The Division of Pulmonary, Critical Care and Sleep Medicine (PCCSM) provides a vigorous, creative basic and clinical science core, with an active clinical service and a high-quality training program. The Division provides services at all three Health Sciences Campus teaching hospitals: LAC+USC Medical Center (LAC+USC), Keck Hospital of USC (KH) and USC Norris Cancer Hospital (Norris). Our 22 nationally and internationally recognized full-time faculty members share the combined research, clinical and teaching mission. The Division provides services in seven Intensive Care Units, three faculty and fellows published XX peer-reviewed research papers and received more than $2.75 million in research funds in 2012-2013.

Pulmonary, Critical Care & Sleep Medicine

Zea Borok, MD
Professor and Chief
Senior Clinical Administrator
Barbara Farrell, MBA

Pulmonary, Critical Care
& Sleep Medicine

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The PCCSM Division remains strongly committed to providing the best possible educational environment and learning opportunities for USC medical students, residents, fellowship trainees and practicing physicians. Daily formal attending rounds are conducted on all division services for medical students, residents and fellows. These rounds take place at the bedside and culminate in multidisciplinary discussions 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, as well as quality improvement. In-depth lectures in clinical and basic research as well as journal clubs 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 PCCSM 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

Professor of Medicine
Debasish Tripathy, MD (Clinical Scholar)  
Art and Priscilla Ulene Chair in Women’s Cancer
Richard G. Barbers, MD (Clinical)
Ahmet Baydur, MD (Clinical)
Zei Borok, MD  
Ralph Edgerton Chair in Medicine
Edward D. Crandall, PhD, MD  
Honoring Professor of Medicine
Kenneth T. Norris Jr. Chair of Medicine
Kwang-Jin Kim, PhD
Janice M. Liebler, MD (Clinical)
Albert H. Niden, MD (Clinical)
Edward D. Crandall, PhD, MD  
Ralph Edgington Chair in Medicine
Richard G. Barbers, MD (Clinical)
Janice M. Liebler, MD (Clinical)
Albert H. Niden, MD (Clinical)
Ami Oren, MD (Clinical)

Associate Professor of Medicine
Thomas C. Boylen, MD (Clinical)
David M. Kelley, MD (Clinical)
Richard L. Lubman, MD
Renli Qiao, MD, PhD (Clinical)
Hidenobu Shigemitsu, MD (Clinical)

Assistant Professor of Medicine
Kamyar Afshtar, DO (Clinical)
Alex A. Balekian, MD (Clinical)
Ching-Fei Chang, MD (Clinical)

Ulf Per Floby, PhD (Research)
Sivagini Ganesh, MD (Clinical)
Teresa C. Hammond, MD (Clinical)
Richard H. Juarez, MD (Clinical)
Santhi Iyer Kumar, MD (Clinical)
Boris L. Medarov, MD (Clinical)
Michael S. Newman, DO (Clinical)
Adapa P. Rao, MD (Clinical)
Robert S. Swinney, MD (Clinical)
Beiyun Zhou, PhD

LAC+USC Medical Center

The PCCSM Division operates three Medical Intensive Care Unit services at LAC+USC. In addition, the Division provides consultative services to inpatients and to intensive care units of other divisions and departments, including internal medicine, surgery (including trauma), neurology, neurosurgery, burns, emergency medicine and cardiology. The Division conducts a weekly Chest Continuity Clinic, at which members and fellows evaluate new patients and provide consults to care for established patients. Each year, members of the Division conduct approximately 4,800 outpatient visits, see approximately 600 consultations and perform about 600 bronchoscopic examinations, as well as numerous other procedures including bronchoalveolar lavage, transbronchial and percutaneous needle biopsy and endobronchial ultrasound (EBUS). The Pulmonary Physiology Laboratory and Sleep Center under the medical direction of the Division performs an average of 5,000 lung function tests and 2,000 sleep studies every year.

