medicine fellow performs all diagnostic and therapeutic procedures. Diagnostic and therapeutic bronchoscopies are performed by the fellow with an attending staff physician supervising the procedure. The Lung Transplantation Center, Adult Cystic Fibrosis Center and Cough Disorders Clinic have been established. Drs. Barbers, Baydur, Borok, Chang, Escalante, Ganesh, Juarez, Liebler, Lubman, Qiao, Rao, Shigemitsu, Soto and Sharma carry out major clinical roles at USCUH and at the Ambulatory Health Center.

USC/NORRIS CANCER HOSPITAL

New programs have been developed in fluorescence bronchoscopy, brachytherapy, lung immunology/transplantation, rehabilitation, cough/asthma and chronic pulmonary diseases. USC/Norris Cancer Hospital provides an unparalleled opportunity in delivering care to a large number of patients with complications related to malignancy, immunosuppression and bone marrow transplantation. Critically ill patients are cared for in the six-bed Intensive Care Unit. The Pulmonary and Critical Care Medicine fellow carries out all consultations and performs all diagnostic, invasive and noninvasive, and therapeutic procedures under the supervision of the attending staff. A new Center for Lung Cancer Management has been established. Drs. Barbers, Chang, Juarez, Rao, Sharma, Soto and Shigemitsu carry out major clinical responsibilities for USC/Norris Cancer Hospital inpatients and outpatients.

SPECIAL CLINICAL SERVICES

The Division of Pulmonary and Critical Care Medicine has established several clinical programs which are primarily located at USC University Hospital and our Ambulatory Healthcare Center, but are also located at USC/Norris Cancer Hospital and LAC+USC Medical Center. Each program offers specialized treatment of various pulmonary disorders as well as an educational setting for fellowship training.

1. Asthma and Allergy Center

The USC Asthma and Allergy Center is a comprehensive clinical program for the diagnosis and management of patients with asthmatic and/or atopic disorders (such as allergic rhinitis and sinusitis), which affect more than 20 million people in this country. The Asthma and Allergy Center is staffed by full-time teaching faculty who are certified in pulmonary, allergic and immunologic diseases. Besides physician specialists, resources include clinical nurse specialists, physical therapists, respiratory therapists, nutritionists, social workers and pharmacologists. A state-of-the-art pulmonary function laboratory has capabilities for airflow measurements, including methacholine challenge studies to detect hyperirritable airway disorders. State-of-the-art skin testing for common pollen allergens, animal dander, dust mites, common molds and common foods is available. Testing by the RAST method for hypersensitivity pulmonary disease, including allergic bronchopulmonary aspergillus, is also offered. In addition, skin testing for hymenoptera hypersensitivity (bee venom) and penicillin allergy is also available. If warranted, immunotherapy (desensitization) can be initiated for selected patients. The Medical Director of the Asthma and Allergy Center is Richard G. Barbers, M.D.

Pulmonary and Critical Care Medicine

2. Cough Disorders Center

The USC Cough Disorders Center is a comprehensive clinical program providing state-of-the-art modalities for the diagnosis and management of patients with unexplained and/or persistent cough, which is a common respiratory symptom affecting tens of millions of people in this country. Cough can be a symptom of asthma, bronchitis, chronic aspiration, lung cancer and other conditions. The USC Cough Disorders Center (CDC) is staffed by certified physician specialists in pulmonary and allergic disorders who are part of the full-time teaching faculty at USC. The latest diagnostic technological tools are available at the CDC, including bronchoprovocation testing, gastrointestinal pH monitoring, and upper and lower airway and esophageal endoscopic procedures, as well as comprehensive state-of-the-art radiologic procedures. The CDC focuses on the unique needs of each patient in order to assure that daily life and function are minimally limited by symptoms or by the underlying disorder that is responsible for the symptoms. The Medical Director of the Cough Disorders Center is Richard G. Barbers, M.D.

3. Emphysema Management and Surgery Program

The USC Division of Pulmonary and Critical Care Medicine has established a program for the diagnosis and management of patients with chronic obstructive lung disease (emphysema). We provide state-of-the-art diagnostic, therapeutic and rehabilitation services. It has recently been discovered that lung volume reduction surgery (LVRS) has successfully improved pulmonary function and quality of life in patients with severe emphysema. LVRS may also be used as a “bridge” to lung transplantation. The USC Division of Pulmonary and Critical Care Medicine, in conjunction with the USC Division of Cardiothoracic Surgery, provides a comprehensive multidisciplinary program for the evaluation and management of patients who have advanced emphysema and qualify for LVRS. The Emphysema Management and Surgery Program is directed by Om P. Sharma, M.D.

4. Sleep Center

The USC Sleep Disorders Program offers comprehensive outpatient and inpatient sleep disorders evaluation. Individuals with sleep irregularities manifested by symptoms or signs such as excessive daytime sleepiness, excessive snoring, witnessed apneas, morning headaches, insomnia and abnormal nocturnal movements or behaviors would benefit from a comprehensive sleep evaluation. The sleep disorders evaluation begins with a thorough history and physical examination, and if indicated, preparations are made for a formal sleep study. The program offers Attended Standard Sleep Studies, CPAP Titration Sleep Studies, and Multiple Sleep Latency Studies, all performed with state-of-the-art equipment. The Medical Director of the Sleep Center is Ricardo Juarez, M.D.

5. Pulmonary Exercise Center

The USC Pulmonary Exercise Program provides outpatient and inpatient exercise evaluations. The exercise studies are performed with state-of-the-art exercise equipment and experienced exercise technologists. Individuals with suspected functional impairment during any type or grade of exercise would benefit from an exercise evaluation to identify the physiologic causes for the impairment. The information obtained from the study can be used to tailor specific exercise regimens and therapeutic strategies. The program offers Standard Pulmonary Stress Tests, Oxygen Denaturation Exercise Studies, Exercise-Induced Bronchospasm Studies and Metabolic Studies. The Medical Director is Ricardo Juarez, M.D.

6. High Altitude Evaluation Test Center

The USC University Hospital High Altitude Simulation Test (HAST) is a specialized type of oxygenation study. This study is performed on individuals who have marginal oxygenation and are considering excursions into high altitudes, including flying in an airplane. The study objective is to determine the quantity of supplemental oxygen that is required for a safe trip at various altitudes. The study is performed at rest and with gradients of activity. The Medical Director is Ricardo Juarez, M.D.

