

National Heart, Lung,
and Blood Institute

CURRENT AND FUTURE RESEARCH NEEDS IN THE ERA OF HIGHLY EFFECTIVE MODULATOR THERAPIES FOR CYSTIC FIBROSIS

**VIRTUAL WORKSHOP
JUNE 2-3, 2022**

PROGRAM BOOK

MEET THE TEAM

NHLBI WORKSHOP PLANNING COMMITTEE

- **Marrah Lachowicz-Scroggins, Ph.D.**, *Program Director Division of Lung Diseases, NHLBI, Planning Committee Lead*
- **Tom Eggerman, M.D., Ph.D.**, *Program Director, Division of Diabetes, Endocrinology, and Metabolic Diseases, NIDDK*
- **Xin-Xing Gu, M.D.**, *Program Director, Respiratory Diseases Branch, NIAID*
- **JP Clancy, M.D.**, *Vice President of Clinical Research, Cystic Fibrosis Foundation*
- **John Engelhardt, Ph.D.**, *University of Iowa, Workshop Co-chair*
- **Susan Birkett, PharmD, Ph.D.** *University of Alabama Birmingham, Workshop Co-chair*
- **Nicole Mayer Hamblett, Ph.D.**, *Seattle Children's Hospital, Workshop Co-chair*
- **Katie Hisert, MD, Ph.D.**, *National Jewish Health, Workshop Co-chair*

ADDITIONAL MEMBERS FROM CYSTIC FIBROSIS FOUNDATION:

- **Dara Riva, MS**, *Director of Clinical Research Awards*
- **Elizabeth Yu**, *Director of Physician Scientist Training Programs*
- **Katherine Tuggle, Ph.D.**, *Sr. Director of Research*
- **Patrick Thibodeau, Ph.D.**, *Vice President of Basic Research*

9:00 AM – 9:05 AM

WELCOME ADDRESS ON BEHALF OF NHLBI

DR. JIM KILEY, PH.D.,
DIRECTOR, DIVISION OF LUNG DISEASES

9:05 AM – 9:15 AM

INTRODUCTION TO WORKSHOP AND MEETING LOGISTICS

DR. MARRAH LACHOWICZ-SCROGGINS, PH.D.,
PROGRAM DIRECTOR, DIVISION OF LUNG DISEASES

CYSTIC FIBROSIS RESEARCH LANDSCAPE IN THE ERA OF HIGH EFFECTIVE MODULATOR THERAPIES

This session will set the stage for the meeting with an overview of the current cystic fibrosis (CF) research landscape and the development pipeline of CFTR-based therapies for all including novel modulators, genetic-based therapies, and readthrough agents. This session will also address how the outcomes and future research needs of those on highly effective modulator therapy (HEMT) will critically inform the research needed when disease modifying therapies are available and accessible to all individuals with CF.

Session Moderator: *Dr. JP Clancy, M.D., Vice President of Clinical Research, Cystic Fibrosis*

9:15 AM – 9:45 AM

DR. JP CLANCY, M.D.,

*VICE PRESIDENT OF CLINICAL RESEARCH,
CYSTIC FIBROSIS FOUNDATION*

DR. STEVEN ROWE, M.D.,

*CHIEF SCIENTIFIC OFFICER, CYSTIC FIBROSIS
FOUNDATION*

9:45 AM – 10:00 AM

DR. DEEPIKA POLINENI, M.D., MPH,

*ASSOCIATE PROFESSOR, PULMONARY,
CRITICAL CARE AND SLEEP MEDICINE,
UNIVERSITY OF KANSAS MEDICAL CENTER &
CHILDREN'S MERCY HOSPITAL*

10:00 AM – 10:15 AM

COMMUNITY MEMBER PERSPECTIVE

MS. MELANIE LAWRENCE,

*PERSON WITH CYSTIC FIBROSIS,
COMMUNITY CONSULTANT*

10:15 AM – 10:30 AM

Q&A

AGENDA: JUNE 2, 2022

DAY 1

SESSION 1: ANIMAL MODEL SYSTEMS TO STUDY HIGH EFFECTIVE MODULATOR THERAPIES

This session will introduce current animal models to study HEMT discussing their capabilities and limitations including CF mouse, rat, ferret, pig and sheep models. Goal is to allow the audience to formulate potential areas of research in CF animal model that can enhance understanding of the CF human condition and inform clinical studies.

Session Moderators: *Dr. Susan Birket PharmD, Ph.D. Assistant Professor, University of Alabama Birmingham & Dr. Ann Harris, Ph.D, Professor, Department of Genetics and Genome Sciences, School of Medicine, Case Western Reserve University*

10:30 AM – 10:45 AM

DR. CRAIG HODGES, PH.D.,

ASSOCIATE PROFESSOR, DEPARTMENT OF GENETICS AND GENOME SCIENCES, SCHOOL OF MEDICINE, CASE WESTERN RESERVE UNIVERSITY

10:45 AM – 11:00 AM

DR. SUSAN BIRKET, PHARM.D, PH.D.

ASSISTANT PROFESSOR, UNIVERSITY OF ALABAMA BIRMINGHAM

11:00 AM – 11:15 AM

DR. JOHN ENGELHARDT, PH.D.,

PROFESSOR OF ANATOMY AND CELL BIOLOGY, UNIVERSITY OF IOWA

11:15 AM – 11:30 AM

SARAH ERNST, B.S.

RESEARCH ASSOCIATE, UNIVERSITY OF IOWA

11:30 AM – 11:45 AM

DR. IRINA POLEJAEVA, PH.D., MS, USTAR

PROFESSOR, UTAH STATE UNIVERSITY

DR. ANN HARRIS, PH.D,

PROFESSOR, DEPARTMENT OF GENETICS AND GENOME SCIENCES, SCHOOL OF MEDICINE, CASE WESTERN RESERVE UNIVERSITY

11:45 AM – 12:15 PM

Q&A

12:15 PM – 12:45 PM

BREAK

SESSION 2: LATE-STAGE CYSTIC FIBROSIS LUNG DISEASE PATHOPHYSIOLOGY AND PROCESSES

The session will discuss what lung pathology of CF is reversible in people with chronic and established lung disease, including structural changes and chronic infection. Cross-talk between endocrine systems, nutrition and metabolism will be addressed and how changes in these systems link to lung disease progression. Goal is to define clinical challenges for CF patients on HEMT with chronic lung disease.

Session Moderators: *Dr. Katie Hisert, MD, Ph.D., National Jewish Health, Workshop Co-chair & Dr. Jessica Alvarez Ph.D., RD, Associate Professor, Division Endocrinology, Metabolism and Lipids, Department of Medicine, Emory University School of Medicine*

12:45 PM – 1:00 PM

DR. FRANK MCKEON, PH.D.,
PROFESSOR, DIRECTOR OF SOMATIC STEM CELL CENTER, AND CPRIT ESTABLISHED INVESTIGATOR IN CANCER RESEARCH, UNIVERSITY OF HOUSTON

DR. WA XIAN, PH.D.,
RESEARCH ASSOCIATE PROFESSOR, STEM CELL CENTER, DEPARTMENT OF BIOLOGY & BIOCHEMISTRY, UNIVERSITY OF HOUSTON

1:00 PM – 1:15 PM

DR. ESZTER VLADAR, PH.D.,
ASSISTANT PROFESSOR, MEDICINE-PULMONARY SCIENCES & CRITICAL CARE, UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

1:15 PM – 1:30 PM

DR. PRADEEP SINGH, M.D.,
PROFESSOR, DIVISION OF PULMONARY, CRITICAL CARE, AND SLEEP MEDICINE, UNIVERSITY OF WASHINGTON

1:30 PM – 1:45PM

DR. ANDREA KELLY, M.D., MSCE,
PROFESSOR OF PEDIATRICS, CHILDREN'S HOSPITAL OF PHILADELPHIA

AGENDA: JUNE 2, 2022

DAY 1

1:45 PM – 2:00 PM

DR. JESSICA ALVAREZ PH.D., RD,
*ASSOCIATE PROFESSOR, DIVISION
ENDOCRINOLOGY, METABOLISM AND LIPIDS,
DEPARTMENT OF MEDICINE, EMORY
UNIVERSITY SCHOOL OF MEDICINE*

2:00 PM – 2:30 PM

Q&A

2:30 PM – 2:45 PM

BREAK

2:45 PM – 3:00 PM

**COMMUNITY PERSPECTIVES, NO ONE LEFT
BEHIND: PERSPECTIVES FOR INDIVIDUALS
NOT ELIGIBLE FOR MODULATOR THERAPIES**

LISA J. HAMBURGER, *PARENT OF SON WITH
CYSTIC FIBROSIS* & **KADE HAMMES** *PARENT OF
CHILD WITH CYSTIC FIBROSIS*

3:00 PM – 4:00 PM

BREAKOUT ONE:

BREAKOUT SESSIONS:

**MAXIMIZING RESEARCH POTENTIAL FOR
PATIENT-DERIVED MODELS AND SYSTEMS.**

*How are we using these tools to study modulators,
infection, epithelial cell damage, genotype/phenotype
relationships, gene therapy, etc.? What are the
advantages/limitations to different models: (airway
cells, 3D Organoids, explants, cells on a chip, etc.)?*

MODERATORS AND DISCUSSANTS:

- DR. MARTINA GENTZSCH, PH.D., *ASSOCIATE
PROFESSOR, MARSICO LUNG INSTITUTE,
UNIVERSITY OF NORTH CAROLINA CHAPEL HILL*
- DR. ANJAPARAVANDA "AP" NAREN PH.D.,
PROFESSOR, CEDARS-SINAI MEDICAL CENTER
- DR. AMY RYAN, PH.D., *ASSOCIATE PROFESSOR
OF ANATOMY AND CELL BIOLOGY, UNIVERSITY
OF IOWA*

BREAKOUT TWO:

**USING ANIMAL MODELS IN THE CONTEXT
OF HEMT INFORM CLINICALLY RELEVANT
KNOWLEDGE GAPS.**

*How do we use animal models to study
modulators, infection, epithelial cell damage,
genotype/phenotype relationships, gene therapy,
etc.? What are the advantages/limitations to
different animal models?*

MODERATORS AND DISCUSSANTS:

- DR. SUSAN REYNOLDS, PH.D., *PRINCIPAL INVESTIGATOR, NATIONWIDE CHILDREN'S HOSPITAL*
- DR. BRUCE STANTON, PH.D., *ANDREW C. VAIL PROFESSOR, GEISEL SCHOOL OF MEDICINE AT DARTMOUTH*
- DR. JOHN ENGELHARDT, PH.D., *UNIVERSITY OF IOWA, WORKSHOP CO-CHAIR*

BREAKOUT THREE:

LATE-STAGE CYSTIC FIBROSIS LUNG DISEASE ON HEMT.

What do we know about infection post-HEMT: what are emerging challenges with known organisms, and do we expect new organisms? Changes in background/maintenance therapy post-HEMT: what is the state of the field? Do we have enough information to know when to start or stop therapies? What are the most important questions for understanding damage to epithelial cells from people with longstanding airways disease, much of which may not be reversed with HEMT?

MODERATORS AND DISCUSSANTS:

- DR. LINDSAY CAVERLY, M.D., *ASSISTANT PROFESSOR, UNIVERSITY OF MICHIGAN HEALTH*
- DR. MANU JAIN, M.D., *PROFESSOR OF MEDICINE (PULMONARY AND CRITICAL CARE) AND PEDIATRICS, NORTHWESTERN MEDICINE*
- DR. GINA HONG M.D., MHS, *ASSISTANT PROFESSOR OF MEDICINE, HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA*

4:00 PM – 4:15 PM

BREAK

4:15 PM – 5:15 PM

REGROUP AND RECAP-BREAKOUT REPORT

9:00 AM – 9:15 AM

**INTRODUCTION AND MEETING LOGISTICS
RECAP DAY ONE AND GOALS FOR DAY TWO**

DR. MARRAH LACHOWICZ-SCROGGINS, PH.D.,
PROGRAM DIRECTOR, DIVISION OF LUNG
DISEASES

**SESSION 3: CONCERNS AND QUESTIONS ABOUT PEOPLE WITH
CYSTIC FIBROSIS AND EARLY LUNG DISEASE**

This session will define clinical challenges for CF patients on HEMT without chronic lung. Topics include: additive therapies for children on HEMT, when to start or stop? Disease monitoring in children starting HEMT including bronchoscopy, imaging, LCI, pathogen monitoring, CFRD screening and non-invasive biomarkers. Effects of HEMT on host-pathogen interactions and extrapulmonary organ systems—multiorgan interactions on the evolution of CF lung disease. Potential use of HEMT in utero and early models to predict disease course.

***Session Moderators:** Dr. Jennifer Bomberger, Ph.D., Associate Professor, Microbiology and Molecular Genetics, University of Pittsburgh & Dr. Terri Laguna M.D., MSCS, Division Head, Pulmonary and Sleep Medicine; Associate Professor of Pediatrics, Northwestern University Feinberg School of Medicine*

9:15 AM – 9:30 AM

DR. TERRI LAGUNA M.D.,
MSCS, DIVISION HEAD, PULMONARY AND SLEEP
MEDICINE; ASSOCIATE PROFESSOR OF
PEDIATRICS, NORTHWESTERN UNIVERSITY
FEINBERG SCHOOL OF MEDICINE

9:30 AM – 9:45 AM

DR. FELIX RATJEN, M.D., FRCP(C),
CHIEF, DIVISION OF PAEDIATRIC RESPIRATORY
MEDICINE, THE HOSPITAL FOR SICK CHILDREN

9:45 AM – 10:00 AM

DR. JENNIFER BOMBERGER, PH.D.,
ASSOCIATE PROFESSOR, MICROBIOLOGY AND
MOLECULAR GENETICS, UNIVERSITY OF
PITTSBURGH

AGENDA: JUNE 3, 2022

DAY 2

10:00 AM – 10:15 AM

DR. CHRISTOPHER FORTNER, M.D, PH.D.,
*ASSOCIATE PROFESSOR OF PEDIATRICS,
UPSTATE MEDICAL UNIVERSITY*

10:15 AM – 10:30 AM

DR. GERRY CUTTING, M.D.,
*PROFESSOR OF GENETIC MEDICINE, JOHN
HOPKINS MEDICINE*

10:30 AM – 11:00 AM

Q&A

SESSION 4: CONSIDERATIONS FOR MODULATOR USE IN SPECIAL POPULATIONS

This session will address modulator use and needs during pregnancy, post-transplant, in patients with ultra-rare mutations and as patients age with risk of age-related co-morbidities (cancer, renal failure, etc.). This session will also address racial disparities in CF including access to medication, representation in clinical trials and known healthcare disparities pre-modulators as a primer for a path forward to high quality clinical care for all patients with CF.

