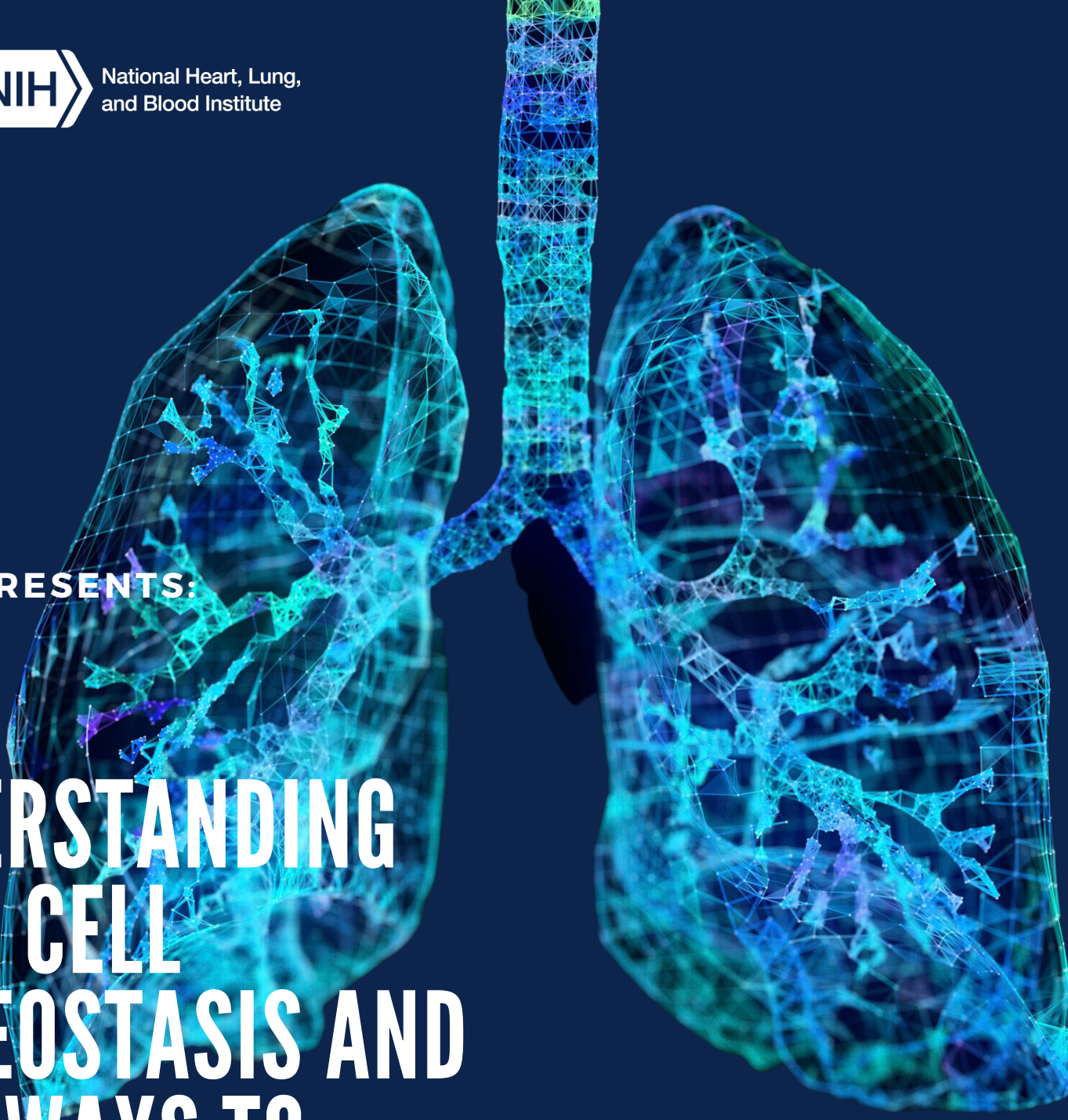
National Heart, Lung, and Blood Institute



NHLBI PRESENTS:

# 2021 UNDERSTANDING LUNG CELL HOMEOSTASIS AND PATHWAYS TO REVERSE LUNG CELL REMODELING

VIRTUAL WORKSHOP
OCTOBER 21 & 22, 2021

PROGRAM BOOK

# PROGRAM AGENDA Day 1: THURSDAY, OCTOBER 21, 2021

**9:00 - 9:10 AM** **Welcome Address and Meeting Logistics**

*Dr. Jim Kiley, Ph.D., Director, Division of Lung Diseases*
*Dr. Marrah Lachowicz-Scroggins, Ph.D., Program Director*

**9:10 - 9:25 AM** **Welcome from Chairs and Charge of Workshop**

*Workshop Co-Chairs:*
*Dr. Brigid Hogan, Ph.D., Professor, Cell Biology and Pediatrics, Duke University School of Medicine*
*Dr. Y.S. Prakash MD, Ph.D., Professor, Anesthesiology and Physiology, Mayo Clinic Rochester*

**Session 1: Realizing the promise of 'omics and other new technologies**

*This session will illustrate how new technologies, including single cell 'omics, spatial transcriptomics and proteomics can be used to elucidate the origin and treatment of respiratory disease, and mechanisms driving normal and abnormal remodeling. The new technologies, as well as mouse models exploiting state-of-the-art lineage tracing and genetic manipulation, can also reveal the dynamic interactions between different cell types in the lung that are required for long term maintenance and repair after injury.*