7. Pulmonary Rehabilitation Program

Nearly all patients with chronic pulmonary disease benefit from participation in a pulmonary rehabilitation program. The USC Pulmonary Rehabilitation Program offers a wide range of services, from single sessions focused upon a specific need (such as training the asthmatic patient in the use of metered dose inhalers), to a comprehensive two afternoon per week program for a total of six weeks. The comprehensive program includes exercise training, patient education in a broad range of subjects (from the pathophysiology of disease to therapy), psychosocial support services, physical therapy, vocational therapy, symptom control techniques and the use of low flow oxygen. In addition, there are specialized programs targeted at patients with particular problems, such as emphysema and pulmonary fibrosis. The Program Medical Director is Ahmet Baydur, M.D.

8. Lung Cancer Management Center

As an integral part of the multidisciplinary Lung Cancer Management Center based at the USC/Norris Cancer Hospital, faculty of the Division of Pulmonary and Critical Care Medicine participate in the evaluation and care of patients with lung cancer. A regular Tuesday afternoon clinic staffed by pulmonary, oncology, thoracic surgery and radiation oncology services is designed to streamline the coordinated assessment of patients with or suspected of having lung cancer.

Fluorescence Bronchoscopy in Early Detection of Lung Cancer

The Lung Imaging Fluorescence Endoscope (LIFE) employs spectral differences of autofluorescence of normal and cancerous tissue. Fluorescence images are amplified and captured by an image-intensified camera. The images are then analyzed and converted into real-time video images that clearly distinguish cancerous from normal tissue. In our experience, the combination of LIFE and routine bronchoscopy has 100 percent sensitivity and 82 percent specificity in endobronchial cancer.

Indications for the procedure are:

1. Patients who are at high risk of developing lung cancer
 - (a) smokers
 - (b) exposure to carcinogen (asbestos, chromium)
 - (c) prior head and neck cancer
 - (d) prior resection of lung cancer
2. Evaluation of patients with abnormal chest x-rays
3. Endobronchial staging of lung cancer

The Medical Director of the LIFE service is Ricardo Juarez, M.D.

High-Dose Brachytherapy for Advance Stage Lung Cancer

In conjunction with the Department of Radiation Oncology, high-dose brachytherapy is available for the treatment of endobronchial malignancies. The placement of multiple after-loading catheters and delivery of local high-dose radiation allow reduction in the number of treatments from usually three bronchoscopic treatments to one. Patients should understand that this treatment is for palliation of symptoms (hemoptysis, dyspnea) and not for cure. Referrals should be directed to Hidenobi Shigemitsu, M.D.

Follow-Up and Chemoprevention of Lung Cancer

Patients with a primary lung malignancy are at increased risk for recurrent disease and second primary lung cancers. Our Division is engaged in trials studying the benefit of chemoprevention with 13 cis-retinoic acid and of the analysis of post-operative sputum using monoclonal antibodies to detect early dysplasia. Patients with completely resected and treated lung cancer are eligible for evaluation, enrollment and follow-up. The LIFE bronchoscope may be used to evaluate patients with abnormal sputum cytology. This service is coordinated by Hidenobu Shigemitsu, M.D.

9. Smoking Cessation Consultation Service

The Division of Pulmonary and Critical Care Medicine at USC is interested in promoting lung health. As tobacco-related lung diseases comprise a significant portion of the pulmonary disorders we see, smoking cessation is paramount in improving overall lung health. Smoking cessation can be achieved through health education, sometimes with medical intervention. Assessment for smoking cessation includes a thorough history and physical examination, personal counseling, appropriate medical intervention (e.g., transdermal nicotine patches) and follow-up. Other interventions (e.g., acupuncture) can be arranged when indicated. Patients appropriate for referral include all adult users of tobacco products, with emphasis on patients with cardiopulmonary and vascular disorders, and especially those smokers anticipating elective surgeries. The physician in charge of assisting patients in smoking cessation is Richard Lubman, M.D.

10. Sarcoidosis and Interstitial Lung Disease Center

Although classified as a lung disease, sarcoidosis can attack any organ in the body. Because of its multisystem nature, sarcoidosis patients appear in offices of medical practitioners of different disciplines. The Sarcoidosis and Interstitial Lung Disease Center at USC deals with the diagnosis and treatment of all types of interstitial lung diseases including sarcoidosis, idiopathic pulmonary fibrosis, hypersensitivity pneumonitis, collagen vascular lung disease, eosinophilic granuloma and pulmonary eosinophilia. Over the last 25 years, services have been provided to patients from all over the world. The Medical Directors of the Center are Om P. Sharma, M.D., and Hidenobu Shigemitsu, M.D.

11. Adult Cystic Fibrosis Center

The Adult Cystic Fibrosis Program of the USC Comprehensive Cystic Fibrosis Center provides direct care or consultation for adults with cystic fibrosis. Outpatients are seen at the USC Ambulatory Health Care Center and inpatients are hospitalized at the USC University Hospital. The cystic fibrosis care team is headed by pulmonologists supported by a full range of consultants, including diabetologists, gastroenterologists, otolaryngologists, infectious diseases experts, general surgeons and cardiothoracic surgeons. Allied health services are provided by pulmonary clinical nurse specialists, dietitians, clinical social workers, physical therapists, occupational therapists and respiratory therapists. State-of-the-art therapies are offered, and there are gateways to research protocols and lung transplantation. The usual hours for outpatient appointments are Friday afternoons, but patients will be seen at other times as necessary. The Medical Director is Adupa P. Rao, M.D.

12. Lung Transplantation Program

Pulmonary transplantation has become a viable treatment option for patients with end-stage pulmonary disease. The USC Cardiopulmonary Transplant Team, headed by Vaughn Starnes, M.D., and Richard Barbers, M.D., is composed of experts in their respective fields of cardiothoracic surgery, cardiology, pulmonary medicine, immunology, critical care medicine, pediatrics, cystic fibrosis, perfusion medicine, immunosuppression, rehabilitation and social/psychological services. Patients eligible for lung transplantation include any person who is severely debilitated by cardiopulmonary disease and is not hampered by any other organ system dysfunction. Candidates frequently have the diagnosis of obstructive lung disease (e.g., emphysema, cystic fibrosis, bronchiectasis), pulmonary hypertension (both primary and secondary) or pulmonary fibrosis (e.g., sarcoidosis, IPF, silicosis).