Session Moderators: *Dr. John Brewington, M.D., Assistant Professor, Department of Pediatrics, Cincinnati Children's & Dr. Meghan McGarry, M.D., MS, Assistant Professor, Pediatrics, University of California San Francisco*

11:00 AM – 11:15 AM

DR. JENNIFER L. TAYLOR-COUSAR, M,D, MSCS,
*MEDICAL DIRECTOR, CLINICAL RESEARCH SERVICES,
PROFESSOR, DIVISION OF PULMONARY, CRITICAL
CARE & SLEEP MEDICINE, NATIONAL JEWISH HEALTH*

11:15 AM – 11:30 AM

DR. KATHY RAMOS M.D., MS
*ASSISTANT PROFESSOR, DIVISION OF
PULMONARY, CRITICAL CARE AND SLEEP
MEDICINE, UNIVERSITY OF WASHINGTON*

11:30 AM – 11:45 AM

DR. CHRISTOPHER GOSS, MD, MS, FCCP,
*PROFESSOR, DIVISION OF PULMONARY,
CRITICAL CARE AND SLEEP MEDICINE,
UNIVERSITY OF WASHINGTON*

AGENDA: JUNE 3, 2022

DAY 2

11:45 AM – 12:00 PM

DR. JOHN BREWINGTON, M.D.,
*ASSISTANT PROFESSOR, DEPARTMENT OF
PEDIATRICS, CINCINNATI CHILDREN'S*

12:00 PM – 12:15 PM

DR. MEGAN MCGARRY, M.D., MS,
*ASSISTANT PROFESSOR, PEDIATRICS,
UNIVERSITY OF CALIFORNIA SAN FRANCISCO*

12:15 PM – 12:45 PM

Q&A

12:45 PM – 1:15 PM

BREAK

SSESSION 5: ADVANCING CLINICAL CARE AND OUTCOMES FOR PATIENTS WITH CF IN THE POST MODULATOR ERA

This session highlights the challenges of detecting outcomes and meaningful endpoints for research in the post-modulator era will include discussion of novel imaging, pathogen detection and remote data capture tools for monitoring lung disease progression in CF as well as defining and treating acute pulmonary exacerbations.

Session Moderators: *Dr. Nicole Mayer Hamblett, Ph.D., Seattle Children's Hospital, Workshop Co-chair & Dr. Margaret Rosenfeld, M.D., MPH, Professor and Associate Vice-Chair for Clinical Research, Department of Pediatrics, Seattle Children's*

1:15 PM – 1:30 PM

DR. ZACKARY CLEVELAND, PH.D.,
*ASSOCIATE PROFESSOR, UC DEPARTMENT OF
PEDIATRICS, CINCINNATI CHILDREN'S*

1:30 PM – 1:45 PM

DR. HEATHER BEAN, PH.D.,
*ASSISTANT PROFESSOR, SCHOOL OF LIFE
SCIENCES, ARIZONA STATE UNIVERSITY*

1:45 PM – 2:00 PM

DR. NATALIE ELLIOTT WEST, M.D., M.H.S.,
*ASSISTANT PROFESSOR OF MEDICINE, JOHNS
HOPKINS MEDICINE*

2:00 PM – 2:15 PM

DR. MARGARET ROSENFELD, M.D., MPH,
*PROFESSOR AND ASSOCIATE VICE-CHAIR FOR
CLINICAL RESEARCH, DEPARTMENT OF
PEDIATRICS, SEATTLE CHILDREN'S*

2:15 PM – 2:30 PM

COMMUNITY PERSPECTIVE

MS. JENNIFER KYLE

PERSON WITH CYSTIC FIBROSIS

2:30 PM – 3:00 PM

Q&A

3:00 PM – 4:00 PM

BREAKOUT SESSIONS

BREAKOUT ONE:

RISKS/BENEFITS OF STARTING IN PWCF WITH MINIMAL DISEASE ON HEMT (+/- ADD-ON THERAPIES) WHEN WE DON'T HAVE LONG TERM SAFETY DATA ON HEMT.

In young patients and people with CF with minimal to mild disease: big question is when to start HEMT? What are the issues around safety? What do we know about stopping/optimizing therapies post-modulator initiation—which could cover a range of classes of therapies from anti-infectives to mucolytics and ACT. What information do we need to determine optimal dosing of HEMT: right now we use a one size fits all, but some patients seems to do better on lower doses with just as much efficacy.

MODERATORS AND DISCUSSANTS:

- DR. RON RUBENSTEIN, M.D., PH.D.,
*PROFESSOR OF PEDIATRICS, DIVISION CHIEF -
DEPARTMENT OF PEDIATRICS ALLERGY AND
PULMONARY MEDICINE, WASHINGTON
UNIVERSITY SCHOOL OF MEDICINE IN ST. LOUIS*
- DR. EDITH ZEMANICK, M.D.,
*ASSOCIATE PROFESSOR, PEDIATRICS-
PULMONARY MEDICINE, UNIVERSITY OF
COLORADO SCHOOL OF MEDICINE*
- DR. JESSICA PITTMAN, M.D., MPH, ASSOCIATE
*PROFESSOR, DEPARTMENT OF PEDIATRICS
ALLERGY AND PULMONARY MEDICINE,
WASHINGTON UNIVERSITY SCHOOL OF
MEDICINE IN ST. LOUIS*

BREAKOUT TWO:

ADVANCING CLINICAL CARE AND OUTCOMES FOR PATIENTS WITH CF IN THE POST MODULATOR

Advancing clinical care we need to take a deeper dive into health equity and innovative ways to support real world studies and clinical trials. Thinking about chronic airways disease, what do we know about the overlap with what is known about non-CF bronchiectasis, how can we leverage this information about what the CF lung may look like as pwCF age on modulator therapies. What tools and knowledge do we have, or even need to develop, to understand CF disease progression? How to best detect changes and outcomes in the post-modulator era when our normal indicators (i.e. LF decline) may not be (a) valid and/or (b) sensitive enough? How do we assess efficacy of new medications when people's lungs seem healthy by current metrics?

MODERATORS AND DISCUSSANTS:

- DR. BONNIE RAMSEY, M.D., *ENDOWED PROFESSOR IN CYSTIC FIBROSIS AND VICE CHAIR FOR RESEARCH, DEPARTMENT OF PEDIATRICS, UNIVERSITY OF WASHINGTON SCHOOL OF MEDICINE*
- DR. RHONDA SZCZESNIAK, PH.D., *ASSOCIATE PROFESSOR, BIostat/EPI & PULM MED CINCINNATI CHILDREN'S HOSPITAL MEDICAL CENTER*
- DR. TIMOTHY CORCORAN, PH.D., *ASSOCIATE PROFESSOR, MEDICINE AND BIOENGINEERING, UNIVERSITY OF PITTSBURGH*

BREAKOUT THREE:

CONSIDERATIONS FOR MODULATOR USE IN SPECIAL POPULATIONS WITH CF:

We know that many people are living longer with CF, what will life look like for pwCF in 10 years? What new disease manifestation, complications or co-morbidities we might expect to arise as diseases of aging or potential under-recognized co-occurring conditions (cancers, renal failure)? What does the future look like for lung transplant? Will patients just be older when they need a transplant? As pwCF are living longer, we need to understand other complex health care needs such as relationships and emotional needs—this would include reproductive needs (fertility, pregnancy, breastfeeding, newborn care) and mental health needs as individuals live longer with the burden of chronic illness.

MODERATORS AND DISCUSSANTS:

- DR. KATHRYN OLIVER, PH.D., ASSISTANT PROFESSOR, DEPARTMENT OF PEDIATRICS, DIVISION OF PULMONARY, ALLERGY/IMMUNOLOGY, CYSTIC FIBROSIS & SLEEP, EMORY UNIVERSITY SCHOOL OF MEDICINE
- DR. GABRIELA OATES, PH.D., ASSISTANT PROFESSOR, DIVISION OF PEDIATRIC PULMONARY & SLEEP MEDICINE, UNIVERSITY OF ALABAMA BIRMINGHAM
- DR. TRACI KAZMERSKI, M.D., M.S., ASSISTANT PROFESSOR OF PEDIATRICS, UNIVERSITY OF PITTSBURGH

4:00 PM - 4:15 PM

BREAK

4:15 PM - 5:15 PM

**REGROUP AND RECAP-BREAKOUT REPORT
WHAT ARE THE GAPS AND
OPPORTUNITIES? WHAT RESEARCH
PROGRAMS ARE NEEDED?**

WELCOME ADDRESS ON BEHALF OF NHLBI

Dr. Jim Kiley, Ph.D.

Director, Division of Lung Diseases



Bio: Dr. James Kiley serves as the Director of the Division of Lung Diseases at the National Heart, Lung and Blood Institute at the National Institutes of Health (NIH). Prior to this position, he was the Director of the National Center on Sleep Disorders Research at NIH. Dr. Kiley received his education and training at St Anselm's College, Kansas State University and the University of North Carolina at Chapel Hill. He is a member of a number of professional organizations and has received numerous honors and awards for his outstanding contributions to advancing pulmonary biology in health and disease, sleep research, and public health. His major areas of interest include control of respiration, sleep, and the pathophysiology of obstructive airways disease. Dr. Kiley is the author or co-author of over 100 scientific articles.

Marrah Lachowicz-Scroggins, Ph.D.

Program Director Division of Lung Diseases,
NHLBI, Planning Committee Lead



Bio: I am a Program Director at the National Institutes of Health at the National Heart, Lung, and Blood Institute, Division of Lung Diseases in the Airway Biology and Disease Branch, mainly overseeing the Institute's Cystic Fibrosis grant portfolio. Before joining NHLBI in 2018, I was an Assistant Research Professor at University of California San Francisco in the Airway Clinical Research Center. I received my Ph.D. in Comparative Pathology at the University of California Davis in 2010 and hold a Graduate Certificate in Clinical Pathology from University of Massachusetts Lowell. Currently, I serve as a Project

Scientist for the Genetic Disease of Mucociliary Clearance Consortium part of the Rare Diseases Clinical Research Network jointly funded by NHLBI and NCATS Office of Rare Disease Research. I also manage grants in the Common Fund Somatic Cell Gene Editing Program (SCGE) for Innovative Technologies to Deliver Genome Editing Machinery to Disease-relevant Cells and Tissues and serve as a NIH SCGE Working Group Member. I am a member of the NHLBI Women's Health Working Group, serving as Co-Chair the Working Group since July 2020. I am also serving as a Coordinating Committee Member on behalf of NHLBI to the Coordinating Committee on Research on Women's Health. I am the Chair of the RECOVER Pathobiology Working Group for addressing the mechanisms of Post-Acute Sequelae of COVID-19 (PASC). I am part of several other Trans-NIH working groups and committees for which I have shared interests. Twitter @LachowiczMarrah

Clinical Expertise

Oversight of NHLBI clinical trials and observational studies in Cystic Fibrosis and other Disorders of Mucociliary Clearance.

CF/Research Expertise

My areas of focus are respiratory medicine, pulmonary physiology and immunology with a concentration in airways diseases Cystic Fibrosis, disorders of mucociliary clearance including ciliopathies and other rare lung diseases. My current portfolio also includes respiratory tract infections/susceptibility, mucins/mucus biology, mucosal immunology, epithelial cell biology, gene editing technologies and women's health. My research skills are in translational bench-to-bedside models using broad application of systems biology, histology and molecular techniques.



SPEAKERS

CYSTIC FIBROSIS RESEARCH LANDSCAPE IN THE ERA OF HIGH EFFECTIVE MODULATOR THERAPIES

JP Clancy M.D.

Vice President of Clinical Research
Cystic Fibrosis Foundation (CFF)



Bio: I was born and raised in Iowa (Go Hawks!) and now live in Cincinnati (Go Bengals!). My pediatric residency was at UVA and my fellowship was at UAB. Prior to joining the CFF in 2018, I was a CF clinician (pediatric pulmonologist) and researcher. I worked from 1993 – 20210 at UAB, and subsequently Cincinnati Children’s Hospital Medical Center (2011 – 2018).

Clinical Expertise

- CF healthcare provider for kids with CF

CF/Research Expertise

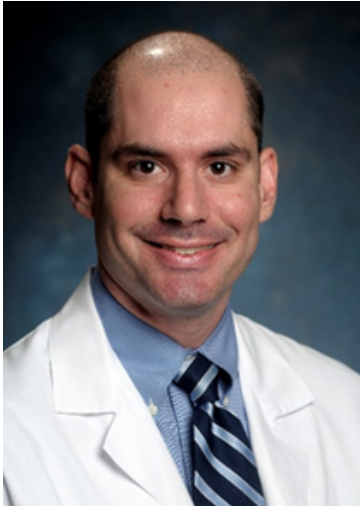
- CFTR and epithelial biology
- MR-based pulmonary imaging
- Clinical outcome measures for CF clinical research

Gaps:

1. Determine short and long-term benefits of initiating highly effective modulators in young children prior to established lung disease
2. Develop novel ways to detect and monitor infection in CF patients receiving HEM
3. Understand mechanisms responsible for variability in clinical response to HEM
4. Define phenotypes of CF patients receiving HEM therapy to guide use of symptomatic therapies

Steven M. Rowe, M.D., MSPH

Professor and Director, Cystic Fibrosis Research Center
University of Alabama at Birmingham



Bio: Steven M. Rowe is Professor with tenure in the Departments of Medicine (Pulmonary and Critical Care), Pediatrics (Pediatric Pulmonology), and Cell Developmental and Integrative Biology. He is completing his tenure as Director of the Gregory Fleming Ja12t for translational science for the Cystic Fibrosis Foundation and has been named Chief Scientific Officer and will assume that role in July 2022 while maintaining his appointment at UAB.

Clinical Expertise

Dr. Rowe specializes in developing new treatments for cystic fibrosis. He maintains expertise in the design and conduct of clinical trials targeting the basic CF defect. Dr. Rowe also has an interest in Biomarkers in CF, including ion transport and the relation between mucus stasis.

