

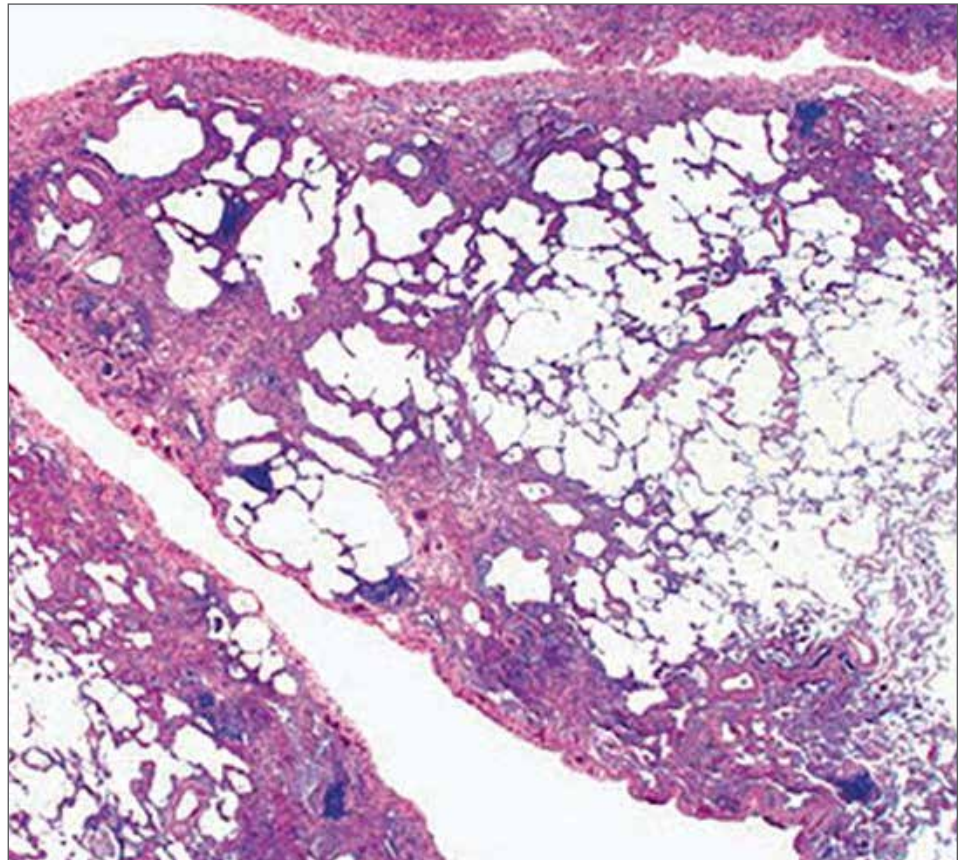
## Therapies for Idiopathic Pulmonary Fibrosis

Multicenter trials conducted at the Icahn School of Medicine at Mount Sinai led to Federal Drug Administration (FDA) approval of pirfenidone, one of the first two approved therapies for idiopathic pulmonary fibrosis (IPF). Maria L. Padilla, MD, Professor of Medicine, Pulmonary, Critical Care, and Sleep Medicine, was the principal site investigator for this and several other trials of therapies for IPF, a chronic, fibrosing lung disease of unknown cause.

Pirfenidone is a small, synthetic nonpeptide molecule of low molecular weight. Although its mechanism of action is not completely understood, data suggest that pirfenidone is a selective regulator of gene expression triggered by signals from a variety of cytokine factors, including transforming growth factor (TGF) - $\beta$ 1, platelet-derived growth factor (PDGF), and tumor necrosis factor-alpha (TNF- $\alpha$ ).

IPF is progressive, debilitating, and occurs predominantly in older adults. The median survival of patients with IPF is 3.8 years from diagnosis. It is estimated to occur in 0.2 percent of individuals older than 75 years, and the incidence in the Medicare population is about 42,000 cases per year.

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Surgical lung biopsy demonstrating septal and peripheral fibrosis consistent with IP pattern. There is intervening normal lung architecture and on higher power, fibroblastic foci are appreciated.

### CLINICAL TRIALS

## New Tools to Help Control and Treat Asthma

Linda Rogers, MD, Clinical Director, Adult Asthma Program at the Mount Sinai - National Jewish Health Respiratory Institute, helped develop and launch the Asthma Health App and the Asthma Mobile Health Study in March 2015. Dr. Rogers worked in collaboration with Apple Inc., Sage Bionetworks, and the Digital Health Team at the Icahn Institute for Genomics and Multiscale Biology.

This study is poised to be one of the largest, ongoing real-time epidemiological studies of asthma across the United States. To date there have been over 50,000 downloads, and more than

7,000 participants have enrolled in the study. The app is currently available for free download online in the App Store.