***Session Chairs:***

*Dr. Nicholas Banovich, Ph.D., Associate Professor, Integrated Cancer Genomics Division at the Translational Genomics Research Institute*

*Dr. Tien Peng, MD, Associate Professor of Pulmonary, Critical Care, Allergy and Sleep Medicine, University of California San Francisco*

**Short Talks: (15 minutes each)**

**9:25 - 9:40 AM** *Dr. Nicholas Banovich, Ph.D., Associate Professor, Integrated Cancer Genomics Division at the Translational Genomics Research Institute*

**9:40 - 9:55 AM** *Dr. Matthew B Buechler, Ph.D., Assistant Professor, Department of Immunology, University of Toronto*

**9:55 - 10:10 AM** *Dr. Tien Peng, MD, Associate Professor of Pulmonary, Critical Care, Allergy and Sleep Medicine, University of California San Francisco*

**10:10 - 10:25 AM** *Dr. Xin Sun, Ph.D., Professor, Pediatrics Section of Cell and Developmental Biology, University of California San Diego*

**10:25 - 10:40 AM** *Maya Kumar, Ph.D., Assistant Professor, Pediatrics-Pulmonary Medicine, Stanford University*

**10:40 - 11:25 AM** **Q&A: (45 minutes each)**

**11:25 - 11:40 AM** **Break: (15 minutes each)**

**Session 2: Embracing cellular diversity**

*This session will illustrate how new 'omics and imaging technologies can reveal diversity in lung cell types and function, and how lung structure changes during remodeling and with progression of disease. Topics will include the identification of new cell types and states in the human lung and their significance for tissue maintenance and disease.*

***Session Chairs:***

*Dr. Purushothama Rao Tata, Ph.D., Assistant Professor of Cell Biology, Duke University School of Medicine*
*Dr. Dean Sheppard, MD, Professor, Department of Medicine University of California San Francisco*

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|---|---|
| | **Short Talks: (15 minutes each)** |
| **11:40 - 11:55 AM** | *Dr. Purushothama Rao Tata, Ph.D., Assistant Professor of Cell Biology, Duke University School of Medicine* |
| **11:55 - 12:10 PM** | *Dr. Joo-Hyeon Lee, Ph.D. Principal Investigator, University of Cambridge Stem Cell Institute, UK* |
| **12:10 - 12:25 PM** | *Dr. Dean Sheppard, MD, Professor, Department of Medicine University of California San Francisco* |
| **12:25 - 12:40 PM** | *Dr. Lida Hariri, MD, Ph.D., Assistant Professor, Harvard Medical School* |
| **12:40 - 12:55 PM** | *Dr. Jichao Chen, Ph.D., Associate Professor, Department of Pulmonary Medicine, Division of Internal Medicine at MD Anderson Cancer Center* |
| **12:55 - 1:25 PM** | **Q&A: (30 minutes each)** |
| **1:25 - 1:55 PM** | **Break: (30 minutes each)** |
| **1:55 - 2:00 PM** | **Breakout Instructions and Assigning Rooms** |
| **2:00 - 3:15 PM** | **Breakout Sessions (1 hour and 15 minutes)** |
| | *Session 1 - Realizing the promise of 'omics and other new technologies*<br>*Session 2 - Embracing cellular diversity* |
| **3:15 - 4:30 PM** | **Reports/Summary (1 hour 15 minutes)** |

# Day 2: FRIDAY, OCTOBER 22, 2021

**9:00 - 9:05 AM** **Welcome from Chairs and Recap from Day1 (Drs. Prakash and Hogan)**

**Session 3: Triggers and paths to remodeling**

*This session will discuss how new technologies are impacting the study of how immune cells function in the normal and damaged lung and contribute to either initiating destructive inflammation or effecting repair; how early life exposures can set the lung up for abnormal remodeling in later life; and how the effects of early exposures could be reversed.*

***Session Chairs:***

*Dr. Jason Rock, Ph.D., Principal Scientist, Immunology Discovery, Genentech*
*Dr. Jennifer Sucre, MD , Assistant Professor, Pediatrics, Vanderbilt*

**Short Talks: (15 minutes each)**

**9:05 - 9:20 AM** *Dr. Alex "Sasha" Misharin, MD, Ph.D., Assistant Professor, Medicine- Pulmonary and Critical Care, Northwestern Feinberg School of Medicine*

**9:20 - 9:35 AM** *Dr. Jason Robert Mock, MD, Ph.D. Assistant Professor, Medicine- Division of Pulmonary Diseases and Critical Care Medicine, UNC Chapel Hill*

**9:35 - 9:50 AM** *Dr. Shaon Sengupta, MBBS, MPH, Assistant Professor, Attending Neonatologist, Children's Hospital of Philadelphia*

**9:50 - 10:05 AM** *Dr. Martijn Nawijn, Ph.D., Professor, Functional Genomics of Chronic Respiratory Diseases, University Groningen*