CF/Research Expertise

Dr. Rowe is a respected international authority in the design and conduct of clinical trials targeting the basic CF defect, and has made key advances in the measurement and interpretation of CFTR function in humans and animals. In a related effort, Dr. Rowe has advanced both the molecular and clinical understanding of suppression of premature termination codons, representing an exciting strategy for treatment of genetic diseases caused by nonsense mutations, which is responsible for ~10% of all genetic diseases. Dr. Rowe has discovered that COPD patient's exhibit 'acquired CFTR dysfunction' through a pathway that causes delayed mucociliary clearance and confers chronic bronchitis. The approach has led to new efforts to evaluate CFTR modulators in patients with chronic bronchitis, potentially leading to a new paradigm for COPD treatment. Dr. Rowe co-invented one-micron resolution optical coherence tomography that captures 3D imaging in real-time at the cellular level, shedding light on disease mechanism through measurements of the functional microanatomy of the airway surface, advancing our understanding of airway disease pathogenesis and novel treatments.

Deepika Polineni

Associate Professor, Pulmonary,
Critical Care and Sleep Medicine



Bio: Dr. Deepika Polineni is an Associate Professor of Internal Medicine in the Division of Pulmonary, Critical Care, and Sleep Medicine at the University of Kansas Medical Center. She received her Bachelor of Arts and Doctor of Medicine degrees from the University of Missouri, Kansas City, and Master of Public Health degree from Boston University. She completed internship and residency in internal medicine at the University of Michigan in Ann Arbor, Mich., fellowship in pulmonary medicine at the University of North Carolina at Chapel Hill, and post-doctoral research in pulmonary medicine at Washington University in St. Louis. Dr. Polineni's research interests include the identification of non-CFTR genetic modifiers of cystic fibrosis lung disease, as well as clinical trials of CFTR modulator therapies. Her long-standing research focus has been in-vivo transcriptome wide association studies and metabolomic studies to identify differential gene expression and metabolite variability associated with CF lung disease severity. These studies are conducted with the goal of advancing personalized CF therapies. She has additionally begun a multi-center clinical trial, through the CF Foundation Success with Therapies Research Consortium, to study novel tele-communication-based methods aimed at improving treatment adherence in complex CF care regimens.

Clinical Expertise

- Cystic Fibrosis, Primary Ciliary Dyskinesia
CF/Research Expertise
 - Genetic modifiers of CF lung disease severity; treatment adherence
-

SESSION 1: ANIMAL MODEL SYSTEMS TO STUDY HIGH EFFECTIVE MODULATOR THERAPIES

Dr. Craig Hodges, Ph.D.

Associate Professor
Case Western Reserve University



Bio: I am an Associate Professor at Case Western Reserve University (CWRU) in the Department of Genetics and Genome Sciences. Before joining CWRU faculty in 2009, I received my B.S. in Biology from Berry College in 1996 and my Ph.D. in Genetics from Case Western Reserve University in 2002. During my postdoctoral studies I used various animal models to study somatic cell nuclear transfer (cows and pigs), meiosis and infertility (mouse) and cystic fibrosis (mouse). I have received training in genetics, developmental biology, cell biology, molecular biology, reproduction and endocrinology. The focus of my research is the creation and use of novel CF mouse models to understand the basic biology of CF as well as test therapeutics to hopefully cure CF. I also direct the Cystic Fibrosis Mouse Resource Center (CFMRC) funded by the Cystic Fibrosis Foundation. The CFMRC serves a unique service to the CF research community as it is the largest creator and distributor of CF and CF-related mouse models in the world. The core maintains over 50 different CF mouse strains at any one time. The production and phenotyping of these various CF mouse strains has allowed us to distribute CF mice and provide CF mouse related services to 267 investigators at 115 universities and 27 companies in 32 states in the USA as well as 16 countries around the world since 2006.

CF/Research Expertise:

My areas of focus are the creation and utilization of novel mouse models of CF to study intestinal dysfunction and growth, nonsense mutations, gene editing, reproduction and fertility and novel therapeutics .

Susan Birket, Pharm.D., Ph.D.

Assistant Professor, Department of Medicine
University of Alabama at Birmingham



Bio: I am an Associate Professor at Case Western Reserve University (CWRU) in the Department of Genetics and Genome Sciences. Before joining CWRU faculty in 2009, I received my B.S. in Biology from Berry College in 1996 and my Ph.D. in Genetics from Case Western Reserve University in 2002. During my postdoctoral studies I used various animal models to study somatic cell nuclear transfer (cows and pigs), meiosis and infertility (mouse) and cystic fibrosis (mouse). I have received training in genetics, developmental biology, cell biology, molecular biology, reproduction and endocrinology. The focus of my research is the creation and use of novel CF mouse models to understand the basic biology of CF as well as test therapeutics to hopefully cure CF. I also direct the Cystic Fibrosis Mouse Resource Center (CFMRC) funded by the Cystic Fibrosis Foundation. The CFMRC serves a unique service to the CF research community as it is the largest creator and distributor of CF and CF-related mouse models in the world. The core maintains over 50 different CF mouse strains at any one time. The production and phenotyping of these various CF mouse strains has allowed us to distribute CF mice and provide CF mouse related services to 267 investigators at 115 universities and 27 companies in 32 states in the USA as well as 16 countries around the world since 2006.

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Susan Birket, Pharm.D., Ph.D.

Assistant Professor, Department of Medicine
University of Alabama at Birmingham



Knowledge gaps:

- What are the long-term effects of HEMT on established infections in the lung?
- Do HEMT correct abnormal mucus in the setting of infection and inflammation?
- Are continued supportive therapies necessary for mucus accumulation and infection?

Readings:

- 1.** Birket SE, Davis JM, Fernandez-Petty CM, Henderson AG, Oden AM, Tang LP, Wen H, Hong J, Fu Lianwu, Chambers A, Fields A, Zhao G, Tearney GJ, Sorscher EJ, Rowe SM. "Ivacaftor Reverses Airway Mucus Abnormalities in a Rat Model Harboring a Humanized G551D-CFTR." *Am J Resp Crit Care Med.* 2020 Nov 1;202(9):1271-1282.
- 2.** Green ME, Lindgren N, Henderson AG, Keith JD, Oden AM, Birket SE. "Ivacaftor partially corrects airway inflammation in a humanized G551D rat." *American Journal of Physiology-Lung Cellular and Molecular Physiology.* 2021 June 1;320(6):L1093:L1100.
- 3.** Keith JD, Henderson AG, Fernandez-Petty CM, Davis JM, Oden AM, Birket SE. "Muc5b contributes to mucus abnormality in rat models of cystic fibrosis." *Frontiers in Physiology.* 2022 Apr;13:884166.
- 4.** Henderson AG, Davis JM, Keith JD, Green ME, Oden AM, Rowe SM, Birket SE. "Static mucus impairs bacterial clearance and allows chronic infection with *Pseudomonas aeruginosa* in the cystic fibrosis rat." *European Respiratory Journal.* Epub ahead of print.



John F. Engelhardt, Ph.D.

Professor and Chair,
Department of Anatomy and Cell Biology
University of Iowa Carver College of Medicine



Bio: Molecular and Cell Engineering, UPenn (Assistant Professor, 1994 – 1997); Anatomy and Cell Biology, University of Iowa (Associate Professor, 1997 – 2001; Professor, 2001 – Present), Director of Center for Gene Therapy, University of Iowa (1998 – Present); Chair of the Department of Anatomy and Cell Biology (2004 – Present).

CF Research Expertise

Lung molecular and cellular biology as it relates to the pathogenesis and treatment of cystic fibrosis (CF) lung disease; the development of transgenic ferret models to study CF lung and pancreatic stem cell biology; viral vectors and gene therapy for CF; pathogenesis cystic fibrosis related diabetes; the study of airway stem cell niches, the regulatory mechanisms that control stem cell proliferation and repair in the airway, and the development of cell-based therapies for CF using stem cells.

Sarah Ernst, B.S.

Researcher
University of Iowa



Bio: I am a member of the CF research group at the University of Iowa. I graduated from the University of Iowa in 2009 with a Bachelor of Science in chemistry. Under the leadership of Mike Welsh and David Stoltz, I have assisted with various projects, publications, and clinical trials.

CF/Research Expertise

•My research experience began with studying ion transport in excised tissues and primary airway cultures from humans and animal models of CF and assessing CFTR function in airway and GI tissues from various models of CF. More recently, I've had the opportunity to design and help characterize a pig model with the G551D mutation and use this model to study effects of modulator therapy.



Irina Polejaeva, Ph.D.

Professor of Developmental Biology
Utah State University



Bio: I am a Professor of Developmental Biology in the Department of Animal, Dairy and Veterinary Sciences at Utah State University (USU) and also a member of the USU Veterinary Diagnostics and Infectious Diseases Team. I received my PhD in Developmental Biology from the National Institute of Animal Science in Moscow, Russia in 1993. Prior to joining USU in April 2011, I worked as the Project Manager for Porcine Nuclear Transfer Program at PPL Therapeutics, Inc. (Blacksburg, VA, USA) and then served for eight years as the Chief Scientific Officer at ViaGen, Inc. (Austin, TX, USA). My research led to the generation of the world's first cloned pigs by SCNT (Nature, 2000. 407: 86-90) the birth of the first 1,3-galactosyl-transferase deficient pigs (Science, 2003. 299: 411-414). More recently my laboratory was the first to report on efficient gene knockouts in goats using CRISPR/Cas9 and generate novel animal models including sheep models for Cystic Fibrosis, goat model for Atrial Fibrillation, surrogate sire goat model and the first trans-chromosomic goats for human polyclonal antibody production. I served on the Board of Governors for the International Embryo Technology Society (2015-2018). Since 2016, I have been also serving as the Chair of the Organizing and Scientific Committee for the Large Animal Genetic Engineering Summit that brings together reproductive biologists, geneticists, molecular biologists, animal model developers, and representatives of federal research and regulatory agencies.

Research Expertise

My primary research interests are:

- The development of genetically engineered large animal models using Somatic Cell Nuclear Transfer (SCNT or cloning) and CRISPR/Cas9 genome editing techniques; and
- Cloning efficiency improvement through understanding the molecular mechanism of epigenetic reprogramming during embryonic genome activation.

Ann Harris Ph.D.

Vice Chair for Research,
Leonard C Hanna Professor
Case Western Reserve University



Bio: BA, MA, University of Oxford, UK. Ph.D. University of London, UK.

Assistant Professor, Pediatric Research Unit, Guy's Hospital Medical School, University of London. 1985-1991. Associate Professor/Professor, Weatherall Institute of Molecular Medicine, University of Oxford. 1991-2005.

Professor, Director, Human Molecular Genetics Program Lurie Children's/Northwestern University, Chicago. 2005-2016. Case Western Reserve 2017-

CF/Research Expertise

- Cell-type specific and temporal regulation of the CFTR gene.
- Functional genomics of human epithelial tissues.
- Human epididymis function and molecular characterization.
- Generation of the CF sheep model and its use for investigating early development of CF disease by cellular/organoid and molecular methods.

Gaps:

Sheep models of HEMT

- Why the sheep?
- What aspects of CF disease does it model well?
- Current main applications of the model.

A sheep model of cystic fibrosis generated by CRISPR/Cas9 disruption of the CFTR gene

Sheep models of F508del and G542X cystic fibrosis mutation show cellular responses to human therapeutics

SESSION 2: LATE-STAGE CYSTIC FIBROSIS LUNG DISEASE PATHOPHYSIOLOGY AND PROCESSES

Frank D. McKeon, Ph.D.

Professor and Director Stem Cell Center, Dept. Biol. & Biochemistry, Univ. Houston



Bio: My laboratory investigates the biology of stem cells in chronic inflammatory diseases and cancer. After undergraduate studies at Pomona College in Los Angeles, I received my doctoral and postdoctoral training in Biochemistry and Biophysics with M. Kirschner at UCSF. I was then hired by Howard Green at the Harvard Medical School to start an independent laboratory focused on cell cycle control and immune signaling. At the time, Prof. Green was engaged in his revolutionary cloning of the epidermal stem cell and exploiting this in regenerative medicine for severe cutaneous burns. The discovery of the

p63 transcription factor in my laboratory and the demonstration, via mouse genetics, of its essential role in all stratified epithelia, suggested that Prof. Green's stem cell approach to regenerative medicine could be adapted to airway diseases. A fortuitous meeting with Wa Xian (w/ Christopher Crum, B&WH), who was seeking cloning approaches to stem cells of ovarian cancer, led to our initiating two laboratories at ASTAR in Singapore devoted to the development of stem cell cloning technologies. This Singapore experience included analyses with H1N1 influenza, which in turn revealed the stunning ability of the lung to regenerate despite >60% loss, and the essential role of a clonogenic p63+ cell from distal airways in this process. Armed with this knowledge, and with the stem cell cloning technologies of Wa Xian that showed these "adult" distal airway cells were intrinsically immortal and genomically stable, we set about with key collaborators to deconstruct the stem cell spectrum of chronic lung diseases including COPD, IPF, severe asthma, and cystic fibrosis. This work is establishing the concept that these serious lung conditions are the result of the emergence of pre-existing stem cell variants whose intrinsic function in normal individuals is to coordinate the innate immune response to incursions by pathogens. Disease states arise when these minor variants, which drive inflammation, fibrosis, and mucin production, become major variants in the lung. Accordingly, we believe these pathogenic variants both dictate the pathology of the respective lung conditions and represent proximal targets of disease mitigation. Our drug discovery efforts are predicated on the belief that effective therapies for cystic fibrosis will involve combinations of drugs targeting the variant combined with edited autologous stem cells.

CF/Research Expertise: Via collaboration with experts

Frank D. McKeon, Ph.D.

Professor and Director Stem Cell Center, Dept. Biol. & Biochemistry, Univ. Houston

Gaps:

Do the animal models that recapitulate CF lung disease show an emergence of pathogenic stem cells akin to those seen in COPD and more recently in CF?

How does the emergence of pathogenic stem cells relate to the onset of severe disease and to the response to CFTR modulators?

If these variant stem cells indeed drive CF and other chronic lung diseases, what are the short- and long-term options for translation?

Regenerative Metaplastic Clones in COPD lung Drive Inflammation and Fibrosis

Dr. Wa Xian, Ph.D.