Asthma Health is one of the first disease apps for the Apple Research Kit, an open source software framework designed for developing iPhone apps for medical research. It contains asthma educational and disease management tools, and daily medication reminders. Simultaneously, it allows participants to engage in asthma research from home on their iPhones. Our long-term vision is to integrate Asthma Health with electronic medical records,

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Charles A. Powell, MD, Chief, Catherine and Henry J. Gaisman Division of Pulmonary, Critical Care and Sleep Medicine, and Janice and Coleman Rabin Professor of Pulmonary Medicine

## Advancing Medicine and Research

The Division of Pulmonary, Critical Care and Sleep Medicine continues to expand its research and clinical programs to investigate the underlying causes of respiratory diseases and discover better ways to treat them. This year's *Chief's Report* features articles on innovative studies by two of our young investigators on, respectively, the effect of early life environmental exposure to various substances and its impact on respiratory disease in later life in India, Bangladesh, Ghana, and New York City; and on improving health care delivery for critically ill patients in the Emergency Room Intensive Care Unit. This *Chief's Report* also highlights clinical trials for the chronic disease Idiopathic Pulmonary Fibrosis (IPF); a new app and mobile health study that we are conducting with Apple Inc. and other participants; and the Center for Advanced Medical Simulation (CAMS), which enhances the education and training of residents and fellows in our division, and throughout the Mount Sinai Health System.

### › Therapies for Idiopathic Pulmonary Fibrosis *continued from page 1*

An IPF diagnosis is established by a pattern of usual interstitial pneumonia (UIP), either by a high resolution CT scan of the chest (HRCT) or by histologic evidence of UIP; and exclusion of alternative causes, including connective tissue disease, chronic hypersensitivity pneumonitis, occupational lung diseases, and drug toxicity. *See slides on pages 1 and 2.*

Over the past two decades, extensive trials have been conducted to find therapies to help manage this disorder, as conventional treatments are ineffective or even harmful. Most trials were negative but provided useful information on the natural course of IPF. They confirmed the survival statistics, defined the complication of acute exacerbation and, more importantly, established the futility or harmful effects of certain therapies once thought to be of some value.

Nintedanib, approved by the FDA in October 2014, also was found to positively affect the course of disease by slowing the rate of decline in pulmonary function as a primary endpoint and by meeting certain predetermined secondary endpoints. Nintedanib is a small molecule that inhibits a spectrum of Tyrosine Kinases Receptors (RTKs) and non-VEGFR (Vascular Endothelial Growth Factor Receptor), PDGFR (Platelet-Derived Growth Factor Receptor), and FGFR (Fibroblast Growth Factor Receptor). All of these growth factor pathways and their downstream



HRCT of UIP demonstrating peripheral and basilar honeycombing and traction bronchiectasis

signal cascades have been demonstrated to be involved in fibrotic lung disease pathogenesis.

Pirfenidone and Nintedanib represent the first approved therapies for IPF. While they hold promise for better outcomes in our pulmonary fibrosis patients, ongoing trials continue for agents that will arrest or

reverse IPF damage. We continue to treat and manage the co-morbidities that affect patients suffering with this illness to improve quality of life and survival, our ultimate goal. Dr. Padilla and Aditi Mathur, MD, are the principal investigators at Mount Sinai of ongoing multicenter trials and other investigations aiming to expand the therapies and approaches to managing IPF.



# Training at the Center for Advanced Medical Simulation

The Center for Advanced Medical Simulation (CAMS), established in 2007 and located at Mount Sinai West and Mount Sinai St. Luke's, provides simulation-based education and training to Pulmonary, Critical Care and Sleep Medicine residents and fellows, and to students attending the Icahn School of Medicine at Mount Sinai. Computerized, high fidelity manikins enable students to respond to a wide range of emergency room scenarios, followed by critiques of their interventions that prepare them for real-life situations.

The CAMS has three simulation laboratories; several procedural arcades; debriefing and conference rooms with several high fidelity manikins; task trainers; and virtual laparoscopic and bronchoscopy equipment. The center is equipped with state-of-the-art audiovisual and video recording equipment to facilitate training and debriefing.

The CAMS is dedicated to improving patient safety and strengthening the quality of health care by teaching teamwork and advanced communication skills, and enhancing clinical decision-making. The CAMS is directed by Hassan Khouli, MD, Associate Professor, Medicine, Pulmonary, Critical Care, and Sleep Medicine.



From left, Pulmonary and Critical Care Fellows Catherine Oberg, MD, The Mount Sinai Hospital; Bashar Mourad, MD, Mount Sinai St. Luke's and Mount Sinai West; and Michael Bergman, MD, The Mount Sinai Hospital, learn the proper techniques for intubation on manikins.

The first and only accredited simulation center in Manhattan, the CAMS is one of fewer than 50 nationwide. The Center, which has received full five-year accreditation in Teaching and Education by the Society for Simulation in Healthcare, also provides training to staff in Emergency Medicine, Anesthesia, Surgery, Nursing,

Respiratory Therapy, Orthopaedic Surgery, and other departments and services.