**10:05 - 10:20 AM** *Dr. Jennifer Sucre, MD , Assistant Professor, Pediatrics, Vanderbilt*

**10:20 - 10:50 AM** **Q&A: (30 minutes each)**

**10:50 - 11:05 AM** **Break: (15 minutes each)**

**Session 4: Taking cells to cures**

*This session will discuss cell and CRISPR based gene therapy in relation to respiratory disease, strategies to achieve therapeutic cell transplantation into the lung, and using human organoids as models for testing gene function and for drug discovery.*

***Session Chairs:***

*Dr. Finn Hawkins, MBBCh, Principal Investigator, Boston University School of Medicine*
*Dr. Tushar Desai, MD, MPH, Associate Professor, Medicine - Pulmonary, Allergy & Critical Care Medicine Stanford University*

**Short Talks: (15 minutes each)**

**11:05 - 11:20 AM** *Dr. Finn Hawkins, MBBCh, Principal Investigator, Boston University School of Medicine*

**11:20 - 11:35 AM** *Dr. Tushar Desai, MD, MPH, Associate Professor, Medicine - Pulmonary, Allergy & Critical Care Medicine Stanford University*

# CONTINUE OF DAY 2: FRIDAY, OCTOBER 22, 2021

**11:35 - 11:50 AM** *Emma Rawlins PhD, Senior Group Leader, Gurdon, University of Cambridge*

**11:50 - 12:05 PM** *Dr. Shahin Rafii, MD, Professor, Medicine- Reproductive Medicine, Weill Cornell Medical College*

**12:05 - 12:20 PM** *Dr. April Kloxin, Ph.D., Associate Professor of Chemical & Biomolecular Engineering and Materials Science & Engineering, University Delaware*

**12:20 - 12:50 PM** **Q&A: (30 minutes each)**

**12:50 - 1:20 PM** **Break: (15 minutes each)**

**1:20 - 1:25 PM** **Breakout Instructions and Assigning Rooms**

**1:25 - 2:40 PM** **Breakout Sessions (1 hour and 15 minutes)**

*Session 3 - Triggers and paths to remodeling*
*Session 4 - Taking cells to cures*

**2:40 - 3:55 PM** **Reports/Summary (1 hour 15 minutes)**

**3:55 - 4:30 PM** **Workshop Closeout**

# SPEAKERS AND CHAIRS

## Workshop Co-Chair/Speaker

DR. BRIGID HOGAN, PH.D., FRS
PROFESSOR,CELL BIOLOGY AND PEDIATRICS
DUKE UNIVERSITY SCHOOL OF MEDICINE

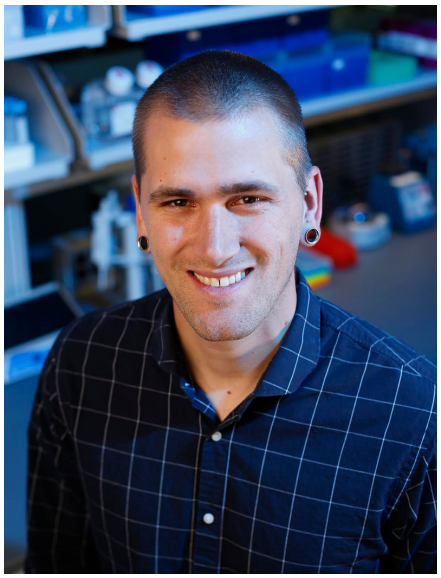
FROM 2002-2018 I WAS AN ENDOWED PROFESSOR AND CHAIR OF THE DEPARTMENT OF CELL BIOLOGY AT DUKE UNIVERSITY MEDICAL SCHOOL. WHEN I STEPPED DOWN AS CHAIR, I DECIDED TO REVERT TO SIMPLE PROFESSOR OF CELL BIOLOGY, WITH A SECONDARY APPOINTMENT IN PEDIATRICS. UNTIL 2019 I RAN A RESEARCH PROGRAM STUDYING LUNG DEVELOPMENT AND THE ROLE OF RESIDENT EPITHELIAL STEM CELLS IN LUNG MAINTENANCE, REPAIR, AND DISEASE, PRIMARILY USING THE MOUSE AS A MODEL GENETIC ORGANISM BUT ALSO TAKING ADVANTAGE OF HUMAN AND MOUSE CELL CULTURE SYSTEMS, INCLUDING ORGANOID CULTURES. I REMAIN ACTIVELY INVOLVED IN RESEARCH IN THE DEPARTMENT, AND WITH TEACHING, ADVISING, EDITING, AND MENTORING. MOST RECENTLY I CO-EDITED, WITH DR MARKO NIKOLIC, UNIVERSITY COLLEGE LONDON, A MONOGRAPH ON LUNG STEM CELLS IN DEVELOPMENT, HEALTH AND DISEASE PUBLISHED IN 2021 BY THE EUROPEAN RESPIRATORY SOCIETY. (SADLY, THE GREAT ARTICLES IN IT ARE NOT ON PUBMED.)