Research Associate Professor, Stem Cell Center,
Dept. Biol. & Biochemistry, Univ. Houston



Bio: My laboratory is focused on developing technologies to clone stem cells in normal and abnormal airways, including those with chronic diseases and cancer. I received my Ph.D. in Molecular Genetics from the MD Anderson Cancer Center, performed postdoctoral studies in breast (J. Rosen, Baylor) and ovarian cancer (C. Crum, B&WH/Harvard), and became Principal Investigator in Molecule Medicine at ASTAR in Singapore. My studies there, in collaboration with F. McKeon, demonstrated the remarkable potential of the lung to regenerate following H1N1 influenza infections, and highlighted the role of a

p63+ stem cell in the terminal bronchioles in the generation of alveoli in this regenerative process (Kumar et al., Cell, 2011). Further work from my laboratory showed that these p63+ cells were both essential for lung regeneration and were readily transplantable via intratracheal delivery in acute injury (Zuo et al. Nature, 2015). More recently, I exploited this cloning technology to demonstrate that COPD lungs display four p63+ stem cells, including the normal p63+ cell seen in normal lungs as well as three pathogenic variants that are separately pro-inflammatory, pro-fibrotic, or hypermucinous, which in aggregate reflect COPD pathology (Rao et al., Cell 2020). My present work focuses on determining the stem cell repertoire of the lungs of cystic fibrosis patients and in drug discovery to target and eliminate these variants, whose pathogenic features appear resistant to CFTR complementation by genetic or therapeutic regimens

CF/Research Expertise

In collaboration with multiple investigators, my laboratory has focused on dissecting the stem cell spectrum of late-stage cystic fibrosis. To date with four cases, we have identified six stem cell variants common to each, including four that overlap with those seen in COPD and two novel variants that are pro-inflammatory versions of those committed to goblet and squamous cell metaplasia. We know that complementation of CFTR in these cells does not alter their pathogenic properties, nor does triple combinations of CFTR modulators. As such, much of my efforts are devoted to the discover of drugs that eliminates these variants coupled regenerative medicine involving corrected autologous cells. In collaboration with Drs. Engelhardt, Parekh, and Rowe, we are developing cloning strategies to identify the homologous stem cell variants in the ferret model of cystic fibrosis.

Eszter Katalin Vladar, Ph.D.

Assistant Professor

University of Colorado Anschutz Medical Campus



Bio: I am an assistant professor in the Departments of Medicine (Division of Pulmonary Sciences and Critical Care Medicine) and Cell and Developmental Biology at the University of Colorado Anschutz Medical Campus. Before joining CU Anschutz in 2018, I was a Research Instructor in the Department of Pathology at Stanford University School of Medicine. I received my PhD in 2007 and trained as a postdoctoral fellow at Stanford University.

CF/Research Expertise

My research focuses on the ciliated cells of the respiratory epithelium, which mediate the mucociliary clearance of the airways as our first line of defense against inhaled threats. My CF research interests are centered on mechanisms of airway epithelial remodeling and mucociliary dysfunction. Active projects investigate: 1) functional and transcriptomic airway epithelial responses to highly effective modulator therapy, 2) remodeling mechanisms due to aberrant activation of developmental signaling programs in CF airway epithelial stem cells, and 3) role of ciliated target cells in the SARS-CoV-2 infection of the CF airway epithelium. The Vladar lab is funded by grants from the NIH, the Cystic Fibrosis Foundation, the American Thoracic Society and the SPARK Program.

Pradeep K. Singh, M.D.

Professor and Director CF Research Development Program
University of Washington School of Medicine



Bio: Singh graduated from Columbia University in New York City, earned his MD at Northwestern University, and received postgraduate clinical and research training at the University of Iowa College of Medicine. He is Professor of Microbiology and Medicine and Director of the CF Research Development Program at the University of Washington.

Clinical Expertise

Singh received postgraduate training in internal medicine and pulmonary and critical care medicine at the University of Iowa College of Medicine, and has been active in CF clinical care.

CF/Research Expertise

Singh's research focuses on the pathogenesis of CF lung infections, the antimicrobial activity of mucosal secretions, antibiotic resistance, and new antimicrobial approaches.

Andrea Kelly, M.D., MS

Professor of Pediatrics

University of Pennsylvania Perelman School of Medicine



Bio: I have been an Attending Physician in the Division of Endocrinology & Diabetes at Children's Hospital of Philadelphia (CHOP) since 2001 when I completed my fellowship in pediatric endocrinology. I am also Professor of Pediatrics at the University of Pennsylvania Perelman School of Medicine, Associate Director of the CHOP Center for Human Phenomic Science and the Director of Research for our Division. I am a mentor for the Cystic Fibrosis Foundation Envision program, whose goal is to train pediatric and adult endocrinologist and reproductive specialists in the care of people with CF.

Clinical Expertise

- Cystic fibrosis related diabetes
- Cystic fibrosis related bone disease

Research Expertise

- Insulin secretion in cystic fibrosis
- Bone accrual
- Body composition

Gaps/Research Question:

Can highly effective CFTR modulator therapy improve, delay, and even prevent CFRD?

Mechanisms, patient characteristics, time frame for & durability

Is the protection against traditional cardiometabolic/cardiovascular risk mitigated by highly effective CFTR modulator therapy?

Can highly effective CFTR modulator therapy improve, delay, and even prevent CFBD?

Mechanisms, patient characteristics, time frame for & durability

Jessica A. Alvarez, Ph.D., RD

Associate Professor of Medicine
Emory University School of Medicine



Bio: I am currently an Associate Professor of Medicine at the Emory University School of Medicine, Division of Endocrinology. I am a registered dietitian with a Master's degree in Clinical Nutrition and a PhD in Nutrition Sciences from the University of Alabama at Birmingham. An overarching goal of my research program in CF is to gain a deep understanding of the role of diet and nutrition, including body composition, on CF clinical outcomes (e.g., CF-related diabetes and lung disease progression) in order to improve CF nutrition standard of care. I have been steadily funded by the NIH NIDDK, the

Cystic Fibrosis Foundation (Clinical Research Award), and other granting mechanisms and have maintained a strong publication record in clinical nutrition research. I served on the 2020 Academy of Nutrition and Dietetics Evidence Analysis Workgroup Expert Committee for Development of Nutrition Guidelines in Cystic Fibrosis. I also serve as Co-Director of the Lifestyle & Behaviors Core of the NIH-funded Georgia Cystic Fibrosis Research and Translation Core Center.

CF Research Expertise

Role of diet/nutrition and body composition on metabolism in cystic fibrosis and other chronic diseases. Research integrates state-of-the-art metabolomics methods with many aspects of nutrition research including rigorous clinical trials, body composition analysis, biomarker assessment, and analysis of dietary intake.

Gaps:

- Optimizing diet in CF: What are macro- and micronutrient needs in CFTR modulator era? How do these differ with comorbidities, such as CFRD? Should we shift focus from diet quality over quantity in CF management?
- Redefining nutrition assessment in CF: Should we shift away from BMI as primary indicator of nutrition status? New studies are needed to better define optimal nutrition status for health and longevity in people with CF. Does lung function remain a good endpoint?
- HEMT effects on nutrition status: What are the long-term effects of HEMT on body composition? Is overweight/obesity a concern for people with CF?

COMMUNITY MEMBER PERSPECTIVE

COMMUNITY PERSPECTIVES, NO ONE LEFT BEHIND: PERSPECTIVES FOR INDIVIDUALS NOT ELIGIBLE FOR MODULATOR THERAPIES

Lisa J. Hamburger

*Parent of son with
Cystic Fibrosis*



***Cystic Fibrosis Maryland Chapter Board
Member - Chair, Outreach and Advocacy***

***Liaison - Cystic Fibrosis Foundation, Maryland
Chapter and CF Care Clinic at Johns Hopkins
Hospital***

***Parent Advisory Board, CF Care Clinic - Johns
Hopkins Hospital***

CFF National Leadership Council - Outreach

MODERATOR

BREAKOUT ONE: MAXIMIZING RESEARCH POTENTIAL FOR PATIENT-DERIVED MODELS AND SYSTEMS.

Dr. Martina Gentsch, Ph.D.

Associate Professor, Marsico Lung Institute,
University of North Carolina Chapel Hill



Bio: Dr. Gentsch is an Associate Professor of Pediatric Pulmonology, Adjunct Associate Professor of Cell Biology and Physiology, and member of the Marsico Lung Institute at UNC. The major goal of Dr. Gentsch's studies is to restore CFTR function in cystic fibrosis (CF). Dr. Gentsch received her PhD from the University of Regensburg, Germany in 1997. Early in her career, she conducted crucial studies on CFTR misfolding at the Mayo Clinic in Scottsdale. Since 2005, she established novel techniques to evaluate rescue of CFTR function by small-molecule compounds in primary human airway epithelial cultures at UNC.

CF/Research Expertise

Dr. Gentsch directs the CFRTCC Molecular/Functional Measurement Core, which supports the translation of therapeutic strategies for CF from basic research to clinical studies, and the CFF RDP CFTR Functional Analysis Core, which utilizes electrophysiological, biochemical, cell- and organoid-based assays to characterize ion channel activity and rescue of CFTR function in human bronchial, nasal, and intestinal epithelial cultures. Currently, Dr. Gentsch is investigating the following: 1) Mechanistic aspects underlying the mode of action of novel CFTR therapeutics, 2) Pharmacological approaches to rescue rare CFTR mutations, 3) Mechanistic details on how the lung environment (bacterial infection, inflammation) affects ion channel function and CFTR rescue, 4) Consequences of CFTR rescue on fluid transfer and mucociliary clearance in CF airways, and 5) Pharmacodynamics and pharmacokinetics of CF therapeutics.

Important Gaps and Research Opportunities:

- Personalized medicine and therotyping
- Specific targeting of relevant CFTR-expressing cells for gene therapy
- Impact of infection and inflammation on efficacy of CFTR therapeutics
- Pharmacodynamics and pharmacokinetics of CF combination therapies

MODERATOR

BREAKOUT ONE: MAXIMIZING RESEARCH POTENTIAL FOR PATIENT-DERIVED MODELS AND SYSTEMS.

Dr. Anjaparavanda "AP" Naren Ph.D.

Professor, Director of Cystic Fibrosis Research Cedars-Sinai Medical Center



Bio: CFTR Biology/Physiology (Assistant, Associate and Full Professor, 2001- Present).

Director, Personalized Cystic Fibrosis Therapy and Research Center (P30- NIH/NIDDK sponsored Program)

Past Director CFF-RDP Program-Cincinnati. Permanent Member NIH-Study section (LCMI 2008-2012).

Permanent Member-NIH/NIDDK Clinical, Integrative and Molecular Gastroenterology (CIMG) Study Section

(2014-2018). North American Cystic Fibrosis Conference (NACFC) Program Planning Committee.

2014-Present.

CF/Research Expertise

Macromolecular complexes of CFTR, Personalized medicine in CF and outcome studies using organoids, CF-organ-on-a-chip and sensors.

MODERATOR

BREAKOUT ONE: MAXIMIZING RESEARCH POTENTIAL FOR PATIENT-DERIVED MODELS AND SYSTEMS.

Dr. Amy Ryan, Ph.D.

Associate Professor of Anatomy and Cell Biology,
University of Iowa



Bio: Associate Professor of Anatomy and Cell Biology: 2021-current; Associate Director for the Center for Gene Therapy of Cystic Fibrosis, University of Iowa: 2021-current; Member: Epithelial Stem Cell Consortium (CFF): 2017-current

CF/Research Expertise

Stem cells, gene-editing, iPSC-derived models, primary airway models, stem cell niche, lung injury, repair and lung regeneration, immune cell interactions

My research program centers on understanding the complex mechanisms that contribute to the pathogenesis

of lung disease, focusing on CF and ciliopathies. I have a background in ion channel regulation and now focus on the regulation of stem cells in lung injury, repair and regeneration. My major contributions to the field include the generation and gene-editing of patient specific induced pluripotent stem cells (iPSCs) and the development of directed differentiation protocols to specify cells comprising the proximal airway epithelium. We are now using these iPSC-based models, in conjunction with primary airway epithelial stem cells, to understand mechanisms of injury and repair of the human airway epithelium, including, but not limited to, progenitor cell specification and differentiation, epithelial barrier function, injury and repair and mucociliary clearance. Recently, we have expanded our focus to understand the impact of the cellular niche, including roles of inflammation and inflammatory cells, in airway regeneration and their potential impact on cellular therapy for CF. Tissue level responses are being evaluated in intact ex vivo tissues as well as human airway-on-chip models.

MODERATOR

BREAKOUT TWO: USING ANIMAL MODELS IN THE CONTEXT OF HEMT INFORM CLINICALLY RELEVANT KNOWLEDGE GAPS.

Dr. Susan Reynolds, Ph.D.

Principal Investigator,
Nationwide Children's Hospital



Bio: Susan D. Reynolds, PhD's research focuses on tissue stem cells that maintain the conducting airway epithelium. Previous work identified a basal cell subtype that functioned as a tissue stem cell in mice. Current research translates these findings to human airways and seeks to use the tissue stem cell as therapy for lung disease, including Cystic Fibrosis.

CF/Research Expertise

Airway epithelial injury and repair

Cell replacement therapy

WNT/b-catenin and Notch regulation of differentiation

MODERATOR

BREAKOUT TWO: USING ANIMAL MODELS IN THE CONTEXT OF HEMT INFORM CLINICALLY RELEVANT KNOWLEDGE GAPS.

Dr. Bruce Stanton, Ph.D.

Andrew C. Vail Professor,
Geisel School of Medicine at Dartmouth



Bio: Bruce Stanton received his Ph.D. from Yale University and did a postdoctoral fellowship at Yale. He has been on the faculty at Dartmouth since 1984. Dr. Stanton is the Director of the Dartmouth Lung Biology Center, is PI of the Cystic Fibrosis (CF) Research Development Program, and Associate Director of an NIH/NIDDK P30 program project on CF. He was the PI of an NIH T32 for 25 years, PI of an NIH/COBRE Lung Biology program project (2003-2018) and PI of the Dartmouth Superfund Program (2008-2018). Dr. Stanton is also the PI on an NIH R25 funded course titled Reproducible and FAIR Analysis of Bioinformatics Data and he and his colleagues have developed several widely used applications to interrogate large data sets. He has written several textbooks for medical students. Dr. Stanton has served on numerous editorial boards, and grant review committees for the NIH and Cystic Fibrosis Foundation.

CF/Research Expertise

Dr. Stanton's laboratory studies host-pathogen interactions in CF. His work is focused on elucidating how bacteria establish and maintain a chronic lung infection in CF. Recent studies are exploring host pathogen interactions that are mediated by the secretion of extracellular vesicles (EVs).

MODERATOR

BREAKOUT TWO: USING ANIMAL MODELS IN THE CONTEXT OF HEMT INFORM CLINICALLY RELEVANT KNOWLEDGE GAPS.

Dr. John Engelhardt, Ph.D.

University of Iowa, Workshop Co-chair



Bio: Molecular and Cell Engineering, UPenn (Assistant Professor, 1994 – 1997); Anatomy and Cell Biology, University of Iowa (Associate Professor, 1997 – 2001; Professor, 2001 – Present), Director of Center for Gene Therapy, University of Iowa (1998 – Present); Chair of the Department of Anatomy and Cell Biology (2004 – Present).