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Living related lobar lung transplantation is unique to our institution and provides an alternative therapy for severely ill patients who are unlikely to survive the waiting period that is often required for cadaveric organs to become available. Since this is an experimental procedure, strict criteria must be met before a patient can qualify for this procedure. Single cadaveric lung transplantation is available for patients up to the age of 65 years. Double lung transplantation is the procedure of choice for patients with suppurative lung disease and severe pulmonary hypertension. Candidates are frequently under 60 years of age in this group of patients. Combined heart-lung transplantation is a procedure reserved for relatively young patients with irreversible cardiac and pulmonary disease. The Sarcoidosis and Interstitial Lung Disease Center at USC deals with the diagnosis and treatment of all types of interstitial lung diseases, including sarcoidosis, idiopathic pulmonary fibrosis and hypersensitivity pneumonitis. Richard Barbers, M.D., is Medical Director.

Educational Activities

FELLOWS

First Year

Mazda Aghamohammadi, M.D.
Ayana Boydking, D.O.
Alfredo Castellanos, M.D.
Mouhammed Farhat, M.D.
Santhi Iyer, M.D.
Haven Malish, M.D.

Second Year

Margarita Bass, M.D.
Michaela Ivan, M.D.
Rizwana Khan, M.D.
Ashish Patel, M.D.
Anthony Pureza, M.D.

Third Year

Kamyar Afshar, D.O.
Hesham Elghannam, M.D.
Willima Le, M.D.
Husein Nassr, M.D.
Nariman Saddad, M.D.

FELLOWSHIP PROGRAM

The Pulmonary and Critical Care Medicine Fellowship Program is designed and balanced to provide each trainee with a range of exposure to the diagnosis and management of chest diseases, the experience and skills required of an intensivist and the opportunity to develop research interests. At the present time, five new fellows are admitted to the program every year. For the most part, clinical and teaching responsibilities encompass most of the first and second years, with the remainder of the three years devoted to research activities. During the clinical phase of the training, fellows devote their time to evaluation, diagnosis and treatment of patients admitted to various USC hospitals. The rotations include LAC+USC Medical Center, USC University Hospital and USC/Norris Cancer Hospital. The fellows assess problems, make appropriate diagnostic and therapeutic recommendations and perform specialized procedures, including fiberoptic bronchoscopy, percutaneous needle biopsy of the lung and pleura, and thoracentesis and pleurodesis. The trainee receives instruction in pulmonary function and x-ray interpretations including high-resolution computerized tomography (HRCT), the principles and techniques of mechanical ventilation and inhalation therapy, and all aspects of pulmonary and critical care medicine. The program encourages the fellow to become an independent thinker and develop an attitude of intellectual scholarship by providing an academic atmosphere. The Division's dedication to excellence in patient care, research and teaching is expressed in every phase of the training program. Numerous full-time and part-time faculty members with national and international reputations share teaching responsibilities while pursuing active research and delivering outstanding clinical care.

TEACHING ACTIVITIES

Our strong commitment to teaching is evident in an extensive daily conference schedule (starting at 8:30 a.m.) consisting of didactic lectures, multidisciplinary case conferences, grand rounds, morbidity and mortality conferences, and research seminars on various aspects of pulmonary and critical care medicine and related sciences. Combined thoracic surgery and thoracic oncology conferences are held every Friday at 12:15 p.m., alternately at USC/Norris Cancer Hospital and USCUIH.

Monthly Journal Clubs stress the importance of evaluating, analyzing and presenting the medical research literature. Guest lectures and seminars with nationally and internationally known physician/scientists are held frequently. Rounds conducted in all the USC hospitals form the cornerstone of our clinical teaching program. These in-depth sessions ensure the highest quality of patient care. Full-time faculty conduct bedside rounds as well as clinical discussions. Housestaff, medical students, fellows and attending physicians participate in these rounds, which take place every day throughout the year.

The Division has also been committed to providing essential teaching for the education of second-year medical students. Both current and former faculty participate in lectures and small group discussions on various topics in respiratory medicine. Beginning in the fall of 2002, the Division implemented a major revision of its curriculum in collaboration with members of the basic sciences departments. This project was undertaken as part of the overall revision for the Years I and II curriculum.

Research Activities

The Division of Pulmonary and Critical Care Medicine published 12 peer-reviewed research papers in 2007-2008. Of these, four studies are especially noteworthy accomplishments in Pulmonary and Critical Care Medicine.

Yacobi NR, DeMaio L, Xie J, Hamm-Alvarez SF, **Borok Z, Kim KJ, Crandall ED**: Polystyrene nanoparticle trafficking across alveolar epithelium. *Nanomedicine* 4:139-145, 2008.

We investigated trafficking of polystyrene nanoparticles (PNP; 20 and 100 nm; carboxylate, sulfate, or aldehyde-sulfate modified [negatively charged] and amidine-modified [positively charged]) across rat alveolar epithelial cell monolayers (RAECM). Apical-to-basolateral fluxes of nanoparticles were estimated as functions of apical PNP concentration ([PNP]) and temperature. Uptake of nanoparticles into RAECM was determined using confocal microscopy. Fluxes increased as charge density became less negative/more positive, with positively charged PNPs trafficking 20-40 times faster than highly negatively charged PNP of comparable size. Trafficking rates decreased with increasing PNP diameter. PNP fluxes tended to level off at high apical [PNP]. Fluxes at 4 degrees C were significantly lower than those at 37 degrees C. Confocal microscopy revealed nanoparticles localized to cell cytoplasm, whereas cell junctions and nuclei appeared free of PNP. These data indicate that (1) trafficking of PNP across RAECM is strongly influenced by charge density, size, and temperature, (2) PNP translocate primarily transcellularly, and (3) PNP translocation requires cellular energy.

Liebler JM, Lutzko C, Banfalvi A, Senadheera D, Aghamohammadi N, **Crandall ED, Borok Z**: Retention of human bone marrow-derived stem cells in murine lungs following bleomycin-induced lung injury. *Am J Physiol*, in press, 2008.