## Workshop Co-Chair/Speaker

DR. Y.S. PRAKASH MD, PH.D.
PROFESSOR, ANESTHESIOLOGY AND PHYSIOLOGY
MAYO CLINIC ROCHESTER

THE RESEARCH GROUP OF Y.S. PRAKASH, M.D., PH.D., STUDIES HUMAN LUNG DISEASES SUCH AS ASTHMA, CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD), EMPHYSEMA, PULMONARY FIBROSIS AND PULMONARY HYPERTENSION. USING STATE-OF-THE-ART TOOLS APPLIED TO HUMAN AND ANIMAL MODELS, DR. PRAKASH'S GROUP IS WORKING TOWARD DEVELOPING NOVEL THERAPIES AND APPROACHES TO TREAT SUCH DISEASES IN BABIES, CHILDREN AND ADULTS, ESPECIALLY IN WOMEN AND OLDER ADULTS.
DR. PRAKASH HAS A UNIQUE TRAINING BACKGROUND AS AN ANESTHESIOLOGIST, PHYSIOLOGIST, AND ELECTRICAL AND BIOMEDICAL ENGINEER, WHICH ALLOWS HIM TO BRING UNIQUE PERSPECTIVES TO RESEARCH ON THE "HOW AND WHY" OF THESE CLINICALLY RELEVANT DISEASES.
DR. PRAKASH WORKS WITH AN OUTSTANDING INTERDISCIPLINARY TEAM OF YOUNG CLINICIAN-SCIENTISTS, RESEARCHERS, GRADUATE STUDENTS AND TECHNICIANS IN HIS PULMONARY CELL BIOLOGY LABORATORY, WITH THE MOTTO "YOU ARE ONLY AS GOOD AS THE PEOPLE YOU WORK WITH."

## Session 1
## Realizing the promise of ‘omics and other new technologies



### Session Chair/Speaker

DR. NICHOLAS BANOVICH, PH.D.
ASSOCIATE PROFESSOR
INTEGRATED CANCER GENOMICS DIVISION
TRANSLATIONAL GENOMICS RESEARCH INSTITUTE

Dr. Banovich received his PhD in Human Genetics from the University of Chicago where he gained expertise in functional genomics. His PhD work focused on identifying genetic variants which are associated with regulatory changed including gene expression (eQTLs), chromatin accessibility (caQTLs), and DNA methylation (meQTLs). After the completion of his PhD, Dr. Banovich jointed TGen where he spent one year in a transitional postdoctoral position before starting his own lab as an Assistant Professor. Dr. Banovich's research is focused on understanding how gene regulatory changes alter disease risk, progression, and treatment response. His lab employs a combination of experimental and computational approaches, integrating molecular biology, genomics, and computational biology. Currently, Dr. Banovich is engaged in an active research effort using single cell RNA sequencing (scRNA-seq) to profile gene expression changes associated with pulmonary fibrosis. As a part of these efforts he is also involved in the Human Cell Atlas as a member of the Lung Biological Network.

## Session Chair/Speaker

DR. TIEN PENG, MD
ASSOCIATE PROFESSOR OF PULMONARY, CRITICAL CARE, ALLERGY AND SLEEP MEDICINE
UNIVERSITY OF CALIFORNIA SAN FRANCISCO

Tien Peng is a physician-scientist with a longstanding interest in the role of the mesenchyme in regulating the microenvironment to maintain organ function. As a principal investigator at UCSF, the Peng lab focuses on the role of the mesenchyme in modulating the stem cell niche in the lung. The approach is to generate novel mouse genetic tools to focus on the adult mesenchyme, examine the heterogeneity of mesenchymal identities through single cell transcriptome analysis, and model epithelial-mesenchymal interactions ex vivo through 3D organoid platforms. The Peng lab is applying these techniques to study alterations in the stem cell niche in age-related pathologies in the lung such as emphysema, fibrosis, and cancer.

## Speaker

DR. XIN SUN, PH.D.
PROFESSOR, PEDIATRICS SECTION OF CELL AND DEVELOPMENTAL BIOLOGY
UNIVERSITY OF CALIFORNIA SAN DIEGO

Dr. Xin Sun obtained her Ph.D. at Yale University and conducted postdoctoral training at University of California, San Francisco. The Sun lab studies the mechanisms of lung development, homeostasis, dysplastic repair and lung disease mechanisms. The focus is on pediatric diseases, both rare disorders and more common conditions including bronchopulmonary dysplasia and asthma. The team uses CRISPR/Cas9 genome editing to generate genetic mouse models of human diseases to interrogate disease mechanisms. Supported by the LungMAP consortium, the team has generated and shared single cell transcriptomic and epigenomic datasets of the pediatric human lung for the community. Extending from their work on pulmonary neuroendocrine cells, a rare but critical sensor cell type in the lung, they have also initiated work to elucidate neural circuit control of lung function.

## Speaker

DR. MATTHEW B BUECHLER, PH.D.
ASSISTANT PROFESSOR
DEPARTMENT OF IMMUNOLOGY
UNIVERSITY OF TORONTO

Matthew Buechler received his PhD in the laboratory of Dr. Jessica Hamerman at the University of Washington. He performed his postdoctoral training with Dr. Shannon Turley at Genentech. Dr. Buechler started a laboratory at the University of Toronto in the Department of Immunology in August 2021. The Buechler Lab studies unknown aspects of the immune system with a particular interest in fibroblasts and macrophages. More information about Matt and the lab can be found at www.buechlerlab.com.