Clinical Activities

Chest Continuity Clinic
The Division conducts a weekly Chest Continuity Clinic, at which members and fellows evaluate new patients and provide consults to care for established patients. Each year, members of the Division conduct approximately 4,800 outpatient visits, see approximately 600 consultations and perform about 600 bronchoscopic examinations, as well as numerous other procedures including bronchoalveolar lavage, transbronchial and percutaneous needle biopsy and endobronchial ultrasound (EBUS). The Pulmonary Physiology Laboratory and Sleep Center under the medical direction of the Division performs an average of 5,000 lung function tests and 2,000 sleep studies every year.

Private Practice

Keck Hospital of USC
The PCCSM Division participates in the care of patients at four Intensive Care Units at KH, involving the care of inpatients with a wide spectrum of lung and critical illnesses. The PCCSM fellow performs all diagnostic and therapeutic procedures, including bronchoscopies, under the supervision of an attending physician. Specialized, multidisciplinary programs that provide patient-centered care include the Lung Transplantation Center, Adult Cystic Fibrosis Center, Center for Advanced Lung Disease, Multidisciplinary Center for Lung Cancer Management, Sleep Center and Pulmonary Hypertension Center.

USC Norris Cancer Hospital
Norris provides an unparalleled opportunity to deliver care to a large number of patients with malignancy, immunosuppression and bone marrow transplantation. The PCCSM fellow carries out all consultations and performs all diagnostic, invasive and noninvasive, and therapeutic procedures under the supervision of the attending staff. Lung cancer patients are seen at the Multidisciplinary Center for Lung Cancer Management.

Special Clinical Services

The PCSM Division has established several clinical programs of excellence, each of which offers specialized treatment of various pulmonary disorders, as well as an educational setting for fellowship training.

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 allergy nurse specialists, respiratory therapists, nutritionists and pharmacologists. A state-of-the-art pulmonary function laboratory has capabilities for airflow measurements, including methacholine challenge studies to detect hyperreactive 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 aspergillosis, 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. Other novel therapeutic interventions offered include omalizumab. The Division is also the first academic program in Southern California to establish Bronchial Thermoplasty as a novel therapeutic option for severe asthmatics under the direction of Dr. Richard Barbers.

This past spring, our division successfully launched the USC Bronchial Thermoplasty Program for the treatment of severe refractory asthma. Between the KH and LAC+USC sites, we have performed 14 of these complicated procedures to date, with excellent results. Drs. Richard Barbers, Ching-Fei Chang, Ricardo Juarez and David Kelley comprise the interventional arm of this program, while Dr. Edward Hu manages the clinical aspects of care. Because of Dr. Barbers’ and Dr. Juarez’s involvement as primary investigators in the original AIR2 study that led to FDA approval of this procedure for asthma, we anticipate developing into a center of excellence for Bronchial Thermoplasty in the near future.

The USC Sleep Disorders Center underwent a dramatic redesign and expansion this year. After incorporation into the Center for Advanced Lung Disease (CALD) and because of increased referrals, the Sleep Center itself doubled its capacity to four beds. Staffing was internalized and a full-time senior technologist, Edwin Valladares, was recruited. KH also extended institutional support for a Sleep Medicine fellowship to commence on July 1, 2014; it will be multidisciplinary but will be housed under the core Internal Medicine program. In terms of research, we were added to the Sleep Translational Science Core, which focuses on translational research in sleep-disordered breathing. We have also conducted the first investigation of transvenous phrenic nerve stimulation for the treatment of central sleep apnea. Further growth is anticipated this year as the Sleep Center expands into limited channel (home) sleep testing, secures laboratory accreditation through the American Academy of Sleep Medicine (AASM) and strengthens community collaborations, such as the one initiated with USC Verdugo Hills Hospital.

The USC Pulmonary Exercise Program provides outpatient exercise evaluations. Exercise studies are performed with state-of-the-art equipment by 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 cause for the impairment. Information obtained from the study can be used to tailor specific exercise regimens and therapeutic strategies. The program offers Standard Pulmonary Stress Tests, Oxygen Desaturation Studies, Exercise-induced Bronchospasm Studies and Metabolic Studies. The Medical Director of Respiratory Services is Dr. David Kelley.