We studied the capacity of adult human bone marrow-derived cells (BMDC) to incorporate into distal lung of immunodeficient mice following lung injury. Immunodeficient NOD/SCID and NOD/SCID/beta(2) microglobulin (beta(2)M)(null) mice were administered bleomycin (bleo) or saline intranasally. One, 2, 3 and 4 days after bleo or saline, human BMDC labeled with CellTracker Green CMFDA (5-chloromethylfluorescein diacetate) were infused intravenously. Retention of CMFDA(+) cells was maximal when delivered 4 days after bleo treatment. Seven days after bleo, <0.005% of enzymatically dispersed lung cells from NOD/SCID mice were CMFDA(+), which increased 10- to 100-fold in NOD/SCID/beta(2)M(null) mice. Preincubation of BMDC with Diprotin A, a reversible inhibitor of CD26 peptidase activity that enhances the stromal-derived factor-1 (SDF-1/CXCL12)/CXCR4 axis, resulted in a 30% increase in the percentage of CMFDA(+) cells retained in the lung. These data indicate that human BMDC can be identified in lungs of mice following injury, albeit at low levels, and this may be modestly enhanced by manipulation of the SDF-1/CXCR4 axis. Given the overall low number of human cells detected, methods to increase homing and retention of adult BMDC, and consideration of other stem cell populations, will likely be required to facilitate engraftment in the treatment of lung injury.

Qiao R, Yan W, Clavijo C, Mehrian-Shai R, Zhong Q, **Kim KJ**, Ann D, **Crandall ED, Borok Z**: Effects of KGF on alveolar epithelial cell transdifferentiation are mediated by JNK signaling. *Am J Respir Cell Mol Biol* 38:239-246, 2008.

Rat alveolar epithelial cells (AEC) in primary culture transdifferentiate from a type II (AT2) towards a type I (AT1) cell-like phenotype, a process that can be both prevented and reversed by keratinocyte growth factor (KGF). Microarray analysis revealed that these effects of KGF are associated with upregulation of key molecules in the mitogen-activated protein kinase (MAPK) pathway. To further explore the role of three key MAPK (i.e., extracellular signal-related kinase (ERK) 1/2, c-Jun N-terminal kinase (JNK) and p38) in mediating effects of KGF on alveolar epithelial cell (AEC) phenotype, primary rat AEC cultivated in minimal defined serum-free medium (MDSF) were treated with KGF (10 ng/ml) from Day 4 for intervals up to 48 hr. Exposure to KGF activated all three MAPK, JNK, ERK1/2, and p38. Inhibition of JNK, but not of ERK1/2 or p38, abrogated the ability of KGF to maintain the AT2 cell phenotype, as evidenced by loss of expression of lamellar membrane protein (p180) and increased reactivity with the AT1 cell-specific monoclonal antibody VIIIb2 by Day 6 in culture. Overexpression of JNKK2, upstream kinase of JNK, increased activation of endogenous c-Jun in association with increased expression of p180 and abrogation of AQP5, suggesting that activation of c-Jun promotes retention of the AT2 cell phenotype. These results indicate that retention of the AT2 cell phenotype by KGF involves c-Jun and suggest that activation of c-Jun kinase may be an important determinant of maintenance of AT2 cell phenotype.

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Zhou B, Ann DK, Li K, **Kim KJ**, Lin H, Minoo P, **Crandall ED**, **Borok Z**: Hypertonic induction of aquaporin 5: novel role of hypoxia inducible factor-1 α . *Am J Physiol* 292:C1280-C1290, 2007.

Aquaporin-5 (AQP5) is a water channel protein expressed on the apical surface of alveolar epithelial type I cells in distal rat lung, suggesting a role for AQP5 in regulating alveolar surface liquid tonicity and/or cell volume. We investigated the molecular mechanisms underlying hypertonic induction of AQP5 in primary rat alveolar epithelial cells (AEC). Steady-state levels of AQP5 mRNA and protein were increased by exposure to sorbitol (200 mM in culture fluid) for 24 h. The increase in AQP5 was not accompanied by changes in mRNA half-life. Transduction of mouse lung epithelial (MLE-15) cells and primary rat AEC with lentivirus vectors encoding AQP5-luciferase demonstrated transcriptional activation of the reporter by exposure to hypertonic sorbitol solution. Hybridization of proteins from sorbitol-treated cells to a transcription factor DNA array demonstrated induction of hypoxia-inducible factor-1 α (HIF-1 α) by hypertonicity, which was confirmed by quantitative RT-PCR. Cotransfections of AQP5-luciferase with HIF-1 α and HIF-1 β expression plasmids in MLE-15 cells led to dose-dependent transcriptional enhancement, which was partially abrogated by mutagenesis of putative HIF-1 α binding sites in the proximal AQP5 promoter. Importantly, hypertonic induction of AQP5 was significantly inhibited by preventing HIF-1 α induction with small interfering RNA. Hypertonicity induced activation of a transiently transfected vascular endothelial growth factor (VEGF) hypoxia response element-driven luciferase construct and increased expression of endogenous VEGF. These results demonstrate that hypertonic induction of both AQP5 and VEGF is transcriptionally regulated and mediated, at least in part, by HIF-1 α , suggesting a novel role for HIF-1 α in modulating cellular adaptive responses to osmotic stress.

OVERVIEW

Basic and clinical research remains a major focus of the Division's interests and activities. A number of investigators are studying pulmonary structure and function at the organ, tissue, cellular and molecular levels. Current areas of investigation include study of mechanisms and regulation of water, solute and macromolecule transport across the pulmonary alveolar epithelium; development of cell-type specific markers for alveolar type I and type II cells using monoclonal antibodies and genetic markers; and regulation of lung cell growth, differentiation and gene expression *in vitro*. In addition, clinical research studies in the fields of sarcoidosis and other granulomatous disorders, acquired immune deficiency syndrome (AIDS), asthma, septic shock, barotrauma, pulmonary edema, acute respiratory distress syndrome (ARDS and tuberculosis) and lung transplantation are underway.

FACULTY RESEARCH AREAS

Richard G. Barbers, M.D.

Mechanisms of Remodeling in Near-Fatal Asthma
Mechanisms of Remodeling in Pulmonary Fibrosis
Novel Therapeutic Interventions for BOS in Lung Transplant Recipients
Novel Therapeutic Interventions in Severe Asthma

Ahmet Baydur, M.D.

Respiratory Mechanics
Control of Ventilation
Neuromuscular Disorders
Acute Respiratory Distress Syndrome
Sarcoidosis

Zea Borok, M.D.

Alveolar Epithelial Cell Function and Differentiation
Modulation of Alveolar Epithelial Cell Phenotype and Recovery Following Lung Injury
Pulmonary Alveolar Epithelial Cell Homeostasis
Stem Cell Biology in Lung Injury
Transport Properties of Pulmonary Alveolar Epithelium

C. Thomas Boylen, M.D.

Oxygen Therapy in COPD
Immunological Diseases of the Lung
Pleural Diseases
Clubbing and Its Evaluation in an Asbestos Contact Population
Nocturnal Oxygen Therapy Trial
Acute Effects of Welding
Effects of Formaldehyde Exposure

Ching-Fei Chang, M.D.