## Speaker

MAYA KUMAR, PH.D.
ASSISTANT PROFESSOR
PEDIATRICS-PULMONARY MEDICINE
STANFORD UNIVERSITY

In my own lab, we explore in depth the cells, cell behaviors and interactions that give rise to pulmonary vascular disease, delineate the molecular pathways that control them, and determine how they can be manipulated to prevent or reverse disease. Using a wide array of approaches -- genetic lineage tracing, clonal analysis, single cell RNA-sequencing, bioinformatic interaction mapping, multiplexed in situ hybridization, immunostaining, deep confocal imaging and staged pharmacologic inhibition – we are unraveling how arteries change in pulmonary hypertension (PH), a disease with no available cure and limited treatment options, characterized by profound vascular remodeling. In PH, pulmonary arteries narrow due to medial thickening and occlusion by neointimal lesions, raising pulmonary vascular resistance and ultimately resulting in right heart failure. Therapies targeting the neointima would represent a significant advance in PAH treatment, and by understanding of the cellular events driving neointima formation, and the molecular pathways that control them, we hope to open the door to new treatments.

## Session 2
## Embracing cellular diversity

### Session Chair/Speaker

DR. DEAN SHEPPARD, MD
PROFESSOR, DEPARTMENT OF MEDICINE
UNIVERSITY OF CALIFORNIA SAN FRANCISCO

Dr. Sheppard research focuses on the molecular mechanisms underlying pulmonary (and other organ) fibrosis, asthma and acute lung injury. One aim of the research is to identify new therapeutic targets to ultimately improve the treatment of each of these common diseases. The work begins with basic investigation of how cells use members of the integrin family to detect, modify and respond to spatially restricted extracellular clues and how these responses contribute to the development of common lung diseases. Utilizing mice with global or conditional knockouts of the epithelial-restricted integrin, avß6, and the widely expressed integrins, a5ß1, a9ß1, avß5 and avß8, the lab has identified important roles for these integrins in models of each common lung disease and key steps upstream and downstream of the integrins that provide potential therapeutic targets. His lab identified the unique roles that 3 integrins, avß1, avß6 and avß8 play in activation of the growth factor, latent transforming growth factor beta (TGFß) and has identified critical roles for this process in acute lung injury, pulmonary fibrosis, post-natal brain development and immunosuppression in the setting of cancer. The lab has partnered with academic colleagues, biotech and pharmaceutical companies to develop novel antibody and small molecule inhibitors of these integrins that are in various stages of pre-clinical and clinical development. Current work employs single cell RNA sequencing and novel murine lineage reporter lines to understand the heterogeneity of cells that contribute to tissue fibrosis.

## Session Chair/Speaker

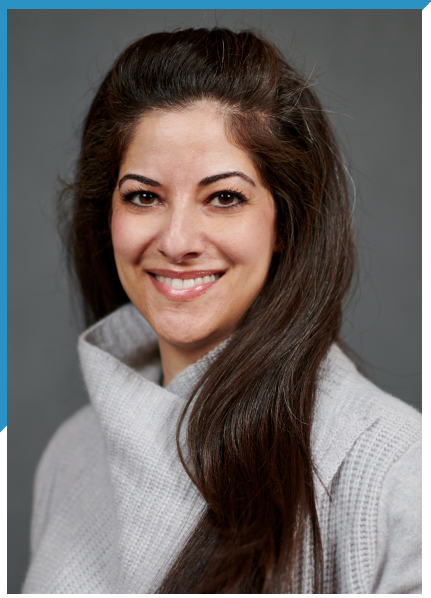
DR. PURUSHOTHAMA RAO TATA, PH.D.
ASSISTANT PROFESSOR OF CELL BIOLOGY
DUKE UNIVERSITY SCHOOL OF MEDICINE

Dr. Tata received his PhD from University of Ulm, Germany and then moved to Massachusetts General Hospital and Harvard Medical School, Boston for his postdoctoral training in the lab of Dr. Jayaraj Rajagopal. During his time in Boston, Dr. Tata uncovered novel communication between stem and progenitors and the cellular plasticity mechanisms that are operant in tissue homeostasis, regeneration, and tumorigenesis. Currently my lab is developing novel technologies to profile and identify cell types in normal and pathological tissues and to uncover the mechanisms guiding tissue repair and resolution following damage.

## Speaker

DR. JOO-HYEON LEE ,PH.D.
PRINCIPAL INVESTIGATOR
UNIVERSITY OF CAMBRIDGE STEM CELL INSTITUTE, UK

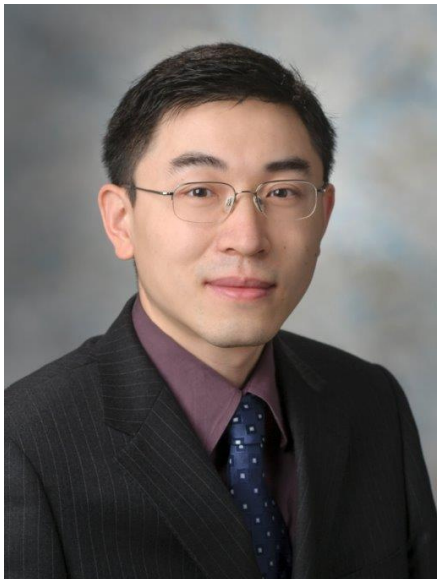
Dr. Joo-Hyeon Lee is a group leader, a Wellcome Trust Senior Research Fellow, and an academic member of the Department of Physiology, Development, and Neuroscience based at the Wellcome – MRC Cambridge Stem Cell Institute, University of Cambridge in UK. Her lab focuses on understanding the mechanisms of stem cell fate dynamics in the lung. They ask fundamental questions involving how stem cells sense environmental changes and determine their cell fate/state, and how niches develop and remodel the local environment during lung regeneration and the early stages of disease progression utilizing combined in vitro organoids, in vivo genetic models, single-cell profiling, and clonal biophysical modeling.