The High-Altitude Simulation Test (HAST) is a specialized type of oxygenation study available in our Pulmonary Function Laboratory at KH. 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, and it is performed at rest and with gradients of activity. The Medical Director is Dr. David Kelley.
The USC Pulmonary Rehabilitation Program based at LAC+USC offers a wide range of services to patients with chronic pulmonary disease, from single sessions focused upon a specific need (such as training in the use of metered dose inhalers) to a comprehensive program consisting of two afternoons per week for a total of six to eight weeks. The comprehensive program includes exercise training, patient education, psychosocial support services, physical therapy, vocational therapy, symptom control techniques and the use of low-flow oxygen. Patients typically referred to the program include those with emphysema and pulmonary fibrosis. The program also offers on-site educational opportunities for pulmonary fellows with emphasis on respiratory physiology, quality-of-life assessment and key aspects of evaluating physical impairment and disability. The Program Medical Director at LAC+USC is Dr. Ahmet Baydur.

The USC Multidisciplinary Lung Cancer Program includes several faculty members from PCCSM who actively participate in the evaluation, diagnosis and management of patients with thoracic cancers. Every Friday morning, Drs. Ching-Fei Chang and Alex Balekian, along with representatives from medical oncology, radiation oncology and thoracic surgery, staff the Multidisciplinary Lung Cancer Clinic at Norris, which is designed to streamline the coordinated assessment of patients with or suspected of having lung cancer. They also provide pulmonary expertise and input at the weekly Thoracic Tumor Board, as well as teaching and guidance in the management of lung cancer patients at the LAC+USC Pulmonary Clinic every Wednesday afternoon. Each faculty member also has a separate private clinic in which they assist with evaluation and management of dyspnea and other respiratory complications, which may arise during the course of oncologic treatment.

Dr. Chang also provides interventional bronchoscopy services for the minimally invasive diagnosis and staging of lung cancer, using state-of-the-art technology such as Endobronchial Ultrasound (EBUS), Electromagnetic Navigation and Medical Thoracoscopy. Not only are these cutting-edge outpatient procedures less invasive and more comfortable for patients than traditional surgical options, but they offer comparable diagnostic yield at a fraction of the cost. Since January 2010, Dr. Chang has successfully performed 180 EBUS procedures under conscious sedation at LAC+USC and KH, with an 80%-90% diagnostic yield for malignancy. This has translated into an estimated cost savings of $2,000 per case of avoided mediastinoscopy at LAC+USC (based on Medicare facility fees) and no major complications to date. As the newly launched USC Lung Cancer Screening Program gains momentum, this trend of improved resource allocation will likely be seen at KH as well.

The USC Center for Advanced Lung Disease is a newly established program that deals with the diagnosis and treatment of all types of complex lung diseases. In addition to cystic fibrosis and sleep breathing disorders, the Center for Advanced Lung Disease houses clinics specializing in chronic obstructive pulmonary disease, sarcoidosis and interstitial lung disease, including idiopathic pulmonary fibrosis, hypersensitivity pneumonitis, collagen vascular lung disease, eosinophilic granuloma, pulmonary eosinophilia and other rare lung diseases. The USC Center for Advanced Lung Disease has recently been designated as an Alpha-1 Foundation Clinical Resource Center. The Medical Director of the Center is Dr. Kamyar Afshar.

The USC Sarcoidosis and Interstitial Lung Disease Center is now housed under the USC Center for Advanced Lung Disease. The Center continues to deal 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 40 years, and led by the late world-renowned expert Dr. Om Sharma, these services have been provided to patients from all over the world.