Interventional Bronchoscopy
Endobronchial Interventions for COPD
Bronchial Thermoplasty for Asthma
Critical Care Ultrasonography
Medical Pleuroscopy
Medical Education

Edward D. Crandall, Ph.D., M.D.

Markers of Rat Alveolar Epithelial Cell Development and Differentiation
Regulation of Pulmonary Epithelial Cell Differentiation
Acute and Chronic Lung Injury and the Factors that Influence Recovery
Transport Properties of Pulmonary Alveolar Epithelium
Cell Pathophysiology of Alveolar Epithelium
Nanoparticle Interactions with Lung

Patricio Escalante, M.D.

Molecular Epidemiology in Tuberculosis
Molecular Genetics and Pathophysiology of Infection of Mycobacterium Tuberculosis
Treatment of Multi-Drug Resistant and Mono-Resistant Drug Tuberculosis
Sleep Disorders and Critical Care Clinical Research

Sivagini Ganesh, M.D.

Lung Transplant
Pulmonary Hypertension

Henry Gong, Jr., M.D.

Health-Related Effects of Air Pollution

Ricardo H. Juarez, M.D.

Mechanical Ventilation in Respiratory Failure
Preoperative Assessment of Obese Patients

Kwang-Jin Kim, Ph.D.

Drug Delivery through the Lung
Tight Junctions in Alveolar Epithelium

Janice M. Liebler, M.D.

Cell-Based Treatment of Lung Diseases
Lung Epithelial Cell Biology
Lung Injury and Repair
Lung Transplantation

Richard L. Lubman, M.D.

Cell-Matrix Interactions by Human Embryonic Stem Cells
Cell-Matrix Interaction by Alveolar Epithelium in Repair of Lung Injury
Regulation of Intracellular pH and CO₂ Transport by Alveolar Epithelium

Albert H. Niden, M.D.

Pathogenesis, Diagnostic Techniques and Treatment of Diffuse Interstitial Lung Disease

Renli Qiao, M.D., Ph.D.

Mechanisms of Alveolar Homeostasis

Adupa P. Rao, M.D.

Cystic Fibrosis
Sepsis

Bertrand J. Shapiro, M.D.

Cystic Fibrosis

Pulmonary and Critical Care Medicine

Om P. Sharma, M.D.

Predictors of Survival in Patients with Sarcoidosis
Long Term Prognosis of Myocardial Sarcoidosis
Neurological Sarcoidosis

Hidenobu Shigemitsu, M.D.

Interstitial Lung Disease

Graciela J. Soto, M.D.

ARDS
Sepsis and Septic Shock
Clinical Uses of Activated Protein C

Robert S. Swinney, M.D.

Clinical Applications of Computers in Critical Care Medicine

SPECIAL BASIC TRANSLATIONAL RESEARCH ACTIVITIES

Zea Borok, M.D.

Associate Director, Will Rogers Institute Pulmonary Research Center

Regulation of Gene Expression in Lung Growth and Differentiation. The alveolar epithelium lining the gas exchange surface of the adult lung consists of two highly specialized cell types, type II and type I cells. These cell types are distinguished from each other by their characteristic morphologic appearances and by expression of unique cell-specific phenotypic markers. Type II cells have been well-characterized with regard to their role in surfactant production. In contrast, despite the fact that type I cells cover ~90% of the gas exchange surface, little is known of their functional properties or of the mechanisms that regulate gene expression specifically in type I cells. Aquaporin-5 (AQP5) is a member of a family of water channel proteins that is expressed in type I, but not type II, cells of the alveolar epithelium. Dr. Borok is studying the mechanisms underlying cell-specific expression of AQP5 in order to elucidate how gene expression is regulated in type I cells. She and her associates have isolated the regulatory (promoter) region of AQP5 from rat genomic DNA. They have mapped the site at which transcription is initiated and, using transient transfections into a lung cell line, have delineated regions of the promoter that appear to be important for high levels of expression in lung. Dr. Borok is also using *in vivo* approaches to evaluate the ability of the AQP5 promoter to regulate expression of a reporter gene in type I cells within the lungs of transgenic mice. These studies will provide important new insights into the mechanisms that regulate gene expression in type I cells. Identification of a promoter that is able to direct gene expression in a cell-specific fashion in type I cells should prove useful for targeted delivery to type I cells of potentially therapeutic genes in order to modulate type I cell function and accelerate restoration of normal alveolar architecture following injury.

Edward D. Crandall, Ph.D., M.D.

Director, Will Rogers Institute Pulmonary Research Center

Gene Regulation in Lung Injury and Repair. Dr. Crandall's research group focuses on the lung's primary barrier between the external environment and the internal milieu, the alveolar epithelium (lining cells of the air sacs). In addition to several specific projects described below that are currently in progress under the supervision of Division faculty, Dr. Crandall and his group are comprehensively studying many additional aspects of alveolar lung cell biology. Current projects include studies on the effects of injury from excess oxygen exposure (hyperoxia) and lack of oxygen (hypoxia) on the alveolar epithelial barrier, on pharmacological agents that can induce the alveolar epithelium to increase water clearance from the lungs, and on the process of alveolar epithelial cell differentiation after lung injury. The ultimate goal of these studies is to develop a better understanding of the pathways of salt and water absorption by the lungs, and to develop new therapeutic approaches for diseases that cause respiratory failure due to excess alveolar fluid (i.e., pulmonary edema). Conditions such as congestive heart failure (CHF) and the adult respiratory distress syndrome (ARDS), two major causes of morbidity and mortality in the U.S., could potentially be ameliorated by manipulation of alveolar fluid balance and modulation of the process of alveolar epithelial cell differentiation.

Kwang-Jin Kim, Ph.D.

Senior Investigator, Will Rogers Institute Pulmonary Research Center

Drug Delivery Through the Lung. The alveolar and airway epithelium (lining cells) form the primary barrier between the relatively dry alveolar air space and aqueous internal milieu. Dr. Kim and associates are currently studying transport of water, ions, peptides, and proteins across the alveolar epithelial barrier using *in vitro* models of the alveolar epithelium, including air-interfaces monolayer cultures of alveolar pneumocytes. Trafficking of white blood cells (leukocytes, lymphocytes, and macrophages) and tuberculous bacteria (mycobacteria) across the alveolar epithelium are also being studied, as are the effects of injurious agents (H₂O₂, NO₂, acrolein, acetaldehyde, and cigarette smoke) on alveolar epithelial barrier properties. These studies are expected to yield important information concerning the mechanisms involved in maintenance of normal alveolar fluid balance, and will help to characterize drug absorption by the alveolar epithelium as an alternative systemic drug delivery route.