## Speaker

DR. LIDA HARIRI, MD, PH.D.
ASSISTANT PROFESSOR
HARVARD MEDICAL SCHOOL

Lida Hariri obtained her MD/PhD at the University of Arizona in 2009, with her doctorate in Biomedical Engineering focused on multimodal optical imaging for early cancer detection. She subsequently completed her pathology residency training and pulmonary and gynecologic pathology fellowships at MGH. She is a practicing pathologist at MGH, specializing in pulmonary pathology. Her research interests focus on fibrotic lung diseases, including interstitial lung disease and fibrotic sequelae of acute lung injury, and the development, translation and clinical application of high-resolution optical imaging for early detection, diagnosis, and monitoring of these fibrotic pulmonary diseases. She is the Chair of the American Thoracic Society Early Career Workgroup in the Clinical Problems Assembly and the Chair-Elect of the College of American Pathologists Digital and Computational Pathology Committee.



## Speaker

DR. JICHAO CHEN, PH.D.
ASSOCIATE PROFESSOR, DEPARTMENT OF PULMONARY MEDICINE, DIVISION OF INTERNAL MEDICINE
MD ANDERSON CANCER CENTER

Dr. Chen laboratory studies lung development using mouse genetics, single-cell genomics, and three dimensional (3D) imaging. I have extensive training at Johns Hopkins and Stanford in the area of organ development and mouse models of human diseases, as well as a Master's degree in bioinformatics. In my own lab, I have established a research program spanning all 4 lung cell lineages: epithelial, endothelial, mesenchymal, and immune, and have developed experimental and computational expertise in single-cell RNA-seq/ATAC-seq. My major research interests include transcriptional and epigenetic control of epithelial cell fates, endothelial cell heterogeneity including our discovery of Car4 endothelial cells (also called aerocytes), mesenchymal cell turnover, and lung evolution. My first and second graduate students have both received an NIH F31 fellowship. A postdoctoral fellow in my lab has been awarded a K99/R00 grant.

## Session 3
## Triggers and paths to remodeling

### Session Chair/Speaker

DR. JENNIFER SUCRE, MD
ASSISTANT PROFESSOR
PEDIATRICS
VANDERBILT

Jennifer Sucre graduated from Harvard Medical School, trained in pediatrics at Washington University in St. Louis, and completed fellowship in Neonatal-Perinatal Medicine at UCLA. Since joining the Vanderbilt faculty in 2016, she has established a research program focused on understanding the molecular mechanisms of lung development and lung disease across the lifespan with a particular focus on developing novel 4D imaging approaches to study alveologenesis and on understanding molecular drivers of bronchopulmonary dysplasia, the leading complication in survivors of preterm birth. Her clinical experience treating premature infants provides a unique perspective for studying lung development, and she has cultivated new ex vivo, in vitro, and in vivo models of lung injury. Dr. Sucre has combined these models with single-cell biology and spatial transcriptomics to gain insights into cellular specialization and dynamics in the developing lung, elucidated age-regulated host susceptibility factors to SARS-CoV-2 infection, and defined previously unrecognized cell types in chronic respiratory diseases.

## Session Chair

DR. JASON ROCK, PH.D.
PRINCIPAL SCIENTIST
IMMUNOLOGY DISCOVERY
GENENTECH

Dr. Rock laboratory studies lung development using mouse genetics, single-cell genomics, and three dimensional (3D) imaging. I have extensive training at Johns Hopkins and Stanford in the area of organ development and mouse models of human diseases, as well as a Master's degree in bioinformatics. In my own lab, I have established a research program spanning all 4 lung cell lineages: epithelial, endothelial, mesenchymal, and immune, and have developed experimental and computational expertise in single-cell RNA-seq/ATAC-seq. My major research interests include transcriptional and epigenetic control of epithelial cell fates, endothelial cell heterogeneity including our discovery of Car4 endothelial cells (also called aerocytes), mesenchymal cell turnover, and lung evolution. My first and second graduate students have both received an NIH F31 fellowship. A postdoctoral fellow in my lab has been awarded a K99/R00 grant.

## Speaker

DR. ALEX “SASHA” MISHARIN, MD, PH.D.
ASSISTANT PROFESSOR MEDICINE- PULMONARY AND CRITICAL CARE
NORTHWESTERN FEINBERG SCHOOL OF MEDICINE

Alexander Misharin is an immunologist and macrophage biologist. His laboratory applies single-cell techniques to causal animal models and specimens obtained from patients with pulmonary diseases to understand multicellular interactions unfolding during lung injury and normal and aberrant lung repair, specifically in the context of pulmonary fibrosis and severe pneumonia, including SARS-CoV-2 pneumonia.