The USC Comprehensive Adult Cystic Fibrosis Center provides direct care and consultation for adult cystic fibrosis patients. The cystic fibrosis care team is headed by pulmonologists supported by a full range of consultants, including endocrinologists, gastroenterologists, otolaryngologists, infectious diseases experts, general surgeons and cardiothoracic surgeons. Allied health services are provided by pulmonary clinical nurse specialists, dieticians, 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. Dr. A. Purush Rao serves as Medical Director and Dr. Kamyar Afshar is the Associate Director.
Lung transplantation is a treatment option for many patients with end-stage pulmonary disease. The USC Lung Transplant Program at Keck Medical Center of USC is comprised of experts in cardiothoracic surgery, cardiology, pulmonary medicine, immunology, infectious disease, critical care medicine, cystic fibrosis, perfusion medicine, immunosuppression pharmacology, occupational and physical rehabilitation, and social/psychological services. Patients eligible for lung transplantation include those severely debilitated by cardiopulmonary disease and not hampered by 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). Living related lobar lung transplantation in adults was pioneered at USC and offers a comprehensive and multidisciplinary approach to patients with this rare and very serious disorder of the blood vessels of the lung. Patients with pulmonary hypertension are frequently not recognized until they have advanced disease because early symptoms can lead to misdiagnosis. A higher level of awareness and development of a comprehensive treatment plan can dramatically improve quality of life and prognosis for patients with this life-threatening condition. Many therapeutic modalities are highly complex and require intensive patient education and ongoing follow-up with subspecialty physicians and nurse specialists. Medical services such as continuous prostanoid therapy, high-dose calcium channel blocker therapy, anticoagulation therapy and home oxygen therapy are provided and coordinated for patients as needed. When appropriate, referrals are made for physical occupational therapies, home health nursing services and rehabilitation services.

Pulmonary hypertension research is rapidly growing, and patient education and communication are essential to support that growth. We have created pulmonary hypertension support groups to help our patients cope with their illnesses and learn more about their diagnoses. We offer the following:

• Knowledge: Medical information delivered by pulmonary hypertension experts and medical professionals.
• Support: Coping skills shared by patients.
• Hope: Opportunity to interact with and meet patients who have been managing their pulmonary hypertension for 20 years or longer.
• Empowerment: A way to get involved, give back and be part of the solution to finding a cure.

Patients with Pulmonary Hypertension are evaluated and followed by Medical Director Sivagini Ganesh, MD, and Renli Qiao, MD.

**Educational Activities**

The PCCSM Fellowship Program is designed to provide each trainee with a range of exposure to the diagnosis and management of pulmonary diseases, the experience and skills required of an intensivist and the opportunity to develop research interests. Seven new fellows are currently admitted to the program every year. Clinical and teaching responsibilities encompass most of the first and second years, with a significant part of the third year devoted to research activities. During the clinical phase of the training, fellows devote their time to evaluation, diagnosis and treatment of patients admitted to LAC-USC, KH and Norris. Fellows assess problems, make appropriate diagnostic and therapeutic recommendations and perform specialized procedures, including fiberoptic bronchoscopy, percutaneous needle biopsy of the lung and pleura, thoracentesis and pleurodesis. The trainee receives instruction in pulmonary function and x-ray interpretation, including high-resolution computerized tomography (HRCT), the principles and techniques of mechanical ventilation and inhalation therapy, and all aspects of pulmonary, critical care and sleep medicine.

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.

**PCCSM Fellows**

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<tr>
<th>First Year</th>
<th>Second Year</th>
<th>Third Year</th>
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<tr>
<td>Joleen Aguen, MD</td>
<td>Vincent Cunanan, MD</td>
<td>Michelle Bussinguer, MD</td>
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<tr>
<td>Ian Lee, MD</td>
<td>Nona Mei, MD</td>
<td>Sam Eljammal, MD</td>
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<td>Nalin Mallik, MD</td>
<td>Marcus Ottochian, MD</td>
<td>Rajiv Philip, MD</td>
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<td>Aniikki Chawla Mittal, MD</td>
<td>Lejeeo Pallicikal, MD</td>
<td>Moshen Rofoogaran, DO</td>
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<td>Anil Perumbeti, MD</td>
<td>Vimal Ponnezhathan, MD</td>
<td>Charanpal Singh, MD</td>
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<td>Mohammed Aref Rashad, MD</td>
<td>Kaveh Rezvan, DO</td>
<td>Natalie Skow, MD</td>
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<tr>
<td>Mark Valdez, MD</td>
<td>Luke White, DO</td>
<td>Owais Zaidi, MD</td>
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**Conferences**

Our strong commitment to teaching is evident in an extensive daily conference schedule, starting at 8:30 am and consisting of didactic lectures, multidisciplinary case conferences, grand rounds, morbidity and mortality conferences, and research seminars on various aspects of pulmonary, critical care and sleep medicine and related sciences. Combined thoracic surgery and thoracic oncology conferences (Tumor Board) are held every Friday at 12:30 pm, alternately at Norris and KH.