Janice M. Liebler, M.D.

Investigator, Will Rogers Institute Pulmonary Research Center

Cell-Based Therapy for Lung Diseases. Although most lung injury is repaired by locally derived progenitor cells, recent information suggests that cells that originate outside the injured organ, presumably derived from the bone marrow, may also repopulate the lung. Dr. Liebler is interested in learning whether human bone marrow-derived cells, in contrast to murine bone marrow-derived cells, are able to promote repair of injured lung tissue. Dr. Liebler is using well-characterized mouse xenograft models to determine the potential of adult human bone marrow-derived cells to migrate to the lungs of immunodeficient mice following a single intravenous infusion. Since previous studies have established the need for lung injury to be present to show significant levels of engraftment, mice are studied with and without bleomycin (bleo)-induced lung injury. These studies may provide important insights into the potential of cell-based therapy in the treatment of lung diseases.

Renli Qiao, M.D., Ph.D.

Investigator, Will Rogers Institute Pulmonary Research Center

Gene Therapy for Acute Lung Injury. Pulmonary edema is a common and severe condition resulting from acute lung injury (ALI) of various causes. In its most severe form, edema fluid fills the alveolar air spaces resulting in hypoxemia and respiratory failure. The resolution of alveolar edema depends on active ion transport (accompanied by water) across the alveolar epithelium driven by basolaterally located Na pumps. Augmentation of active Na transport via upregulation of Na pump activity through gene transfer of Na pump subunit(s) in the alveolar epithelial cells (AEC) is a potential strategy for enhancing alveolar fluid clearance following ALI and is the focus of Dr. Qiao's research. Currently, he is trying to 1) develop a lentivirus vector that can efficiently infect AEC, and 2) investigate the best strategy of gene delivery to AEC for upregulating functional Na pumps. Since functional Na pumps consist of two structurally and functionally distinct subunits, to achieve augmentation of Na pump activity, genes of both subunits have to be delivered simultaneously into each target cell. Dr. Qiao has successfully incorporated two different genes into the backbone plasmid of a lentivirus vector and in pilot experiments has demonstrated that both genes are efficiently made by this construct. He has determined that the best route of administration of lentivirus to transfect AEC is from the alveolar side (instead of basolateral side) which is encouraging for the development of inhalational strategies for gene delivery. He is currently evaluating lentivirus vectors generated with these plasmids to overexpress functional Na pump in cultured AEC and *in vivo*.

SPECIAL CLINICAL RESEARCH ACTIVITIES**Richard G. Barbers, M.D.**

Chronic Inflammation and Remodeling in Asthmatics. Remodeling may occur in mild, moderate and severe asthmatics and may be a reason for persistent and refractory asthma episodes. However, not all asthma patients manifest remodeling. There may be differences in the inflammatory and immune responses. In order to define these processes in the airways, severe asthma subjects will undergo bronchoscopy, bronchoalveolar lavage (BAL) and proximal airway biopsies. The cellular and protein material retrieved by BAL as well as airway biopsies are studied in the laboratory. Our research will attempt to show that abnormal repair processes and growth factors eventually lead to airway fibrosis (remodeling). The information obtained will provide insight into pathogenesis as well as potential therapeutic interventions for severe asthmatics. In addition, with researchers at the University of Washington, Dr. Barbers is exploring similar mechanisms of remodeling in pulmonary fibrosis. This collaborative effort will examine the effect of inhibitors in the fibrotic process.

Ahmet Baydur, M.D.

A New Noninvasive Method for Evaluating Upper Airway Collapse in Sleep Apnea. The major pathophysiologic factor contributing to the generation of sleep disordered breathing is increased upper airway collapsibility. Expiratory compliance of the upper airway is higher than inspiratory compliance and is higher in obstructive sleep apnea syndrome (OSAS) than in normal subjects. Assessment of flow dynamics during expiration, therefore, should provide information about the degree of airway collapse or occlusion. Demonstration of expiratory flow limitation (EFL) has been facilitated by the introduction of the negative expiratory pressure (NEP) technique. In this approach, a small negative pressure (-3 to -5 cm H₂O) is applied at the start of expiration during tidal breathing. In normal subjects, an increase in expiratory flow is observed. In subjects with EFL the flow measured during the application of NEP will not exceed spontaneous flow. This simple, noninvasive, effort independent and fast technique can be applied in any body position. EFL has been found to correlate with the desaturation index in OSAS and the severity of OSAS, suggesting that the greater the EFL over tidal expiration, the higher is the collapsibility of the upper airway in apneic/hypopneic patients. This phenomenon has been observed more commonly in the supine position. There remain, however, problems in interpreting the presence of EFL in patients with OSAS and those with intrathoracic obstructive airway disease (COPD and asthma). Patients with the latter condition also exhibit EFL, although their expiratory flow pattern can sometimes be distinguished from those with OSAS. Because of these interpretive difficulties, the potential usefulness of the NEP technique as a diagnostic tool in daily clinical practice is unknown. The purpose of this study, therefore, is to determine the operating characteristics of the NEP technique in detecting OSAS in snoring patients, and to determine differences in the expiratory flow pattern during tidal breathing between patients with intrathoracic airway obstruction and those with extrathoracic airway obstruction. The measurements are recorded in seated and supine postures.

Pulmonary and Critical Care Medicine

Edward D. Crandall, Ph.D., M.D.

Gene Therapy. Cystic fibrosis (CF) is an inherited disease that causes severe lung disease in children and young adults. Abnormalities in the transport of salt and water within the patient's airways result in the production of thickened bronchial secretions and respiratory infection. Repeated lung infections cause destruction of lung tissue, resulting in progressive breathlessness, disability and mortality. We are developing programs for treating salt and water transport defects in patients using gene therapy. One object of this therapy is to introduce the normal form of a defective transport channel into the cell membranes of CF airway cells. The DNA sequence of the gene for this channel, known as the Cystic Fibrosis Transmembrane Regulator (CFTR), has been described. Following insertion of copies of this gene into a non-infectious carrier virus and introduction of the vector into airway cells having abnormal CFTR, the abnormal cell will produce normal CFTR. It is hoped that production of the normal channel will correct the transport defect and eliminate the pulmonary abnormalities seen in cystic fibrosis. Other publications of gene therapy are aimed at introducing genes into alveolar epithelial cells that will enhance clearance of pulmonary edema.