CF Research Expertise

Lung molecular and cellular biology as it relates to the pathogenesis and treatment of cystic fibrosis (CF) lung disease; the development of transgenic ferret models to study CF lung and pancreatic stem cell biology; viral vectors and gene therapy for CF; pathogenesis cystic fibrosis related diabetes; the study of airway stem cell niches, the regulatory mechanisms that control stem cell proliferation and repair in the airway, and the development of cell-based therapies for CF using stem cells.

MODERATOR

BREAKOUT THREE: LATE-STAGE CYSTIC FIBROSIS LUNG DISEASE ON HEMT.

Dr. Lindsay Caverly, M.D.

Assistant Professor,
University of Michigan Health



Bio: Dr. Lindsay Caverly is an Assistant Professor of Pediatric Pulmonology at the University of Michigan Medical School, and C.S. Mott Children's Hospital. She attended medical school at The Ohio State University, and then completed her pediatrics residency and pediatric pulmonary fellowship at Children's Hospital Colorado. Dr. Caverly's research focuses on lung microbiome and nontuberculous mycobacterial infections in cystic fibrosis, and she is the co-director of the *Burkholderia cepacia* Research Laboratory and Repository.

Clinical Expertise

Pediatric pulmonology
Cystic fibrosis
Nontuberculous mycobacterial infections

CF/Research Expertise

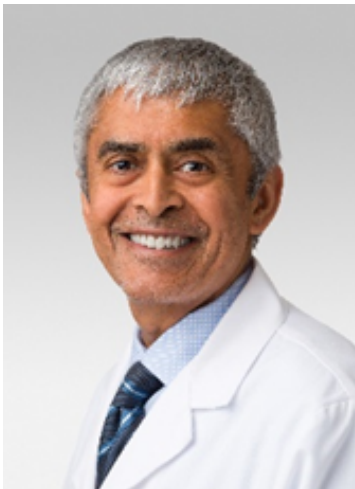
CF lung microbiome

MODERATOR

BREAKOUT THREE: LATE-STAGE CYSTIC FIBROSIS LUNG DISEASE ON HEMT.

Dr. Manu Jain, M.D.

Professor of Medicine
(Pulmonary and Critical Care) and Pediatrics,
Northwestern Medicine



Bio: Pulmonary Critical Care (Assistant, Associate and Full Professor, 1996- Present).

Adult CF program director (NU), Site-PI TDN site NU, Past Chair of PRC (TDN), co-Chair Guidelines Steering Committee (CFF), Adult Program Representative to Center Committee (CFF). Co-Chair of Genetic Therapy Working Group (CFF)

Clinical Expertise

Adult CF and non-CF bronchiectasis. Intensivist with interest in acute lung injury and repair

CF/Research Expertise

Heterogeneity in CF outcomes, transcriptomics, wearable technology for patient monitoring, clinical trials, genetic therapies

MODERATOR

BREAKOUT THREE: LATE-STAGE CYSTIC FIBROSIS LUNG DISEASE ON HEMT.

Dr. Gina Hong M.D., MHS

Assistant Professor of Medicine,
Hospital of the University of Pennsylvania



Bio: Dr. Gina Hong is an Assistant Professor of Medicine at the University of Pennsylvania Perelman School of Medicine in Philadelphia, PA and adult cystic fibrosis physician. She received her M.D. at Rutgers University- New Jersey Medical School and then completed her internal medicine residency training and chief medical residency at the University of Chicago. She completed her pulmonary and critical care fellowship and Master of health sciences at the Johns Hopkins University. Dr. Hong has focused her research efforts in the study and diagnosis of *Aspergillus fumigatus* and its role and impact on CF lung disease

Clinical Expertise

Cystic Fibrosis and non-cystic fibrosis bronchiectasis
Allergic bronchopulmonary aspergillosis

CF/Research Expertise

Detection and diagnosis of fungal infections in cystic fibrosis

SPEAKERS

SESSION 3: CONCERNS AND QUESTIONS ABOUT PEOPLE WITH CYSTIC FIBROSIS AND EARLY LUNG DISEASE

Terri Laguna, M.D., MSCS

Division Head, Pulmonary and Sleep Medicine
Ann & Robert H. Lurie Children's Hospital of Chicago



Bio: I received my MD from UCSF, completed my Pediatric Residency and Chief Residency at the University of Washington and completed my Pediatric Pulmonology Fellowship at the University of Colorado where I also obtained a Master's Degree in Clinical Science. After spending 10 years at the University of Minnesota, I moved to Chicago to join Lurie Children's as Division Head. I have been involved in CF clinical care and research for over 15 years and am passionate about equity, diversity and inclusion initiatives.

Clinical Expertise

- Cystic fibrosis, asthma, interstitial lung disease, primary ciliary dyskinesia (Director, PCD Center of Excellence)

CF/Research Expertise

- Clinical and translational research in early lung disease in CF
- Current NIH RO1 and CFF funded work on early infections in the CF airway and the role of anaerobic communities in the development of lung disease
- Mentor in the Clinical Research Scholars Program (CRSP)

[SIMPLIFY & Recent advances in the early treatment of cystic fibrosis: Bridging the gap to highly effective modulator therapy.](#)

Felix Ratjen, M.D. Ph.D. FRCP(C) FERS

Head, Division of Respiratory Medicine
The Hospital for Sick Children



Bio: I am the Division Chief of Paediatric Respiratory Medicine at The Hospital for Sick Children (SickKids) and Professor of Paediatrics at the University of Toronto. I am also the Program Head and Senior Scientist in the Translational Medicine research program at SickKids Research Institute. I am co-leading the CF Centre at SickKids with Christine Bear, another Senior Scientist in the Molecular Medicine Program. I completed a majority of my medical education in Germany, along with a research fellowship at the Children's Hospital in Boston. I subsequently worked at the University of Essen, where I

was appointed Deputy Chief of the Department of Paediatrics in 1998 and Professor of Paediatrics in 2001. Until 2005 I was the chief executive of the scientific board of the German CF foundation before relocating in Canada in the same year. I am involved in the organizing committees of the major respiratory meetings (American Thoracic Society, European Respiratory Society and the North American CF conference). I also work on multiple grant review panels and am a member of the several editorial boards including the American Journal of Respiratory and Critical Care Medicine, Thorax, Pediatric Pulmonology Lancet Respiratory Medicine and the Journal of Cystic Fibrosis.

CF/Research Expertise

I am conducting multiple clinical trials addressing cystic fibrosis lung disease including new therapeutic strategies to target the underlying defect, treatment of airway infections such as first infection with *Pseudomonas aeruginosa*, airway inflammation and other important aspects of the disease. While some of these studies are single centre studies within the CF centre at SickKids or in collaboration with the adult centre at St. Michael's Hospital, many of them include both national and international collaborations with centres in Canada, the U.S., Europe and Australia. In addition, I am involved in developing and validating new outcome measures to quantify important aspects of CF lung disease that can be utilized in clinical trials. I also study other lung diseases and over the recent years have developed an interest in the clinical evaluation of Hereditary Hemorrhagic Telangiectasia (HHT), for which I am leading one of the largest dedicated pediatric clinics.

Jennifer Bomberger, Ph.D.

Associate Professor
University of Pittsburgh



Bio: I am currently an Associate Professor of Microbiology and Molecular Genetics, and Clinical and Translational Science at the University of Pittsburgh. In fall 2022, I will begin a position as Professor of Microbiology and Immunology at the Geisel School of Medicine at Dartmouth. I currently serve as the Director of the University of Pittsburgh Cystic Fibrosis Research Development Program and Vice Chair of Graduate Education. I joined the faculty at Pitt in 2011, after receiving my Ph.D. in Cellular and Molecular Physiology at Michigan State University and completing my postdoctoral training at the Geisel School of Medicine at Dartmouth. I have been active in the Cystic Fibrosis (CF) research community for over 15 years, participating in many national committees and leading local CF programs. I currently chair the CF Foundation's Infection Research Initiative and the Best Junior Investigator Basic Science Award at the annual NACFC, as well as serve on the NACFC program planning committee and research training study section for the CFF. I have mentored a number of CF scientists and physician scientists on CFF fellowships and transition awards and am dedicated to training the next generation of CF scientists.

CF/Research Expertise

Areas of focus include airway biology, CF microbiology and virology, innate immune responses to infection.

My laboratory studies host-pathogen interactions in the lung, focusing on the modulation of airway epithelial cell biology by respiratory pathogens and the pathogen's response to the host. My laboratory performs translational research to define microbial community dynamics and evolution in the upper (paranasal sinuses) and lower (airways) respiratory tract in CF. We also use specialized in vitro models to study polymicrobial interactions in the respiratory tract. Our long-term research goals are to elucidate the cellular and molecular mechanisms whereby CF pathogens and respiratory viruses synergize to impact CF lung disease and, ultimately, identify new therapeutic approaches to control combined chronic *P. aeruginosa* and respiratory virus infections in people with CF.

Christopher Fortner, M.D., Ph.D.

Cystic Fibrosis Care Center Directory
SUNY Upstate Medical University, Syracuse, New York



Bio: Chris Fortner, MD, PhD is an Associate Professor of Pediatric Pulmonology. He is the CF Care Center Director, TDN Site Director, and Pediatric CF Program Director at SUNY Upstate. Prior to joining SUNY Upstate, he was faculty at Duke University. He completed pediatric pulmonology fellowship and pediatric residency at Duke. His interest in cystic fibrosis began during medical school at the University of Cincinnati's MD, PhD training program.

Clinical Expertise

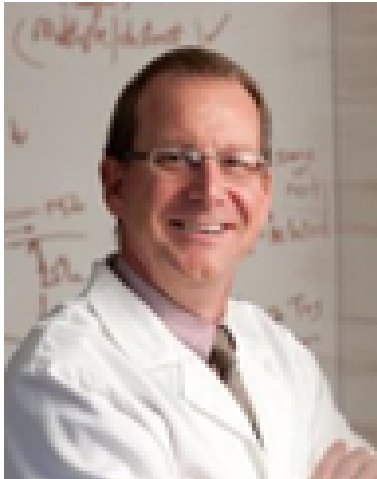
Cystic fibrosis, asthma, chronic cough, flexible bronchoscopy

CF/Research Expertise

His research interests include clinical trials of CFTR modulators and quality improvement of CF newborn screening. He has the privilege of taking care of two of the youngest CF patients ever exposed to CFTR modulators, both born to mothers with CF who were on Trikafta® during their pregnancies. Each of these children showed minimal clinical features of CF in the newborn period, likely due to the modulators helping preserve some CFTR function during fetal development.

Garry R. Cutting, M.D.

Professor of Genetic Medicine, Pediatrics and Medicine
Johns Hopkins University



Bio: I am the Aetna/U.S. Healthcare Professor of Medical Genetics, Pediatrics and Medicine in the McKusick-Nathans Department of Genetic Medicine of the Johns Hopkins University School of Medicine. I have been the Medical Director of the DNA Diagnostic Laboratory of Johns Hopkins Genomics since 1995. I directed the Medical Genetics Residency Program at Hopkins from 1995 to 2004 and Clinical Genetic Laboratory Training Program from 1995 to 2018. As Editor of the journal *Human Mutation*, I oversee the review and publication of manuscripts reporting the mechanism, distribution and phenotype consequences of variation in our genomes. I have been very active in the Human Variome Project, an international effort to document all variation in human DNA (Board of Directors (2016-present), Co-Chair of the Board (2018-present), Co-Chair of the International Scientific Advisory Committee (2015-present) and Chair of the Reporting of Sequence Variants Working Group (2018-present)). I have published more than 200 peer-reviewed articles and 50 reviews and book chapters. I was a founding (1991) Member of the American College of Medical Genetics. Elected to the Society of Pediatric Research (1992), the American Society of Clinical Investigation (1995) and the Association of American Physicians (2017).

CF/Research Expertise

My primary research interests lie in the interpretation of DNA variation and their effect upon human phenotypes. My lab focuses on the effect of common and rare variants in the CFTR gene that cause the single gene disorder cystic fibrosis (CF). Our team operates the CFTR2 database, a resource composed of clinical and genetic data on almost 90,000 individuals with CF world-wide. My laboratory also studies the effect of clinically approved and novel modulators upon CFTR protein bearing disease-causing variants. My laboratory is a leader in the identification and characterization of genetic modifiers of CF. Our group is currently collaborating with teams at UNC and UW, Seattle to identify common and rare modifier variants of disease severity by whole genome sequencing. I am the recipient of the Paul di Sant'Agnese Distinguished Scientific Achievement Award from the Cystic Fibrosis Foundation and a MERIT award from the National Institutes of Health.

SESSION 4: CONSIDERATIONS FOR MODULATOR USE IN SPECIAL POPULATIONS

Jennifer L. Taylor-Cousar, M.D., MSCS, ATSF

Professor, Departments of Medicine and Pediatrics
National Jewish Health



Bio: Adult and Pediatric Pulmonology, UNM 2006-2009 (Assistant Professor), NJH 2009-present (Assistant, Associate, Professor with tenure); Medical Director of Clinical Research Services (2019-present), Medical Staff President-elect (2021-), Co-Director (2015-present)/TDC Director (2017-present) of the Adult CF Program

Clinical Expertise

Adult and pediatric pulmonology; care of adults with CF; orangutan respiratory disease syndrome

CF/Research Expertise

Clinical trial development, design and conduct; unique health needs of women with CF; sexual and reproductive health in CF

CFF/CF TDN Committees:

- Advisor to the Board of Trustees (2021-present), Racial justice working group (2020-present), ResearchCon Executive Planning Committee (2019-2021), Chair-Sexual Health, Reproduction and Gender Research Working group (2019-present), CREC/CRAB (2018-present), PRC (2011-2018)
- Other: SAB, Emily's Entourage; Associate editor, J Cystic Fibrosis

Gaps:

- 1.** Are the unknown risks of CFTR modulators in pregnancy balanced by the risk to the health of the mother of clinical deterioration following modulator cessation?
- 2.** Based on the amount of modulator exposure during lactation, is routine cataract examination and liver function testing necessary for infants exposed to modulators via breast feeding?
- 3.** Does parenthood adversely impact the health of mothers with CF and is the adverse impact mitigated by modulator use?