Monthly Journal Clubs stress the importance of evaluating, analyzing and presenting medical research literature. Guest lectures and both clinical and basic research seminars featuring 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 patient care. Full-time faculty conduct bedside rounds as well as clinical discussions. House staff, medical students, fellows and attending physicians participate in these daily rounds.

**Research Activities**

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, macromolecule and nanoparticle 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; transcriptional regulation of lung cell growth, differentiation and gene expression in vitro and in vivo; the role of epithelial cell plasticity in pulmonary fibrosis and stem cells in lung injury and repair; and epigenetic regulation of alveolar epithelial cell differentiation. 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), tuberculosis, cystic fibrosis, lung transplantation, pulmonary hypertension and health care outcomes are underway.

Dr. Zea Borok is Associate Director of the Will Rogers Institute Pulmonary Research Center, the major research operation of the Division. The primary focus of the laboratory has been on understanding the function of the cells lining the lung, known as alveolar epithelial cells (AEC), in order to understand how the lung repairs itself following...
Faculty Research Areas

C. Thomas Boylen, MD
Biology of Lung Stem Cells
Role of Alveolar Epithelium in Pulmonary Modulation of Alveolar Epithelial Cell Transcriptional and Epigenetic Regulation of

Zea Borok, MD
Neuromuscular Disorders
Control of Ventilation
Respiratory Mechanics

Ahmet Baydur, MD
Novel Therapeutic Interventions (Bronchial Potential Therapies for Remodeling in
Mechanisms of Remodeling in Near-Fatal

Richard G. Barbers, MD
Outcomes and Cost-Effectiveness of Care for
Alex A. Balekian, MD
COPD/Alpha-1 Antitrypsin Deficiency
Lung Transplantation

Kamyar Afshar, DO
Injury
Plasticity
Alveolar Epithelial Cell Differentiation/

Kwang-Jin Kim, PhD
Lung Epithelial Cell Biology
Cell-Based Therapy for Lung Diseases
Regulation of Tight Junctions in Alveolar
Active and Passive Transport Properties of
Pulmonary Drug Delivery

Kong-Jin Kim, PhD
Pulmonary Drug Delivery
Active and Passive Transport Properties of
Airway and Alveolar Epithelium
Regulation of Tight Junctions in Alveolar Epithelium

Renli Qiao, MD, PhD
Mechanisms of Alveolar Homeostasis and Pulmonary Vascular Diseases
Pulmonary Hypertension

A. Purush Rao, MD
Architectural Fibrosis
Mechanisms of Remodeling in the Lung

Hidenobu Shigematsu, MD
Sarcoidosis
Veno-veno-venous Bacterial Disease
Pulmonary Hypertension
Intestinal Lung Disease

Robert S. Swinney, MD
Obesity Effects on Respiratory Function
Control of Ventilation
Ami Oren, MD
Rare Lung Diseases
Interventional Bronchoscopy
Cystic Fibrosis
Chronic Obstructive Pulmonary Disease
Lung Rehabilitation

Edward D. Crandall, PhD, MD
Mechanisms of Remodeling in Near-Fatal Asthma
Potential Therapies for Remodeling in Pulmonary Fibrosis
Novel Therapeutic Interventions (Bronchial Thermoplasty) in Severe Asthma

Ahmet Baydar, MD
Respiratory Mechanics
Control of Ventilation
Neurovascular Disorders
Chronic Obstructive Pulmonary Disease
Lung Rehabilitation

Zea Borok, MD
Transcriptional and Epigenetic Regulation of Alveolar Epithelial Cell Differentiation/Plasticity
Modulation of Alveolar Epithelial Cell Phenotype and Recovery Following Lung Injury
Role of Alveolar Epithelium in Pulmonary Fibrosis
Biology of Lung Strom Cells
Transport and Barrier Properties of Pulmonary Airway Epithelium
Alveolar Epithelium
C. Thomas Boylen, MD
Oxygen Therapy in COPD