Patricio Escalante, M.D.

Molecular Epidemiology and Genetics in Tuberculosis. It is estimated that one third of the world's population is infected with *Mycobacterium tuberculosis*. Most TB cases and deaths occur in under-developed countries. An increased number of TB cases in the United States are foreign-born. Dr. Escalante and colleagues are pursuing a genetic characterization of *Mycobacterium tuberculosis* isolated with matching fingerprints from different geographic regions and studying mycobacterial genetic factors that could influence TB in humans using the isoniazid-resistant katG gene natural model.

Henry Gong, Jr., M.D.

Health-Related Effects of Air Pollution. Dr. Henry Gong directed the Environmental Health Service (EHS) at Rancho Los Amigos National Rehabilitation Center. The EHS primarily investigates health-related effects of air pollution. Clinical research remains a major focus of the EHS's interests and activities in which human health effects are investigated using controlled environmental chambers and exposing volunteers to different pollutants, such as ozone, nitrogen dioxide, particulates, sulfur dioxide and carbon monoxide. This work aims to provide a sound scientific basis for establishing regulatory policies that protect susceptible people. These projects are important to the citizens of Los Angeles County because of the need for high-quality information on the clinical and public health consequences of polluted air. Such information is essential to regulatory decision makers who must balance needs for public health protection with costs and competing concerns. The information is also important to physicians who must advise patients about protective strategies against air pollution.

Albert H. Niden, M.D.

Idiopathic Pulmonary Fibrosis Research Study. Idiopathic Pulmonary Fibrosis (IPF) or Usual Interstitial Pneumonia (UIP) is a not uncommon, slowly progressive disease of unknown etiology, which responds poorly to current available therapy. It is also a disease that is difficult to diagnose short of an open lung or thoracoscopic lung biopsy. Tumor Necrosis Factor (TNF), an inflammatory cytokine, has been shown to be associated with inflammation and fibrosis in patients with IPF. TNFR:Fc (Etanercept, Enbrel®) blocks TNF and has been shown to be safe and effective in treating patients with refractory rheumatoid arthritis. Dr. Niden and co-workers are utilizing a transthoracic core needle biopsy of the lung as an outpatient procedure to pathologically establish the diagnosis of IPF in patients with diffuse interstitial lung disease who have failed to respond to steroid therapy. Patients with TNFR are being treated and their response to therapy with serial pulmonary function and arterial blood gases are being objectively monitored. The study also correlates pathologic changes with lung HRCT and PET scan findings and assesses their ability to monitor response to therapy. Dr. Niden's group is also initiating a study to identify the cytokines, which promote inflammation and or fibrosis and are present in lung tissue from patients with various diffuse interstitial lung diseases. The researchers hope to identify patterns of cytokine deposition that may be specific for the various disease entities. This would lead to future studies with treatment targeted against specific cytokines to more effectively treat these diseases.

Om P. Sharma, M.D.

Predictors of Survival in Patients with Sarcoidosis. Sarcoidosis is a multi-organ system disease of unknown etiology that primarily affects the lungs, causing severe respiratory impairment in many individuals. Dr. Sharma and colleagues are currently analyzing 100 patients with sarcoidosis who have been closely observed for the last 15 years, with only those patients who have had at least once-a-year lung function evaluation included in the study. Changes in FVC (forced vital capacity), FEV1 (forced expiratory volume at one second)/FVC ratio, DLCO (diffusing capacity), and P(A-a)O₂ (alveolar-arterial O₂ difference) are being evaluated as predictors of survival in patients with sarcoidosis. A 10% increase in FVC, 20% increase in DLCO (single breath), 10% increase in FEV1/FVC ratio, and <5 mm Hg decrease in P(A-a)O₂ will define improvement. Kaplan-Meier survival plots and Cox proportional hazard regression model will be used to analyze survival time after one, three, and five years with and without therapy. This study will provide a rationale for the need and effectiveness of therapeutic regimens for individual patients, and the basis for future comparative therapy trials. Long term follow-up studies are in progress related to diagnosis and effects of new therapies in myocardial and neurological sarcoidosis.

Hideobu Shigemitsu, M.D.

Pathogenesis of Sarcoidosis. Sarcoidosis is still a disease of unclear etiology with protean clinical manifestations. One of the hypotheses for pathogenesis is an imbalance of T cell subtypes. We are actively investigating this link by collecting gammaglobulin levels prospectively in a large cohort of sarcoidosis patients in order to elucidate a pattern of sarcoidosis associated with abnormalities in gammaglobulin. In a prospective observational study, patients with sarcoidosis will be screened for pulmonary hypertension (PAH) by echocardiogram using the systolic pulmonary arterial pressure (PAP) and Tei-index. In patients with systolic PAP > 35mmHg, right heart catheterization (RHC) will be performed for confirmation. It is anticipated that PAH will be prevalent among patients with advanced radiographic findings, pertinent physical findings, and pulmonary function impairments. In these patients, measurement of systolic PAP in conjunction with Tei-index by echocardiography will accurately reflect the measurements by RHC.

Graciela J. Soto, M.D.

RCT of Activated Protein C for Treatment of Acute Lung Injury (ALI). Acute lung injury is a syndrome consisting of acute hypoxemic respiratory failure with bilateral pulmonary infiltrates that is associated with both pulmonary and nonpulmonary risk factors and that is not primarily due to left atrial hypertension. Once the hypoxemia is more severe, this syndrome is called Acute Respiratory Distress Syndrome (ARDS). Despite advances in the understanding of the pathophysiology, treatment, and long-term outcomes of ALI and ARDS, the only treatment modality shown to decrease mortality is lung protective mechanical ventilation with low tidal volumes. This is a concern due to recent data that show that ALI has a substantial public health impact in the U.S.—the incidence of ALI in the U.S. is 78 in 100,000 person-years with an in-hospital mortality of 38.5%. This translates into 190,600 cases of ALI which are associated with 74,500 deaths and 3.6 million hospital days. Recently, the pathophysiology of ALI and ARDS has been related to that of sepsis. The inflammatory cascade with its stimulation of the coagulation system and suppression of fibrinolysis seems to play a role in lung injury. Activated Protein C (APC) is an FDA approved new therapy for patients with severe sepsis and septic shock that has anti-inflammatory, anti-coagulant, and profibrinolytic activities *in vivo*. Dr. Soto and colleagues are part of a multicenter NHLBI-funded trial looking at the efficacy of APC for improving clinical outcomes in patients with ALI.