Parenthood impacts short-term health outcomes in people with cystic fibrosis

Fertility, Pregnancy and Lactation Consideration for Women with CF in the CFTR Modulator Era

Jennifer L. Taylor-Cousar, M.D., MSCS, ATSF

Professor, Departments of Medicine and Pediatrics
National Jewish Health



Drug exposure to infants born to mother taking Elexacaftor, Texacaftor, and Lvacaftor

A case report of CFTR modular administration via carrier mother to treat meconium ileus in a f508del homozygous fetus

Normal pancreatic function and false-negative CF newborn screen in a child born to a mother taking CFTR modulator therapy during pregnancy.



Kathleen J. Ramos, M.D. MS

Assistant Professor
University of Washington

UW Medicine
SCHOOL OF MEDICINE



Bio: Dr. Kathleen ("Kathy") Ramos is an Assistant Professor in the University of Washington Division of Pulmonary, Critical Care, and Sleep Medicine. She was the co-chair and lead author of the committee that wrote the Cystic Fibrosis Foundation Lung Transplant Referral Consensus Guidelines in 2019. She also co-chaired the International Society for Heart and Lung Transplantation committee to revise the lung transplant candidate selection criteria in 2021. She is a steering committee member for the Cystic Fibrosis Foundation's Lung Transplant Consortium.

Clinical Expertise

Dr. Ramos is a physician-scientist with clinical responsibilities and research focus in both cystic fibrosis and lung transplantation.

CF/Research Expertise

Timing of lung transplant for people with CF in the era of highly effective modulators

Investigator-designed educational website to inform individuals with CF about lung transplant and empower shared decision making about transplant

Use of elexacaftor/tezacaftor/ivacaftor after lung transplant

Evaluation of clinical outcomes after lung transplant

Christopher Goss, M.D., MS, FCCP,

Professor of Medicine and Pediatrics
University of Washington & Seattle Children's
Hospital

UW Medicine

UW SCHOOL
OF MEDICINE



Bio: I am a Professor of Medicine and Pediatrics at the University of Washington in Seattle WA. I also am the Co-Executive Director of the Cystic Fibrosis Therapeutics Development Network Coordinating Center at Seattle Children's Research Institute. I also lead the NIDDK P30 Clinical Core at UW and serve as the Medical Director of the CTSA/ITHS Network Capacity Team. I am also the Associate Adult CF Clinic Director at the University of Washington. Currently I serve as the Chair of the CF Foundation Patient Registry and Co-Chair of the CF Genetic Therapies Working Group.

Clinical Expertise

Adult cystic fibrosis clinical care
Adult pulmonary and critical care medicine

CF/Research Expertise

Clinical trial design in CF
Acute pulmonary exacerbation in CF
Novel therapeutics (focus on anti-infectives) in CF
Translational research in CF

John Brewington, M.D., MS

Assistant Professor of Pediatrics
Cincinnati Children's Hospital Medical Center



Bio: I am an Assistant Professor of Pediatrics at the University of Cincinnati College of Medicine and Cincinnati Children's Hospital in the division of Pediatric Pulmonary Medicine. Following my MD at Wake Forest University, I subsequently completed my pediatrics residency, chief residency, and pulmonary fellowship at Cincinnati Children's before joining as faculty. I am a physician-scientist with a focus on translational research in Cystic Fibrosis, utilizing patient-derived samples to generate laboratory models of disease and treatment response. Through this work I direct the CF Foundation's Nasal Cell Model Outcomes National Resource Center, which provides national access to theratyping efforts, as well as research support to CF investigators. I am also highly engaged in education, with a focus on pediatric flexible bronchoscopy training.

Clinical Expertise

- Care of children with lung and airways diseases, including CF
- Diagnostic and interventional pediatric flexible bronchoscopy

CF/Research Expertise

- Personalized medicine and theratyping/repurposing existing drugs
- Patient-derived model systems to study CF
- Translational CF studies and assays (e.g., NPD, LCI)
- Impacts of polypharmacy on CFTR function in the CF airway

Meghan E. McGarry, M.D., M.A.S.

Assistant Professor of Pediatrics
University of California San Francisco



Bio: Dr. McGarry is a board-certified Pediatric Pulmonologist at University of California San Francisco with training in Pediatric Clinical Pharmacology and Clinical Research. She is a clinical researcher in health disparities in cystic fibrosis with emphasis on health disparities in Hispanic children with CF.

Clinical Expertise

- Pediatric Pulmonology
- Cystic Fibrosis
- Health Disparities
- Clinical pharmacology, Personalized medicine

CF/Research Expertise

- Cystic Fibrosis Researcher supported by NHLBI, NIMHD, CF Foundation
- Health Disparities in Racial and Ethnic Minorities with CF
- Racial and Ethnic Differences in Newborn Screening For CF
- Unequal Access to CFTR Modulators

Left behind: The potential impact of CFTR modulators on racial and ethnic disparities in cystic fibrosis

Cystic fibrosis patients of minority race and ethnicity less likely eligible for CFTR modulators based on CFTR genotype

SESSION 5: ADVANCING CLINICAL CARE AND OUTCOMES FOR PATIENTS WITH CF IN THE POST MODULATOR ERA

Zackary I. Cleveland, Ph.D.

Cincinnati Children's Hospital Medical Center



Bio: Dr. Cleveland is an Associate Professor in the Center for Pulmonary Image Research at Cincinnati Children's Hospital and has appointments in Pulmonary Medicine, Radiology, Pediatrics, and Biomedical Engineering. He holds a B.S. (chemistry) from The University of Montana, a Ph.D. in physical chemistry (Colorado State University), and was a postdoctoral fellow in Radiology at Duke University. Dr. Cleveland specializes in using MRI to quantify pathophysiology in lung diseases including CF and receives funding from the CFF and NHLBI.

CF/Research Expertise

- Quantitative imaging
- Hyperpolarized gas MRI of lung function (ventilation and gas exchange)
- Structural lung imaging with ultra-short echo-time (UTE) MRI

Heather D. Bean, Ph.D.

Assistant Professor
School of Life Sciences, Arizona State University



Bio: I am a bioanalytical chemist who specializes in untargeted metabolomics and biomarker discovery. I received a PhD in Chemistry from Georgia Tech in 2008, then conducted postdoctoral research at the University of Vermont and Dartmouth College as a Postdoctoral Fellow for the CF Foundation. In 2015 I joined the School of Life Sciences at Arizona State University as an Assistant Professor. My research team at ASU studies the metabolomes of polymicrobial communities in chronic lung infections and in other natural and engineered environments. In the context of CF lung infections, the Bean Lab focuses on identifying breath volatile metabolites that correspond to the dominant infection species, clinically-relevant infection phenotypes, microbe-microbe interactions, and host-microbiome interactions in the lung. I am a co-PI of the IMproving P. Aeruginosa deteCTion using Breath-based diagnostics (IMPACT-Breath) study (Jane Hill, PI; Edith Zemanick, co-PI), which is analyzing breath samples from persons with CF to identify and validate breath biomarkers for P. aeruginosa diagnosis.

CF/Research Expertise

- Breath-based diagnostics for lung infections, with a focus on Pseudomonas aeruginosa and Staphylococcus aureus
- Bioactivity of volatile metabolites and their impacts on microbial growth and virulence

Heather D. Bean, Ph.D.

Assistant Professor

School of Life Sciences, Arizona State University



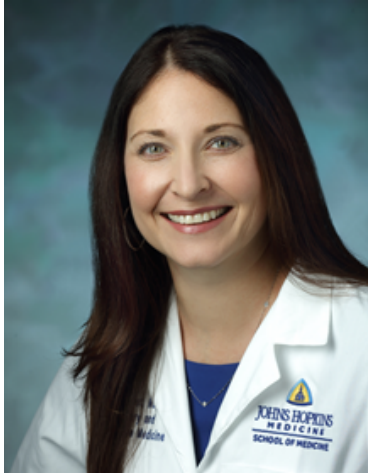
Gaps & Opportunities for Session 5: New methods for CF pathogen detection, specifically related to breath-based diagnostics:

- Direct detection of microbial nucleic acids from exhaled breath condensate has been demonstrated, but clinically-meaningful thresholds for positive vs. negative results need to be established.
- The clinical validation of the infection biomarkers and the identification of biomarkers for other infections is reliant upon access to sputum (or lavage).
 - Opportunity to leverage existing CF clinical studies to access sputum producers (breath sampling is non-invasive, i.e., easy to add to IRB approvals)
 - Opportunity to leverage other patients with structural lung diseases, such as persons with non-CF bronchiectasis
- There is strong governmental, NGO, industry interest in breath analysis right now, but efforts are fragmented/siloed. More inter-agency governmental collaboration would speed progress.



Natalie E. West, M.D. MHS

Assistant Professor of Medicine
Johns Hopkins University



Bio: I am a Pulmonary/Critical Care physician at Johns Hopkins University and received a Masters in Health Science at the Johns Hopkins Bloomberg SPH. I am a national investigator with the Standardized Treatment of Pulmonary Exacerbations (STOP) program in which we design and conduct clinical trials to establish evidence to better treat CF exacerbations. I am one of 5 founding members of the Sexual Health, Reproduction, and Gender Research (SHARING) Working Group, whose aim is to prioritize research around health issues that impact women with CF.

Clinical Expertise

- Critical Care
- Pulmonary - Cystic Fibrosis, Lung Transplant

CF/Research Expertise

- Standardized Treatment of Pulmonary Exacerbations (STOP) Program
- Role of Inhaled Antibiotics in CF Exacerbations
- Sex Differences in CF Pulmonary Exacerbations Outcomes
- Clinical Trials in CF
- Sexual Health, Reproduction, and Gender Research (SHARING) Working Group

Natalie E. West, M.D. MHS

Assistant Professor of Medicine
Johns Hopkins University



Gaps and Opportunities – Pulmonary Exacerbations in the Post-Highly Effective Modulator Therapy (HEMT) Era

- What is the true pulmonary exacerbation (PEX) rate in people with CF (PwCF) on HEMT?
 - While HEMT decreases rates of PEX, the rate of PEX seen in the past 2 years is more than we would expect (likely related to masking, social distancing with COVID).
 - How are PwCF presenting when they have a PEX? How do symptoms compare to the pre-HEMT era?
 - How should we be treating PEX in PwCF who are on HEMT? Many PwCF have stopped all or most of their inhaled chronic therapies – should we add these back back, or only treat with systemic antibiotics?
 - Are PEX in PwCF on HEMT similar to those with non-CF bronchiectasis? If so, this creates an opportunity to conduct clinical trials across diseases to study treatment of PEX
 - Is the lung function drop at the time of diagnosis of a PEX the same as in the pre-HEMT era? Similarly, only 65% of people with CF get back to within 90% of their baseline lung function after treatment for a PEX – is this still occurring?
 - There is an opportunity to define the common symptoms and/or lung function decline that people with CF present with at the time of a PEX, as well as evaluating for the optimal management of PEX.
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Margaret Rosenfeld, M.D., MPH

Professor and Associate Vice Chair for Clinical Research
Department of Pediatrics,
University of Washington School of Medicine



Bio: I am a pediatric pulmonologist and physician-scientist. My research program focuses on multicenter clinical and observational trials in CF and other disorders of mucociliary clearance, with an emphasis on early intervention strategies. I also have a focus on remote clinical trial endpoints, which has become a higher priority since the start of the pandemic. I am the PI of the CFF-sponsored OUTREACH study, a multicenter study of the accuracy, feasibility and acceptability of home spirometry as a clinical trial endpoint, and co-chair the CFF Remote Endpoints Taskforce.

Clinical Expertise

- I am a pediatric pulmonologist who cares for children with cystic fibrosis and other chronic and acute respiratory conditions

CF/Research Expertise

- Multicenter clinical trials and observational studies in CF and other disorders of mucociliary clearance
- Remote endpoints for decentralized clinical trials
- Lung function endpoints for clinical trials
- Early intervention in CF
- Newborn screening for CF

Remote Monitoring Tools for Decentralized Clinical Trials and Disease Monitorin

Gaps:

- Accuracy and variability of remote measurements
- How to optimize participant experience to maximize adherence
- Regulatory approval of remote endpoints

Opportunities

- Improve participant diversity
- Decrease burden of participation by “bringing the trial to the patient”
- Evaluate treatment effects on “real world” endpoints

Margaret Rosenfeld, M.D., MPH

Professor and Associate Vice Chair for Clinical Research
Department of Pediatrics,
University of Washington School of Medicine

References:

Clinical validation of digital biomarkers for pediatric patients with asthma and cystic fibrosis - Potential for clinical trials and clinical care.

Kruizinga MD, Essers E, Stuurman FE, Yavuz Y, de Kam ML, Zhuparris A, Janssens HM, Groothuis I, Sprij AJ, Nuijsink M, Cohen AF, Driessen GJA. Eur Respir J. 2021 Dec 9;2100208. doi: 10.1183/13993003.00208-2021. Online ahead of print. PMID: 34887326

A comparison of clinic and home spirometry as longitudinal outcomes in cystic fibrosis.

Paynter A, Khan U, Heltshe SL, Goss CH, Lechtzin N, Hamblett NM. J Cyst Fibros. 2022 Jan;21(1):78-83. doi: 10.1016/j.jcf.2021.08.013. Epub 2021 Aug 31. PMID: 34474987

The effect of elexacaftor/tezacaftor/ivacaftor (ETI) on glycemia in adults with cystic fibrosis.

Scully KJ, Marchetti P, Sawicki GS, Uluer A, Cernadas M, Cagnina RE, Kennedy JC, Putman MS. J Cyst Fibros. 2022 Mar;21(2):258-263. doi: 10.1016/j.jcf.2021.09.001. Epub 2021 Sep 14. PMID: 34531155

COMMUNITY MEMBER PERSPECTIVE

Ms. Jennifer Kyle

Person with Cystic Fibrosis



Bio: Jennifer Kyle has a M.S in Sports Administration from Montclair State University, a B.S. in Health, Physical Education and Sports Studies and a B.A. in Dance from Douglass College. She taught Dance and PE for 16 years in the New Jersey public schools and Dance four years as an adjunct professor at Montclair State University. Jennifer is a Past President for the New Jersey Association for Health, Physical Education, Recreation and Dance, now known as SHAPE NJ, and served as the VP of Dance for the Eastern District Association for the national SHAPE organization. Since retiring on disability with Cystic Fibrosis, she takes care of dogs and volunteers for the Cystic Fibrosis Foundation and has participated in 5 clinical trials for Cystic Fibrosis. She currently serves on the Governance Board for the Cystic Fibrosis Sexual and Reproductive Health Collaborative helping to create research for sexual and reproductive health to better the lives of people living with CF. Jennifer is also involved in an Outreach Study as a patient advocate to help improve tele-health appointments for patients with Cystic Fibrosis. Her love of dance brought her to South Plainfield Drama Department where she volunteered to help choreograph the fall fund raiser All Together Now and the spring production of Mamma Mia.