Immunological Diseases of the Lung
Fleural Diseases
Nocturnal Oxygen Therapy Trial
Effects of Formaldehyde Exposure

Chung-Fei Chang, MD
Interventional Bronchoscopy
Medical Thoracoscopy
Bronchial Thermotherapy for Asthma
Critical Care Ultrastructural Pathology
Medical Education

Edward D. Crandall, PhD, MD
Acute and Chronic Lung Injury and Factors that Influence Recovery
Barrier Properties of Pulmonary Alveolar Epithelium
Nanoparticle Interactions with Lung
Regulation of Pulmonary Alveolar Epithelial Cell Differentiation

UBP Per Flodby, PhD
Development of Transgenic Mouse and Rat Models for Lung Research
Lung Injury and Repair of Alveolar Epithelium
Lung Ion Transport
Alveolar Epithelial Tight Junction Regulation

Svyatos Ganedi, MD
Lung Transplantation
Pulmonary Hypertension

Ricardo H. Juarez, MD
Mechanical Ventilation in Respiratory Failure
Endothelial Inhibition in the ICU

Kwang-Jin Kim, PhD
Pulmonary Drug Delivery
Active and Passive Transport Properties of
Airway and Alveolar Epithelium
Regulation of Tight Junctions in Alveolar Epithelium

Janice M. Liebler, MD
Cell-Based Therapy for Lung Diseases
Lung Epithelial Cell Biology

Lung Injury and Repair
Lung Transplantation
Critical Care Medicine

Richard Lubman, MD
Rare Lung Diseases

Albert H. Niden, MD
Pathogenesis, Diagnosis, and Treatment of Diffuse Interstitial Lung Disease

Ami Oren, MD
Physiology in Health and Disease Control of Ventilation
Obesity Effects on Respiratory Function

Renli Qiao, MD, PhD
Mechanisms of Alveolar Homeostasis and Pulmonary Vascular Diseases
Pulmonary Hypertension

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Edward D. Crandall, PhD, MD, Director, Will Rogers Institute Pulmonary Research Center
Regulation of Alveolar Epithelial Cell Differentiation and Phenotypic Plasticity in Lung Injury, Fibrosis and Repair.
The alveolar epithelium lining the gas exchange surface of the adult lung consists of two highly specialized cell types, type I and type II. These cell types are distinguished from each other by their characteristic morphologic appearances and by expression of unique cell-specific phenotypic markers. Aquaporin-5 (AQ5) 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 that regulate cell-specific expression of AQ5 in order to understand how gene expression is regulated in type I cells. She and her associates have isolated the regulatory (promoter) region of AQ5 from rat genomic DNA and are using this promoter as a prototype for type I cell genes to investigate the role of candidate transcription factors in regulating phenotypic transitions between type II and type I cells. Dr. Borok has also recently demonstrated that alveolar epithelial cells (AEC) exhibit plasticity, and that following treatment with certain growth factors they can be induced to acquire mesenchymal characteristics, thereby contributing to development of lung fibrosis. Strategies to inhibit this transition (e.g., through inhibition of Wnt signaling pathway) and prevent fibrosis are being explored. These studies, which are funded by NIH/NHLBI, will provide important insights into mechanisms that regulate repair of the alveolar epithelium following injury and could lead to the development of novel therapeutic approaches for lung fibrosis by preserving the epithelium. Dr. Borok is also investigating the role of epigenetic changes in regulation of phenotypic transitions of AEC. In addition, she is using genetically modified mouse models to investigate regulatory pathways in normal and abnormal alveolar epithelial cell differentiation.

Edward D. Crandall, PhD, MD, Director, Will Rogers Institute Pulmonary Research Center
Genes and Environment 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). Dr. Crandall and his group are comprehensively studying many additional aspects of alveolar lung cell biology and lung interactions with nanomaterials. Current projects include studies on interactions of inhaled nanoparticles with the alveolar epithelial barrier, on mechanisms of alveolar fluid clearance from the lungs, and on alveolar epithelial cell differentiation after lung injury. The ultimate goal of these studies is to better understand interactions between environmental factors and the lung and to develop new therapeutic approaches for diseases that cause respiratory failure due to excess alveolar fluid (i.e., pulmonary edema).
The Division published XX peer-reviewed research papers in 2012-2013, and XX more are in press. Of these, three studies are especially noteworthy accomplishments.