Several courses—taught by certified faculty from several Mount Sinai Health System pulmonary and critical care divisions with special expertise in simulation training—focus on team training; procedural training such as central line insertion, intubation and airway management; bronchoscopy and laparoscopy training; medical code training; chest tube insertion; and a wide range of case-based training.

New fellows from across the Mount Sinai Health System complete a one-day “boot camp” at CAMS. They use deliberate practice techniques, standardized evaluation tools and checklists, and validated debriefing methods. This creates uniform training at all Mount Sinai Health System sites in several domains, including airway management,

central line insertion, and introduction to bronchoscopy training.

The CAMS has been awarded several government, private foundation, and industry research grants that have yielded publications in major peer-reviewed journals and presentations at national meetings.

## › New Tools to Help Control and Treat Asthma *continued from page 1*

creating a powerful research and clinical tool for identifying asthma patients at risk for exacerbations and intervening early to prevent these episodes.

Additionally, for the 5 to 10 percent of patients with refractory asthma, the Mount Sinai - National Jewish Health Respiratory Institute is offering phase 2 and phase 3 clinical trials of novel treatments, including a variety of new biological therapies targeting key asthma pathways. Dr. Rogers and Gwen Skloot, MD, from the Respiratory Institute Asthma team have launched VOCALS, a study of Lebrikizumab (anti-IL13) as a steroid-sparing treatment for patients with steroid-dependent asthma. Additionally, a study of the biological therapy Dupilimab (anti-IL4 receptor alpha) opened for enrollment in December 2015 for

patients with severe asthma not controlled with two forms of controller therapy.

The Asthma Health App study's principal investigator is Yu-Feng Yvonne Chan, MD, PhD, Director of Personalized Medicine and Digital Health. Dr. Rogers, Eric Schadt, PhD, Professor and Chair, Genetics and Genomic Sciences, Director, Icahn Institute for Genomics and Multiscale Biology, The Mount Sinai Hospital, and Joel Dudley, PhD, Director of Biomedical Informatics are co-principal investigators.

The Asthma Health App patient dashboard gives users feedback on asthma control levels and warns them about possible local environmental asthma triggers.



RESEARCH FRONTIERS

## Studying the Role of Environment in Lung Disease



Alison Lee, MD

Alison Lee, MD, Assistant Professor, Medicine, Pulmonary, Critical Care, and Sleep Medicine, the Icahn School of Medicine at Mount Sinai, has performed research in India, Bangladesh, Ghana, and New York City, striving to understand how environmental exposures, both chemical (e.g., air pollution, arsenic) and non-chemical (e.g. psychosocial stress), in critical periods of development may predispose children toward chronic respiratory disease persisting into adulthood.

Dr. Lee focuses on household air pollution exposures from burning solid fuels in traditional cook stoves. Her research in Ghana was highlighted in *ATSNews*, <http://news.thoracic.org/?p=6129> and has resulted in first authored manuscripts in *Environmental Research*, *Annals of Global Health* and a *Lancet Respiratory Medicine* editorial.

Under the mentorship of Rosalind Wright, MD, MPH, Professor, Medicine, Pulmonary, Critical Care, and Sleep Medicine, Dr. Lee is investigating the influence of ambient air pollution and stress exposures on childhood asthma outcomes. She co-authored an article published in the *American Journal of Respiratory and Critical Care Medicine* that was the first to identify mid-gestation as a sensitive window of ambient air pollution exposure for asthma risk. Dr. Lee's research has also demonstrated that children exposed to increased pre- and postnatal maternal stress were 2- and 3-times more likely, respectively, to develop asthma (in press, *Journal of Asthma and Clinical Immunology*).

## Driving Quality Care In Intensive Care Units



Kusum S. Mathews, MD, MPH

Kusum S. Mathews, MD, MPH, Assistant Professor of Medicine at the Icahn School of Medicine at Mount Sinai—with a dual appointment in Emergency Medicine—is a young clinical investigator focusing on the triage, throughput, and care of critically ill patients originating from The Mount Sinai Hospital's Emergency Department and hospital wards.

Her research in improving health care delivery in the Intensive Care Unit (ICU), published in the *Annals of the American Thoracic Society* at <http://www.atsjournals.org/action/doSearch?AllField=kusum+mathews>, demonstrates that sizable gains in patient outcomes can be achieved by improving ICU and hospital operations efficiency. Dr. Mathews' research efforts also harness the power of Big Data and innovative computer engineering tools, utilizing large scale national datasets as well as Mount Sinai's own expansive 12-year patient data warehouse, which encompasses more than four million patients. They help us understand health care utilization patterns and improve in-hospital mortality, decrease length of stay, and ensure timely access to higher-level services.

Her research has also overlapped extensively with ongoing Medical ICU quality improvement projects, supporting data-driven change in processes and care practices. Broadening to clinical trials within the ED and ICU, she is one of Mount Sinai's co-investigators within the Prevention and Early Treatment of Acute Lung Injury (PETAL) Network at Mount Sinai. She is completing her Masters of Science in Clinical Research at the Icahn School of Medicine at Mount Sinai.



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