## Speaker

DR. JASON ROBERT MOCK, MD, PH.D.
ASSISTANT PROFESSOR MEDICINE- DIVISION OF PULMONARY DISEASES AND CRITICAL CARE MEDICINE
UNC CHAPEL HILL

Dr. Mock research interests focus on how the immune system promotes lung repair. Acute Respiratory Distress Syndrome (ARDS) is a disease process characterized by lung cell damage, low oxygen delivery to the body, and high mortality. Little information is known about how the lung recovers from these types of injuries; however, recently, there has been considerable interest in investigating the cell types involved in repair after injury. A subset of immune cells, Foxp3+ regulatory T lymphocytes (Tregs), are essential in repair in several experimental models of lung injury and resolution. Furthermore, our group and others have shown that Tregs increase in the lung of patients with ARDS—suggesting that they may be necessary for the human immunological response to ARDS.

Current areas of investigation include examining the newly defined tissue reparative role of Tregs in lung resolution and investigating the impact of Treg interactions with the distal epithelium, specifically type II alveolar epithelial cells. We are also determining the role of specific Treg populations during acute lung injury resolution and testing the hypothesis that potential mechanisms include the proliferation of lung-resident Tregs (either thymically-derived or peripherally-induced) and recruitment of Tregs from sites outside the lung.

Our studies identifying and elucidating mechanisms of lung resolution will provide a clearer understanding of Treg-specific contributions to the reparative process. They may uncover new targets to help accelerate recovery and improve the quality of repaired lung tissue for patients with lung diseases.

## Speaker

DR. SHAON SENGUPTA, MBBS, MPH
ASSISTANT PROFESSOR
ATTENDING NEONATOLOGIST
CHILDREN'S HOSPITAL OF PHILADELPHIA

Shaon Sengupta is a neonatologist and physician scientist with a long-standing interest in lung health. The two areas of investigation in my lab are: (1) Mechanisms underlying the circadian regulation of lung inflammation, injury and repair/regeneration, and (2) effect of early life exposures on the development (or maldevelopment) and function of pulmonary circadian networks in adulthood. We have previously shown that the circadian clock affects outcomes of influenza A infection by modulating the host tolerance. This circadian protection is in fact lost when the lungs are challenged early in life with hyperoxia. Our lab employs a multidisciplinary approach to study lung injury and recovery combining latest tools and insights from virology, immunology, pulmonology and circadian biology.

## Speaker

DR. MARTIJN NAWIJN, PH.D.
PROFESSOR
FUNCTIONAL GENOMICS OF CHRONIC RESPIRATORY DISEASES
UNIVERSITY GRONINGEN

Dr. Nawijn is fascinated with the impact of genetic variation on the function of the innate and adaptive immune system and the consequences thereof for chronic, respiratory diseases. He performed translational research into the contribution of genetic variation, environmental exposures and the interaction between innate and adaptive immune cells with the structural cells of the airways in the inception, exacerbations and remission of asthma and COPD. This research is embedded in the translational Groningen research Institute of Asthma and COPD (GRIAC), and includes a combination of advanced mouse models to functionally characterize gene function, multi-omic characterization of lung tissue samples obtained from patients with lung disease and control subjects, supplemented with ex vivo primary cell culture models of both bronchial epithelial and hematopoietic cells from these patient categories.

## Session 4
## Taking cells to cures

### Session Chair/Speaker

DR. FINN HAWKINS
MBBCH PRINCIPAL INVESTIGATOR
BOSTON UNIVERSITY SCHOOL OF MEDICINE

Dr. Finn is a an Assistant Professor, physician-scientist in the Center for Regenerative Medicine (CReM) and the Pulmonary Center at Boston University. From a medical perspective I direct the Interstitial Lung Disease (ILD) clinic at Boston University Medical Center. My overall research interest is developing improved models of human lung disease to advance our understanding and therapeutic options for patients with lung diseases.
A central focus of our laboratory is to derive lung epithelium from human iPSCs in vitro by recapitulating key development milestones through a process termed directed differentiation. My postdoctoral research work culminated in a detailed characterization of the earliest human lung progenitors derived from iPSCs and methods to generate lung epithelial organoids from iPSCs that can further be patterned into alveolar or airway organoids and a novel platform to study lung diseases. I established my independent laboratory in 2018 and we have two main research priorities; 1) define the molecular program of human lung development including the cell fate decisions that give rise to specialized cell types of the lung epithelium, and 2) apply these advanced models of human lung tissue to the study of genetic and acquired lung diseases including pulmonary fibrosis, cystic fibrosis (CF) and primary ciliary dyskinesia (PCD). To tackle these goals we employ patient-specific human iPSC lung organoid in vitro models, primary human tissue and in vitro cultures, gene-editing and multi-omic analyses.

## Session Chair/Speaker

DR. TUSHAR DESAI, MD, MPH
ASSOCIATE PROFESSOR MEDICINE
INSTITUTE FOR STEM CELL BIOLOGY & REGENERATIVE MEDICINE
STANFORD UNIVERSITY SCHOOL OF MEDICINE

Tushar Desai is a pulmonary physician-scientist with clinical interest in ILD and research interests in lung development, stem cells, injury repair, pulmonary fibrosis and adenocarcinoma.

His undergraduate studies were in Psychology, after which he received an MD and MPH from Tufts Medical School. He completed a residency in Internal Medicine at University of Michigan followed by a fellowship in Pulmonary & Critical Care at Boston University. He then moved to Stanford for a postdoctoral fellowship in Biochemistry after which he joined the faculty in the Department of Medicine. Tushar is also a member of the Stanford Institute for Stem Cell Biology and Regenerative Medicine and serves as the Director of Graduate Education for an interdisciplinary PhD program in stem cell biology.