Highlighted Publications

Ulf Per Flodby, PhD, Investigator, Will Rogers Institute Pulmonary Research Center

Development of Transgenic Mice and Rat Models for Modulation of Gene Expression in Alveolar Epithelial Cells. Dr. Flodby is using in vivo approaches to modulate gene expression in alveolar epithelial cells. Capitalizing on the efficient Cre/LoxP DNA recombination system, he is using state-of-the-art approaches to develop mouse and rat models in which genes can be deleted specifically in type I cells, or in type II cells, or in both cell types. Development of these animal models will facilitate investigation of the contribution of type I and/or type II cells to alveolar homeostasis and the role of specific genes in alveolar epithelial cell function and biology. Genes of specific interest are involved in active ion transport, formation and function of tight junction complexes or in lung fibrosis. Dr. Flodby has gained considerable experience from in vivo analyses to evaluate effects of gene deletions (knockouts) on pulmonary function in these animal models. These experiments will result in important insights into mechanisms that regulate alveolar homeostasis in health and disease.

Beiyun Zhou, PhD, Investigator, Will Rogers Institute Pulmonary Research Center

Transcriptional Regulation of Alveolar Epithelial Cell (AEC) Differentiation and Epithelial-Mesenchymal Transition (EMT)/Fibrosis. Dr. Zhou’s research focuses on alveolar epithelial cell biology in general and delineation of mechanisms regulating AEC function and differentiation in the context of lung injury and repair. A major focus has been to elucidate pathways (e.g., Wnt/β-catenin, FoxO3a and GATA6) that regulate normal differentiation of the alveolar epithelium in order to understand how they are altered in disease and injury. She has demonstrated that the alveolar epithelium has considerable phenotypic plasticity, and recently reported that the alveolar epithelium itself can undergo EMT and express mesenchymal markers in response to TGF-β signaling or injuries (e.g., endoplasmic reticulum [ER] stress), suggesting a direct contribution of the epithelium to the pathogenesis of pulmonary fibrosis. These studies have capitalized on in vitro models developed using isolated rat, mouse or human type II cells which, when placed in culture, undergo differentiation to a type I cell-like phenotype. Studies have been expanded to explore epigenetic mechanisms that regulate AEC plasticity and understand their roles in EMT/fibrosis using integrated transcriptomic and epigenomic analysis in collaboration with the Epigenome Center at USC. Elucidating transcriptional/epigenetic mechanisms that regulate gene expression within the alveolar epithelium should provide novel insights into mechanisms of alveolar epithelial cell homeostasis under both normal and pathologic conditions and also offers the potential for future translational application to lung disease through modulation of signaling pathways and epigenetic changes with various small-molecule inhibitors.

Richard G. Barbers, MD

Chronic Inflammation and Remodeling in Asthma. Remodeling may occur in mild, moderate and severe asthma and may be a reason for persistent and refractory asthma episodes. However, not all asthma patients manifest remodeling. There may be differences in the genetic, inflammatory and immune responses. In order to delineate these processes in the airways, severe asthmatic subjects undergo 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 attempts to show abnormal repair processes (which include inflammatory and immune mechanisms) and growth factors eventually lead to airway fibrosis (remodeling). Collaborative efforts with basic and translational scientists will eventually yield results that can lead to successful interventions to alter the remodeling process in the airways.