MODERATOR

BREAKOUT ONE: RISKS/BENEFITS OF STARTING IN PWCF WITH MINIMAL DISEASE ON HEMT (+/- ADD-ON THERAPIES) WHEN WE DON'T HAVE LONG TERM SAFETY DATA ON HEMT

Dr. Ron Rubenstein, M.D., Ph.D.

Professor of Pediatrics, Division Chief - Department of Pediatrics Allergy and Pulmonary Medicine, Washington University School of Medicine in St. Louis



Bio: Ronald C. Rubenstein, MD, PhD is a Professor of Pediatrics at the Washington University School of Medicine in St. Louis, where he is also Chief of the Division of Allergy and Pulmonary Medicine and holds the Robert C. Strunk Endowed Chair for Lung and Respiratory Research. Dr. Rubenstein's research interests focus on novel therapeutic strategies for Cystic Fibrosis, with a central hypothesis that drugs or small molecules can affect repair of function of mutant CFTR proteins. Dr. Rubenstein's work with one such agent, Sodium 4-Phenylbutyrate (4PBA), provided a critical proof of concept that served as a foundation for the development of now approved modulator agents such as Orkambi, Symdeko and Trikafta. His laboratory's present research focuses on the mechanisms by which the biogenesis of CFTR and other epithelial ion channels and secreted proteins relevant to CF are regulated by a 4PBA-regulated chaperone of the endoplasmic reticulum. Dr. Rubenstein remains active in clinical trials that aim to translate this approach to CF therapeutics into useful therapies, as well as in research that aims to understand the mechanisms underlying the development of CF-related diabetes and the risk factors for aminoglycoside-induced hearing loss in CF. Through this work, Dr. Rubenstein is both an advocate for people with CF, and a mentor and teacher for dozens of trainees and junior faculty as they develop their careers. He is also a Member of the Cystic Fibrosis Foundation (CFF) Medical Advisory Council and Chair of the CFF Clinical Research Committee, serving in this role since 2003.

MODERATOR

BREAKOUT ONE: RISKS/BENEFITS OF STARTING IN PWCF WITH MINIMAL DISEASE ON HEMT (+/- ADD-ON THERAPIES) WHEN WE DON'T HAVE LONG TERM SAFETY DATA ON HEMT

Dr. Edith Zemanick, M.D.

Associate Professor, Pediatrics-Pulmonary Medicine,
University of Colorado School of Medicine



Bio: Dr. Edith Zemanick, MD MSCS is an Associate Professor of Pediatrics in the Section of Pulmonary and Sleep Medicine in the Department of Pediatrics at the University of Colorado. She is Clinical Research Director for the Breathing Institute, Director of the Cystic Fibrosis (CF) Foundation Therapeutics Development Center, and Associate Director of the Pediatric CF Center at Children's Hospital Colorado. Her research has included studies of airway infection in CF including *Pseudomonas aeruginosa* detection, airway microbiome, pulmonary exacerbations and the association of lung infection and clinical outcomes.

More recently, her research has expanded to include clinical trials and multicenter studies examining sweat chloride response and clinical outcomes to CFTR modulator. Her research has been supported by the NIH/ NHLBI and the Cystic Fibrosis Foundation.

Gaps:

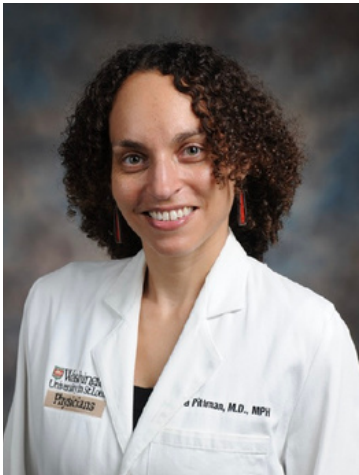
1. Should the management of pulmonary exacerbations differ for people on elexacaftor/tezacaftor/ivacaftor? Should the threshold for antibiotics differ? How should factors such as underlying lung disease, airway bacterial and viral infections be accounted for in treatment decisions?
2. What are the risks of delaying ETI therapy for people with minimal evidence of lung disease?
3. Does early initiation of elexacaftor/tezacaftor/ivacaftor reduce the risk of acquiring pathogens including *Pseudomonas*, *Burkholderia*, NTM? Is the risk of chronic infection reduced?

MODERATOR

BREAKOUT ONE: RISKS/BENEFITS OF STARTING IN PWCF WITH MINIMAL DISEASE ON HEMT (+/- ADD-ON THERAPIES) WHEN WE DON'T HAVE LONG TERM SAFETY DATA ON HEMT

DR. JESSICA PITTMAN, M.D., MPH

Associate Professor, Department of Pediatrics Allergy and Pulmonary Medicine, Washington University School of Medicine in St. Louis



Bio: Dr. Pittman graduated from Oberlin College in 1998, and earned her M.D. from Washington University in St. Louis School of Medicine in 2004. She received her training in pediatrics at Seattle Children's Hospital before moving to the University of North Carolina at Chapel Hill for her fellowship in Pediatric Pulmonology, where she also received a Master's in Public Health in Epidemiology. Dr. Pittman remained on faculty at the University of North Carolina as an Assistant Professor before joining the Division of Allergy, Immunology, and Pulmonary Medicine at Washington University in St. Louis School of Medicine

in 2014, where she is now an Associate Professor. Her roles at Washington University School of Medicine include Co-Director of the WUSM/SLCH Cystic Fibrosis Therapeutics Development Center, Associate Program Director for Diversity and Inclusion for the WUSM/SLCH Pediatric Residency Program and DEI Faculty Leader through the WUSM Office of Diversity, Equity, and Inclusion.

Dr. Pittman's primary research interest is early cystic fibrosis lung disease, specifically improving diagnosis and detection of disease in infancy/early childhood through novel outcome measures. She is a past recipient of the Cystic Fibrosis Foundation Leroy Matthews Physician/Scientist Award, a WUSM Omics of Inflammatory Airways Disease K12 Award, a WUSM Children's Discovery Institute Award and a CFF Clinical Research Scholars Program Award. Dr. Pittman has participated in numerous research studies involving children with cystic fibrosis and primary ciliary dyskinesia, and is currently involved with several longitudinal studies of children with CF through the CFF Therapeutics Development Network.

MODERATOR

BREAKOUT TWO: ADVANCING CLINICAL CARE AND OUTCOMES FOR PATIENTS WITH CF IN THE POST MODULATOR

DR. BONNIE RAMSEY, M.D.

Endowed Professor in Cystic Fibrosis and Vice Chair for Research, Department of Pediatrics, University of Washington School of Medicine



Bio: Dr Bonnie Ramsey is an Endowed Professor and Vice Chair for Research in the Department of Pediatrics at the University of Washington School of Medicine in Seattle, Washington. She is a pediatric pulmonologist and clinical scientist with over 30 years of experience in translational research and therapeutic development in the field of cystic fibrosis (CF). She was a lead investigator for development of key therapies in CF including inhaled tobramycin, dornase alpha, and ivacaftor. She has been acknowledged for her contributions to CF including the Paul D'Sant Agnese Award (1998) and the Lifetime Achievement Award (2013) from the Cystic Fibrosis Foundation, the Lifetime Achievement Award from the American Thoracic Society (2014), elected to the National Academy of Medicine in 2015, and received the Warren Alpert Foundation Prize (2018). As the Vice Chair for Research, Dr Ramsey plays a key role in faculty mentorship programs.

MODERATOR

BREAKOUT TWO: ADVANCING CLINICAL CARE AND OUTCOMES FOR PATIENTS WITH CF IN THE POST MODULATOR

DR. RHONDA SZCZESNIAK, PH.D.

Associate Professor,
Biostat/Epi & Pulm Med
Cincinnati Children's Hospital Medical Center



Bio: Rhonda and her research lab work closely with clinical researchers, providers, patients, families and other community stakeholders on translating statistical methods and tools for early detection of changes in personalized and precision health outcomes. Rhonda serves as co-Chair of the CF Foundation (CFF) Clinical Research Award Committee and is a member of the CFF Patient Registry/Comparative Effectiveness Research Committee. She also serves as Statistical Editor for BMJ-Thorax, Annals of ATS and JCF, and is an Academic Editor for PLOS ONE.

CF/Research Expertise

- Empirical investigations of longitudinal models of lung function decline in CF
- Point-of-care forecast tool co-production and testing for early detection/prevention of rapid lung-function decline
- Identifying phenotypes of rapid lung disease progression
- Biomarker discoveries and mapping environmental exposure (geo-) markers predictive of rapid CF disease progression
- Pragmatic approaches to test paradigms aimed at reducing treatment burden

MODERATOR

BREAKOUT TWO: ADVANCING CLINICAL CARE AND OUTCOMES FOR PATIENTS WITH CF IN THE POST MODULATOR

Dr. Timothy Corcoran, Ph.D.

Associate Professor, Medicine and Bioengineering,
University of Pittsburgh



Bio: Dr. Corcoran is an Associate Professor of Medicine, Bioengineering, and Chemical Engineering at the University of Pittsburgh in the Division of Pulmonary, Allergy, and Critical Care Medicine. His primary research interests include aerosol drug delivery and functional imaging of the lung. His work includes the application of nuclear imaging techniques to measure mucociliary clearance in the lung and he has participated in multiple studies that applied these techniques to test new therapies for Cystic Fibrosis as part of a Cystic Fibrosis Foundation Consortium. He has also applied these techniques in studies of participants with asthma, COPD, ciliopathies, and muscular dystrophy. His research group developed and tested a novel multi-probe aerosol-based imaging technique for measuring changes in airway liquid absorption and epithelial permeability simultaneous to measures of mucociliary clearance. He has an interest in developing *in silico* models based on outcomes from these imaging studies. He has also been involved in the development of aerosol drug delivery devices for infants and children. He has been the principal investigator of NIH K25, R01, and U01 awards on topics related to Cystic Fibrosis. He also serves as a Vice Chair of the University of Pittsburgh Institutional Review Board.

MODERATORS

BREAKOUT THREE: CONSIDERATIONS FOR MODULATOR USE IN SPECIAL POPULATIONS WITH CF

Dr. Kathryn Oliver, Ph.D.

Assistant Professor, Department of Pediatrics, Division of Pulmonary, Allergy/Immunology, Cystic Fibrosis & Sleep, Emory University School of Medicine



Bio: B.S. (Zoology) & M.S. (Microbiology), Auburn University

- Ph.D. (Genetics), University of Alabama at Birmingham
- Postdoctoral Fellowship (Functional Genomics), Emory University School of Medicine
- Certificate Program in Translational Research, Georgia Clinical & Translational Science Alliance
- Assistant Professor
 - Department of Pediatrics, Emory University School of Medicine
 - Center for CF & Airways Disease Research, Emory and Children's Healthcare of Atlanta

CF/Research Expertise:

Research focuses on delineating mechanistic and therapeutic impact of targeting specific ribosomal proteins (and other genetic factors) as a means to rescue defects in CFTR polypeptide synthesis and mRNA metabolism. Attention is placed on rare CFTR variants ineligible for highly effective modulator therapy (HEMT).

Member of the national CFF Guidelines Steering Committee; CFF Guidelines Committee for CFTR-Related Metabolic Syndrome (CRMS) and CF Screen Positive Inconclusive Disorder; and the Georgia Department of Public Health Newborn Screening CF Subcommittee.

Mother to a young child with CF, who is currently receiving reduced dosage of HEMT due to experiencing an adverse reaction upon initiation of treatment.

Gaps/opportunities in Research

- Impact of HEMTs on multiorgan disease progression and development of co-morbidities
- Evolving approaches to clinical care influenced by HEMT use
- Research strategies for maximizing eligibility and access to HEMTs for all people with CF
- Methods for optimizing effectiveness of HEMTs (adherence, environmental exposures, social issues)

MODERATORS

BREAKOUT THREE: CONSIDERATIONS FOR MODULATOR USE IN SPECIAL POPULATIONS WITH CF

Dr. Gabriela Oates, Ph.D.

Assistant Professor, Division of Pediatric Pulmonary & Sleep Medicine, University of Alabama Birmingham



Bio: I am a medical sociologist with expertise in the social determinants of health (SDH) and experience in the application of SDH measures, tools, and data for health services and outcomes research. My work is funded by grants from the National Institutes of Health, the Cystic Fibrosis Foundation, and the Alabama Department of Public Health

CF/Research Expertise

- Epidemiologic studies that assess the role of multi-level demographic, socioeconomic, and environmental factors for CF outcomes
- Health disparities research
- Tobacco smoke exposure and smoking cessation interventions in CF
- Interventions that support CF self-management and patient-centered care

MODERATORS

BREAKOUT THREE: CONSIDERATIONS FOR MODULATOR USE IN SPECIAL POPULATIONS WITH CF

Dr. Traci Kazmerski, M.D., MS,

Assistant Professor of Pediatrics,
University of Pittsburgh



Bio: Traci M. Kazmerski, MD, MS is an Assistant Professor at the University of Pittsburgh School of Medicine in the Department of Pediatrics and Division of Adolescent and Young Adult Medicine. She is a pediatric pulmonologist and health services researcher at UPMC Children's Hospital of Pittsburgh and serves as the Chair of the institutional Transition Task Force. Her research centers on the improvement of comprehensive health care for adolescents and young adults with pediatric-onset chronic disease. As incoming Vice Chair of the CF Foundation Therapeutics Development Network Sexual Health, Reproduction, and Gender Research (SHARING) Working Group, her current projects focus on improving the sexual and reproductive health care of people with cystic fibrosis.

NHLBI WORKSHOP PLANNING COMMITTEE

- **Marrah Lachowicz-Scroggins, Ph.D.**, *Program Director Division of Lung Diseases, NHLBI, Planning Committee Lead*
- **Tom Eggerman, M.D., Ph.D.**, *Program Director, Division of Diabetes, Endocrinology, and Metabolic Diseases, NIDDK*
- **Xin-Xing Gu, M.D.**, *Program Director, Respiratory Diseases Branch, NIAID*
- **JP Clancy, M.D.**, *Vice President of Clinical Research, Cystic Fibrosis Foundation*
- **John Engelhardt, Ph.D.**, *University of Iowa, Workshop Co-chair*
- **Susan Birkett, PharmD, Ph.D.**, *University of Alabama Birmingham, Workshop Co-chair*
- **Nicole Mayer Hamblett, Ph.D.**, *Seattle Children's Hospital, Workshop Co-chair*
- **Katie Hisert, M.D., Ph.D.**, *National Jewish Health, Workshop Co-chair*

ADDITIONAL MEMBERS FROM CYSTIC FIBROSIS FOUNDATION:

- **Dara Riva, Ph.D.** *Director of Clinical Research Awards*
- **Elizabeth Yu**, *Director of Physician Scientist Training Programs*
- **Katherine Tuggle, Ph.D.**, *Sr. Director of Research*
- **Patrick Thibodeau, Ph.D.**, *Vice President of Basic Research, Cystic Fibrosis Foundation*

Marrah Lachowicz-Scroggins, Ph.D.