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Uchiyama T, Fujita T, Gukasyan HJ, **Kim KJ**, **Borok Z**, **Crandall ED**, Lee VHL: Functional characterization and cloning of amino acid transporter B0,+ (ATB0,+) in primary cultured rat pneumocytes. *J Cellular Physiol* 214:645-654, 2008.

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Sharma OP, Shigemitsu H: Diagnosis and treatment of sarcoidosis: 2008. Position Paper, California Thoracic Society/American Lung Association, 2008.

Type	Number Appeared	Number in Press	Number Submitted
Peer Reviewed Publications	12	4	2
Book and Book Chapters	4	2	0
Other Publications	8	0	0
Abstracts	27	4	4

Federal and Agency Grants

Principal Investigator	Agency Name	Title of Account or Grant	Annual Direct	Annual Indirect	Total	Beg Date	End Date
Baydur, Ahmet	University of California Tobacco-Related Disease Research Program	Role of Pneumocystis in COPD Progression	\$ 122,995	\$ 77,479	\$ 200,474	7/1/05	6/30/08
Borok, Zea	National Heart, Lung and Blood Institute	GATA-6: Key Regulator of AEC Transdifferentiation	90,868	57,121	147,989	9/1/86	11/30/07
Borok, Zea	National Heart, Lung and Blood Institute	Role of Fox P2 in AEC Transdifferentiation	219,220	138,109	357,329	8/15/00	7/31/09
Crandall, Edward	National Heart, Lung and Blood Institute	AT1 vs. AT2 Cells: Differential Roles in Alveolar Function and Biology	243,635	153,490	397,126	1/15/91	6/30/11
Crandall, Edward	National Heart, Lung and Blood Institute	Absorption Mechanisms for Peptide/Protein Drugs via the Lung	340,853	214,738	555,591	9/30/99	7/31/09
Demaio, Lucas	American Heart Association	Toxicity and Translocation of Nanoparticle in Lung	62,884	6,288	69,172	1/1/07	12/31/10
Escalante, Patricio	University of California, San Diego	Role of Pneumocystis in COPD Progression	98,631	62,137	160,768	7/1/05	6/30/08
Escalante, Patricio	University of Cincinnati	Serum Antibodies to Recombinant Pneumocystis Antigens	19,843	12,832	32,675	9/15/05	2/28/10
Rao, Adupa	Children's Hospital of Los Angeles	Clinical Research Facilitation Award	20,000	1,600	21,600	12/1/06	11/30/07
TOTAL:			\$ 1,218,929	\$ 723,794	\$ 1,942,723		

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Other Grants

Principal Investigator	Agency Name	Title of Account or Grant	Annual Direct	Annual Indirect	Total	Beg Date	End Date
Barbers, Rick	Asthmatx	Alair System for Asthma	\$ 14,868	\$ 3,717	\$ 18,585	1/27/06	Present
Barbers, Rick	Genentech	Xolair for Asthma Inadequately Controlled by Advair	2,376	594	2,970	3/1/06	Present
Barbers, Rick	Genentech	Xolair (Omalizumab) for Moderate to Severe Asthma	2,570	643	3,213	6/23/06	Present
Barbers, Rick	Altana Pharma	Effect of Roflumilast on Exacerbation Rate in Patients with COPD	1,237	309	1,546	7/11/06	Present
Barbers, Rick	Actelion	Bosentan for Idiopathic Pulmonary Fibrosis	640	160	800	10/12/06	Present
Barbers, Rick	Novartis Pharmaceuticals	Efficacy, Safety and Tolerability of Two Doses of Indacaterol	4,680	1,170	5,850	1/15/08	Present
Baydur, Ahmet	HRA	Seed Grant	1,974	493	2,467	2/14/08	Present
Ganesh, Sivagini	Novartis	TIFACOGIN (Recombinant Tissue Factor Pathway Inhibitor) Administration for Severe Community-Acquired Pneumonia	36	9	45	3/4/08	Present
Liebler, Janice	Artisan Pharma	ART-123 for Sepsis and Disseminated Intravascular Coagulation	5,846	1,462	7,308	8/6/07	Present
Rao, Adupa	Solvay Pharmaceuticals	Pancrelipase for Pancreatic Exocrine Insufficiency due to Cystic Fibrosis	2,637	659	3,296	1/18/08	Present
Rao, Adupa	Altus Pharmaceuticals	ALTU-135 Treatment for Cystic Fibrosis-Related Exocrine Pancreatic Insufficiency	10,025	2,506	12,531	2/28/08	Present
Rao, Adupa	Inspire Pharmaceuticals	Denufosal Tetrasodium Inhalation Solution for Cystic Fibrosis Lung Disease and FEV1	9,009	2,252	11,261	3/4/08	Present

Principal Investigator	Agency Name	Title of Account or Grant	Annual Direct	Annual Indirect	Total	Beg Date	End Date
Rao, Adupa	Genentech	Pulmozyme Withdrawal on Exercise Tolerance in Cystic Fibrosis Subjects with Severe Lung Disease	6,000	1,500	7,500	9/14/07	Present
Rao, Adupa	Mpex Pharmaceuticals	Pharmacokinetic Profile of MP-376 at Three Dose Levels Delivered by the Pari Eflow Electronic Nebulizer to Stable Cystic Fibrosis Patients	13,700	3,425	17,125	8/28/07	Present
Shigemitsu, Hidenobu	Pfizer	Linezolid for Nosocomial Pneumonia due to Methicillin-Resistant Staphylococcus Aureus	936	234	1,170	2/7/05	Present
Shigemitsu, Hidenobu	Intermune	Pirfenidone in Patients with Idiopathic Pulmonary Fibrosis	5,834	1,459	7,293	11/27/06	Present
Shigemitsu, Hidenobu	Pricara	Nosocomial and Ventilator-Associated Pneumonia in Hospitals where Pseudomonas Aeruginosa May be Prevalent	3,200	800	4,000	3/10/08	Present
Soto, Graciela	University of California, San Francisco	Activated Protein C for Acute Lung Injury	830	208	1,038	3/22/06	Present
Soto, Graciela	Takeda	TAK-242 in Adults with Severe Sepsis	2,912	728	3,640	1/18/07	Present
TOTAL:			\$ 89,310	\$ 22,328	\$ 111,638		