A. Purush Rao, MD

Cystic Fibrosis. The adult Cystic Fibrosis (CF) program was established in 1994 and has expanded in volume to 194 patients. The program has been accredited by the Cystic Fibrosis Foundation (CFF) and actively participates in CFF-sponsored research and quality improvement programs. The expansion of this program has provided an opportunity for multiple faculty members to be involved in research studies of CF patients. The program has increased the number of investigator-initiated studies to include studies of drug distribution, delivery and metabolism in CF patients, and therapeutic factors important in maintaining lung function.
Functional relevance for alveolar differentiation. Our incorporation of epigenetic data allowed specific identification of transcription factors that are potential direct upstream regulators of the differentiation process, demonstrating the power of this approach. Integration of epigenomic data with transcriptomic profiling has broad application for the identification of regulatory pathways in other models of differentiation.

**Division Highlights**

**Zea Borok, MD**  
- Associate Editor, American Journal of Respiratory Cell and Molecular Biology  
- Member, Lung Injury Regeneration and Repair (LIRR) NIH Study Section  
- Member, Planning Committee, Assembly on Respiratory Cell and Molecular Biology of the American Thoracic Society

**Kamyar Afshar, DO**  
- Assisted with television story lines on Grey’s Anatomy, Royal Pains and Army Wives.  

**Alex Balekian, MD, and Ching-Fei Chang, MD**  
- The USC Multidisciplinary Lung Cancer Program including Dr. Chang and Dr. Balekian successfully organized and hosted its first CME regional symposium on state-of-the-art advances in this rapidly changing field.  
- Drs. Chang and Balekian have also lectured as a team at many community-outreach events, including the “Health Matters” series and a college course at California State University in Pomona.

**Terese Hammond, MD**  
- Participated in an “Alternative Therapies for Sleep Apnea” Community Forum at Verdugo Hills Hospital in Glendale, California, on February 7, 2013. More than 100 people attended this successful event.

**Janice Liebler, MD**  
- Member, International Conference Program Planning Committee, Critical Care Assembly of the American Thoracic Society  
- Basic and Translational Sciences Section Head for the online Journal Club, Critical Care Assembly of the American Thoracic Society  
- Principal Investigator, USC site for the Critical Illness Outcomes Study (CIOS), a multicentered study of 52 ICUs across the U.S. This study is part of the U.S. Critical Illness and Injury Trials (USCIIT) Group, which is an NIH-funded organization that fosters investigator-initiated hypothesis testing for critical care topics at the national level.

**Renli Qiao, MD, PhD**  
- Global Advisor, American College of Chest Physicians  
- General Secretary, International Advisory Committee, Chinese Society of Respiratory Medicine and Respiratory Branch, Chinese Medical Association  
- Member, Joint Steering Committee for PCCM fellowship training in China, American College of Chest Physicians and Chinese Society of Respiratory Medicine

**Major Lectures**

**Kamyar Afshar, DO**  
April 2013 – Sarcoidosis: Treatment of Pulmonary and Extra-Pulmonary Disease, Interstitial Lung Disease and Pulmonary Hypertension: 2013 State-of-the-Art for the Clinician, Cedars-Sinai Medical Center/Harvey Morse Conference Center, Los Angeles, CA

**Richard Barbers, MD**  
April 2013 – Bronchothermoplasty for Difficult Asthma Management: Back to the Future, L.A. American Lung Association, Los Angeles, CA

**Zea Borok, MD**  
October 2012 – Epithelial-Mesenchymal Transition (EMT) in Pulmonary Fibrosis: Manifestation of Alveolar Epithelial Cell Injury? Second Annual Munich Lung Conference, Munich, Germany

**Ching-Fei Chang, MD**  
May 2013 – Impact Factor “X”: Introduction of Advanced Bronchoscopic Procedures, Harbor-UCLA Medical Center, Los Angeles, CA

**Renli Qiao, MD, PhD**  
April 2013 – Pulmonary Embolism in 2013, Peking Union Medical College-American College of Chest Physicians Summit Conference on Respiratory Medicine, Beijing, China

**Awards & Honors**

**Edward D. Crandall, PhD, MD**  
Best Doctors of America

**Swagun Gaberdi, MD**  
Best Doctors of America

**David Kelly, MD**  
Teacher of the Year, Division of Pulmonary, Critical Care and Sleep Medicine  
Faculty Teaching Incentive Award, Department of Medicine

**Renli Qiao, MD**  
Robert McCallum Humanitarian Award, American College of Chest Physicians