Program Director Division of Lung Diseases,
NHLBI, Planning Committee Lead



Bio: I am a Program Director at the National Institutes of Health at the National Heart, Lung, and Blood Institute, Division of Lung Diseases in the Airway Biology and Disease Branch, mainly overseeing the Institute's Cystic Fibrosis grant portfolio. Before joining NHLBI in 2018, I was an Assistant Research Professor at University of California San Francisco in the Airway Clinical Research Center. I received my Ph.D. in Comparative Pathology at the University of California Davis in 2010 and hold a Graduate Certificate in Clinical Pathology from University of Massachusetts Lowell. Currently, I serve as a Project

Scientist for the Genetic Disease of Mucociliary Clearance Consortium part of the Rare Diseases Clinical Research Network jointly funded by NHLBI and NCATS Office of Rare Disease Research. I also manage grants in the Common Fund Somatic Cell Gene Editing Program (SCGE) for Innovative Technologies to Deliver Genome Editing Machinery to Disease-relevant Cells and Tissues and serve as a NIH SCGE Working Group Member. I am a member of the NHLBI Women's Health Working Group, serving as Co-Chair the Working Group since July 2020. I am also serving as a Coordinating Committee Member on behalf of NHLBI to the Coordinating Committee on Research on Women's Health. I am the Chair of the RECOVER Pathobiology Working Group for addressing the mechanisms of Post-Acute Sequelae of COVID-19 (PASC). I am part of several other Trans-NIH working groups and committees for which I have shared interests. Twitter @LachowiczMarrah

Clinical Expertise

Oversight of NHLBI clinical trials and observational studies in Cystic Fibrosis and other Disorders of Mucociliary Clearance.

CF/Research Expertise

My areas of focus are respiratory medicine, pulmonary physiology and immunology with a concentration in airways diseases Cystic Fibrosis, disorders of mucociliary clearance including ciliopathies and other rare lung diseases. My current portfolio also includes respiratory tract infections/susceptibility, mucins/mucus biology, mucosal immunology, epithelial cell biology, gene editing technologies and women's health. My research skills are in translational bench-to-bedside models using broad application of systems biology, histology and molecular techniques.



Tom Eggerman, M.D., Ph.D.,

Program Director, Division of Diabetes,
Endocrinology, and Metabolic Diseases, NIDDK



Bio: I am the program officer for NIDDK Cystic Fibrosis grants and Centers programs,. The focus is on the non-pulmonary aspects of Cystic Fibrosis. I am also the program director for the Human Islet Research Network (HIRN) Enhancement Center, the Integrated Islet Distribution Program, the Rare Metabolic Disease Program and the Advanced Artificial Pancreas Clinical Trial Program. I am also the Scientific Officer for the Collaborative Islet Transplantation Registry, the Lysosomal Disease Network, and the Post Covid New Onset Diabetes Program. Previously I was the NIDDK scientific officer for the Clinical Islet Transplantation Consortium (CIT), which was comprised of 13 clinical centers and a coordinating center. This consortium was interested in supporting multidisciplinary cellular therapy approaches for controlling blood glucose in patients with type 1 diabetes. Nine protocols were developed including two successful pivotal (phase III) studies over its almost 15-year existence.

Clinical Expertise

Adult Endocrinologist

Oversee clinical grants involving Cystic Fibrosis, artificial pancreas technology, rare metabolic diseases and cellular therapies for type 1 diabetes

Oversee the Collaborative Islet Transplantation Registry which collects world-wide clinical information on autologous and allogeneic islet transplantation

CF/Research Expertise

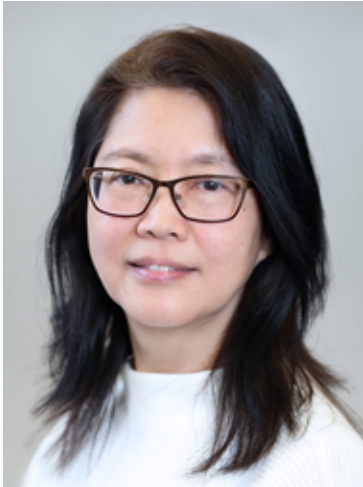
Cystic fibrosis grants involving the abdominal organs, especially diabetes, general research involving CF and also the Cystic Fibrosis Centers program

Oversee basic grants involving other rare metabolic diseases

Xin-Xing Gu, M.D.

Program Officer

National Institute of Allergy and Infectious Diseases



Bio: I am a Program Officer at the National Institute of Allergy and Infectious Diseases, Division of Microbiology and Infectious Diseases in the Respiratory Diseases Branch, managing diversity grant portfolios and contracts of bacterial respiratory diseases. Before joining NIAID in 2010, I was a Principle Investigator/Staff Scientist at NIDCD. I received my medical degree from Shanghai Medical University in 1983, followed by postdoctoral trainings at Shanghai Institute of Biological Products and US Food and Drug Administration. Currently, I serve as a Program Officer, COR, Scientific Lead or Subject Matter Expert for grants, contracts or clinical trials of bacterial respiratory pathogens at NIAID, CDC, FDA, CARB-X, etc.

Clinical Expertise

Oversight of clinical research and trials for diagnosis, treatment and prevention of bacterial respiratory diseases

CF/Research Expertise

Translational/clinical research and vaccine development

JP Clancy M.D.

Vice President of Clinical Research
Cystic Fibrosis Foundation (CFF)



Bio: I was born and raised in Iowa (Go Hawks!) and now live in Cincinnati (Go Bengals!). My pediatric residency was at UVA and my fellowship was at UAB. Prior to joining the CFF in 2018, I was a CF clinician (pediatric pulmonologist) and researcher. I worked from 1993 – 20210 at UAB, and subsequently Cincinnati Children’s Hospital Medical Center (2011 – 2018).

Clinical Expertise

- CF healthcare provider for kids with CF

CF/Research Expertise

- CFTR and epithelial biology
 - MR-based pulmonary imaging
 - Clinical outcome measures for CF clinical research
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John F. Engelhardt, Ph.D.

Professor and Chair,
Department of Anatomy and Cell Biology
University of Iowa Carver College of Medicine



Bio: Molecular and Cell Engineering, UPenn (Assistant Professor, 1994 – 1997); Anatomy and Cell Biology, University of Iowa (Associate Professor, 1997 – 2001; Professor, 2001 – Present), Director of Center for Gene Therapy, University of Iowa (1998 – Present); Chair of the Department of Anatomy and Cell Biology (2004 – Present).

CF Research Expertise

Lung molecular and cellular biology as it relates to the pathogenesis and treatment of cystic fibrosis (CF) lung disease; the development of transgenic ferret models to study CF lung and pancreatic stem cell biology; viral vectors and gene therapy for CF; pathogenesis cystic fibrosis related diabetes; the study of airway stem cell niches, the regulatory mechanisms that control stem cell proliferation and repair in the airway, and the development of cell-based therapies for CF using stem cells.

Dr. Susan Reynolds, Ph.D.

Principal Investigator,
Nationwide Children's Hospital



Bio: Susan D. Reynolds, PhD's research focuses on tissue stem cells that maintain the conducting airway epithelium. Previous work identified a basal cell subtype that functioned as a tissue stem cell in mice. Current research translates these findings to human airways and seeks to use the tissue stem cell as therapy for lung disease, including Cystic Fibrosis.

CF/Research Expertise

Airway epithelial injury and repair

Cell replacement therapy

WNT/b-catenin and Notch regulation of differentiation



Nicole Mayer Hamblett, Ph.D.

*Professor, Pediatrics; Adjunct Professor,
Biostatistics, University of Washington
Co-Executive Director, CF TDNCC,
Seattle Children's Research Institute*



Bio: Nicole Mayer Hamblett, PhD, is a Professor of Pediatrics and Adjunct Professor of Biostatistics at the University of Washington. She is the interim Co-Director of the Center for Clinical and Translational Research and Co-Executive Director of the Cystic Fibrosis Therapeutics Development Network (CF TDN) Coordinating Center at Seattle Children's Research Institute. She has led the design and analysis of numerous clinical studies which have advanced clinical care and outcomes in CF. Dr. Hamblett directs the TDN Consulting Program which partners with industry sponsors and regulators to strategize on complex drug development issues relevant to rare diseases. She is currently a principal investigator on therapeutic trials optimizing treatment regimens in CF and studies to advance biomarkers supporting therapeutic development for novel CFTR modulator therapies.

CF/Research Expertise

Study design, drug development, clinical trials, outcome measure development

Katie Hisert, M.D., Ph.D.

Assistant Professor, Department of Medicine
National Jewish Health



Bio: Katie Hisert is a physician scientist whose clinical practice and translational research program focus on helping people with cystic fibrosis (CF). Her over-arching research goal is to better understand chronic bacterial airway infections and associated inflammation that occur in CF and other chronic airways diseases. Dr. Hisert completed a combined MD-PhD degree at the Weill Cornell /Rockefeller/ Sloan Kettering Tri-Institutional MD- PhD Program, and then performed internship and residency in Internal Medicine at Columbia University Medical Center. During fellowship

training in Pulmonary, Critical Care, and Sleep Medicine at University of Washington, Dr. Hisert benefited from the mentorship of expert CF physicians and researchers. She began basic and translational studies to understand how monocytes and macrophages contribute to CF lung pathology, and she joined the faculty at University of Washington in 2016 as part of the Adult CF Clinical Team. In August 2019, Dr. Hisert moved to Denver to become an Assistant Professor in the division of Adult Pulmonary, Critical Care and Sleep Medicine at National Jewish Health. Dr. Hisert continues to treat adult patients with CF and to build her research program. She currently studies how heterogeneous monocyte and macrophage populations contribute to CF airways disease, and why people with CF demonstrate increased susceptibility to pulmonary nontuberculous mycobacterium infections.

Clinical Expertise

Adult cystic fibrosis, NTM lung infections

CF/Research Expertise

Macrophage heterogeneity in the lung

Host pathogen interactions : NTM and innate immune cells

Mechanisms of airway inflammation

Effects of CFTR modulator therapy of CF airway inflammation and inflammatory cells

Dara Riva, M.S.

Director of Clinical Research Awards
Cystic Fibrosis Foundation



Bio: Director of Clinical Research Awards, CFF (2017 – present), Science Officer for Congressional Directed Medical Research Programs supporting the PH/TBI Research Programs and Military Operational Medicine Research Programs (2014 – 2016), Clinical Research Associate at the Neutrophil Monitoring Laboratory at Frederick National Laboratory supporting NIAID (2008 -2014). Johns Hopkins Family Advisory Board member, parent to two children with CF. Currently, I oversee the Clinical Research Program’s academic portfolio and the funding opportunities related to Clinical Research Committee, co-lead the Infection Research Initiative, member of the TDN’s Sexual Health, Reproduction, and Gender Research (SHARING) Working Group.

Clinical Expertise

Grants management of academic clinical research projects, RFA and research program development, research program management

CF/Research Expertise

Manifestations of cystic fibrosis, particularly understudied complications related to GI, endocrine, mental health, and infection

Elizabeth Yu, Ph.D.

Director, Physician Scientist Training Programs
Cystic Fibrosis Foundation



Bio: I joined the Cystic Fibrosis Foundation at the start of 2020 as the Foundation's Director of Physician Scientist Training Programs. My goals with the Foundation are to support and develop a cohort of physician scientists with an understanding of CF who are capable of carrying forward critical CF research questions and caring for people with CF. Before joining the CF Foundation, I worked at the Congressionally Directed Medical Research Programs managing grants, coordinating review meetings, and facilitating the development of ground-breaking and patient-relevant research. I received my PhD from the University of Pittsburgh in Molecular Biophysics and Structural Biology where I studied the role of protein mutations on structure and stability, and impacts for disease and treatment.

CF/Research Expertise

My primary focus within the CF space is to encourage the development and advancement of physician scientists across the research spectrum, from basic to translational to clinical research. My scientific training is focused in basic protein structure and stability research.

Katherine Tuggle, Ph.D.

Senior Director of Research
Cystic Fibrosis Foundation



Bio: At the CF Foundation I lead a range of basic science research programs, including programs focused on supporting trainees with an interest in CF research as well as a number of investigator-initiated research funding mechanisms. I also oversee the Research Development Programs (RDP), a network of basic science research centers that bring together scientists and clinicians to improve our understanding CF. Since joining the CF Foundation, I have co-organized a number of meetings and workshops, including the NHLBI/CFF Workshop: Advancing Gene Editing Technologies for the Treatment of Cystic Fibrosis Lung Disease and the NIDDK/CFF Cystic Fibrosis-Related Diabetes Scientific Workshop. Before joining the CF Foundation, I completed my PhD in Environmental Health Sciences at the University of Alabama at Birmingham (UAB) followed by a Postdoctoral Fellowship at the Gregory Fleming James Cystic Fibrosis Research Center at UAB where I characterized the first rat model of cystic fibrosis.

CF/Research Expertise

My current portfolio spans a broad array of research areas that are of importance to people with CF including lung infections, inflammation, mucins/mucus biology, as well as gastrointestinal and endocrine manifestations of the disease. I have long-standing research interest in the development and utilization of animal models and other model systems, such as ex vivo and organ chip-based technologies, to enable CF research.

Patrick Thibodeau, Ph.D.

Vice President, Basic Research
Cystic Fibrosis Foundation



Bio: I am the VP of Basic Research for the Cystic Fibrosis Foundation, overseeing the academic basic and translational science portfolio. Before joining the CFF in 2021, I was faculty at the University of Pittsburgh School of Medicine in the Department of Microbiology and Molecular Genetics. My research program focused on questions related to protein biosynthesis and structure-function relationships. I received my Ph.D. in Molecular Biophysics from the University of Texas Southwestern Medical Center at Dallas in 2006.

CF/Research Expertise

My research utilized a variety of computational and biophysical approaches to study questions related to protein folding and function. This included intracellular processing of CFTR and other ABC-transporters and the role of secreted bacterial proteins on the extracellular environment in the CF airway.



National Heart, Lung,
and Blood Institute