Tushar's lab focuses on applying basic science technologies to understand the pathogenesis of and devise novel molecular and cellular therapies for a variety of lung diseases.

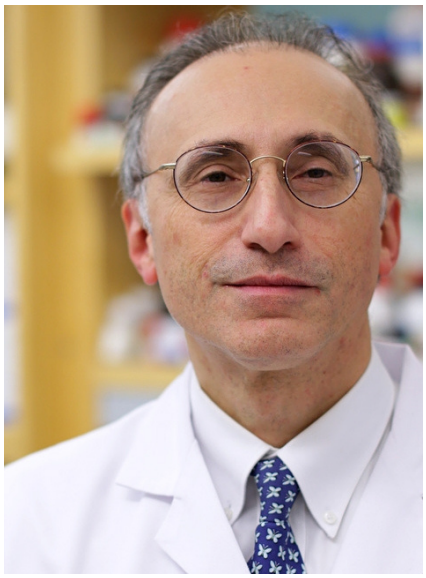
## Speaker

EMMA RAWLINS PH. D.
SENIOR GROUP LEADER GURDON
UNIVERSITY OF CAMBRIDGE

Emma Rawlins is a Senior Group Leader and MRC Senior non-clinical Fellow based at the Gurdon Institute, University of Cambridge and her laboratory works on lung developmental and stem cell biology and regeneration.

Specific questions addressed include: How are our lungs built and maintained? How does this go wrong in disease? Can we use our insights from developmental biology to induce effective lung regeneration? Or to promote improved maturation of premature lungs?

The laboratory uses a combination of human embryonic lung organoids and mouse genetics as model systems. They perform multiple techniques including, in vitro and mouse genetics, lineage-tracing, microscopy, live-imaging, cellular and molecular techniques. They have recently adapted several CRISPR techniques for efficient use in human organoids.



## Speaker

DR. SHAHIN RAFII, MD
PROFESSOR MEDICINE- REPRODUCTIVE MEDICINE
WEILL CORNELL MEDICAL COLLEGE

Shahin Rafii, MD is Arthur B. Belfer Professor of Genetic Medicine, Director of Ansary Stem Cell Institute and Division Chief of Regenerative Medicine at Weill Cornell Medicine. His research focuses on identifying cellular and molecular pathways involved in organ regeneration and tumor targeting. His group has spearheaded the concept that tissue-specific endothelial cells by supplying paracrine factors, known as "angiocrine factors" directly specify and maintain self-renewal and differentiation of hematopoietic, liver and lung stem and progenitor cells without provoking maladaptive fibrosis or tumorigenesis. His laboratory has developed innovative technologies to generate abundant adaptable and hemodynamic organotypic endothelial cells to uncover the molecular determinants of vascular heterogeneity and that could be therapeutically transplanted for organ regeneration or targeted for blocking tumor growth.

## Speaker

DR. APRIL KLOXIN, PH.D.
ASSOCIATE PROFESSOR OF CHEMICAL & BIOMOLECULAR ENGINEERING AND MATERIALS SCIENCE & ENGINEERING
UNIVERSITY DELAWARE

April M. Kloxin, Ph.D., is the Thomas and Kipp Gutshall Development Professor of Chemical and Biomolecular Engineering, an Associate Professor in Chemical and Biomolecular Engineering and Materials Science and Engineering at the University of Delaware (UD), and a member of the Breast Cancer Research Program at the Helen F. Graham Cancer Center and Research Institute in the Christiana Care Health System. She obtained her B.S. and M.S. in Chemical Engineering from North Carolina State University and Ph.D. in Chemical Engineering from the University of Colorado, Boulder, as a NASA Graduate Student Research Program Fellow, and trained as a Howard Hughes Medical Institute Postdoctoral Research Associate at the University of Colorado, Boulder. Her multi-disciplinary group creates unique materials with multiscale property control and applies them in conjunction with other innovative molecular tools for addressing outstanding problems in human health, with a focus on understanding dynamic cell-microenvironment interactions in wound healing, fibrosis, and cancer. She is a recipient of the 2019 Biomaterials Science Lectureship, 2018 ACS PMSE Arthur K. Doolittle Award, a NIH Director's New Innovator Award, a Susan G. Komen Foundation Career Catalyst Research award, a NSF CAREER award, and a Pew Scholars in Biomedical Sciences award.

**NHLBI Division of Lung Diseases Reverse-Remodel Workshop Planning Committee and Workshop Co-Chairs:**
**Dr. Josh Fessel, MD, Ph.D., NHLBI**
**Dr. Marrah Lachowicz-Scroggins, Ph.D., NHLBI**
**Dr. Aaron Laposky, Ph.D., NHLBI**
**Dr. Sara Lin, Ph.D., NHLBI**
**Dr. Jining Lu, Ph.D., NHLBI**
**Dr. Qing Lu, DVM, Ph.D., NHLBI**
**Dr. Brigid Hogan, Ph.D., FRS, Professor, Cell Biology and Pediatrics, Duke University School of Medicine**
**Dr. Y.S. Prakash MD, Ph.D., Professor, Anesthesiology and Physiology, Mayo Clinic Rochester**



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