Sponsored by:

University of Pittsburgh School of Medicine
Center for Continuing Education in the Health Sciences

Division of Pulmonary, Allergy & Critical Care Medicine

PITTSBURGH INTERNATIONAL LUNG CONFERENCE

METABOLISM AND THE LUNG: HOMEOSTASIS, IMMUNITY, AND DISEASE

THURSDAY, SEPTEMBER 8-FRIDAY, SEPTEMBER 9, 2022

UNIVERSITY CLUB
123 UNIVERSITY PLACE
PITTSBURGH, PENNSYLVANIA 15260

Course Directors:
Alison Morris, MD, MS
Janet S. Lee, MD
Tomeka Suber, MD, PhD

WELCOME AND OVERVIEW

Welcome to the 20th Anniversary Celebration of our **Pittsburgh International Lung Conference**!

The meeting was first launched by *Dr. Augustine Choi*, then Division Chief of Pulmonary, Allergy and Critical Care Medicine at the University of Pittsburgh School of Medicine and it quickly became a leading meeting in the field. With a focus on the presentation of cutting-edge topics in clinical, translational, and basic research, the **Pittsburgh International Lung Conference (PILC)** brings together leaders from institutions across the country and internationally to participate in scientific discussion, foster collaboration, and develop the next generation of pulmonary scientists.

This year's conference, Metabolism and the Lung: Homeostasis, Immunity, and Disease, will focus on new insights on the critical role of the metabolism of the cells, tissues, and the microenvironment in a wide range of lung diseases.

We are pleased to welcome colleagues and leaders from multiple partner institutions including the *Royal College of Surgeons in Ireland*, *Harvard University*, *Johns Hopkins University*, the *University of Pennsylvania*, and many others. In addition, we look forward to including panelists from the *Journal of Clinical Investigation* and the *American Society for Clinical Investigation* for a discussion about *Changing Patterns of Publications and Its Impact on Academic Success*.

As part of our 20th anniversary celebration, we are delighted to honor Dr. Augustine Choi, Stephen and Suzanne Weiss Dean of Weill Cornell Medicine and Provost for Medical Affairs at Cornell University as our keynote dinner speaker.

We look forward to your participation in the conference.

Alison Morris, MD, MS
Janet S. Lee, MD
Tomeka Suber, MD, PhD

2022 Pittsburgh International Lung Conference

Metabolism and the Lung: Homeostasis, Immunity, and Disease

PROGRAM AGENDA

Thursday, September 8, 2022

WiFi Network: **UClub-Guest**
Password: **PittConferenceGuest**

7:00 – 8:00 AM **Registration and Refreshments**
Lobby & Ballroom A, First Floor

Main Meeting Session: Ballroom B, Second Floor:

8:00 – 8:10 AM **Welcome and Opening Remarks**
Alison Morris, MD, MS; University of Pittsburgh
Janet S. Lee, MD; University of Pittsburgh
Tomeka Suber, MD, PhD; University of Pittsburgh

Session 1:	**The State of Metabolism Research in Health Sciences: Metabolism, Bioenergetics, and the Tools of the Trade**
Session Chairs:	*Janet S. Lee, MD; University of Pittsburgh* *Anuradha Ray, PhD; University of Pittsburgh* *Nathaniel Weathington, MD, PhD; UPMC*

8:10 – 8:20 AM **Session Chair Introduction**

8:20 – 8:40 AM **Aging, Metabolism and Autophagy**
Toren Finkel, MD, PhD
University of Pittsburgh

8:40 – 8:45 AM Q&A

8:45 – 9:05 AM **Overview of Metabolomics Analysis**
Stacy Gelhaus Wendell, PhD
University of Pittsburgh

9:05 – 9:10 AM Q&A

9:10 – 9:30 AM **Cellular Measurements and Metabolism**
William M. Oldham, MD, PhD
Harvard Medical School

9:30 – 9:35 AM Q&A

9:35 – 9:55 AM **Refreshment Break**
Ballroom A, First Floor

Thursday, September 8, 2022 *(continued)* WiFi Network: **UClub-Guest**
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MAIN MEETING SESSION: BALLROOM B, SECOND FLOOR:

Session 2:	**ALTERATIONS TO METABOLISM AS A DRIVER OF PULMONARY VASCULAR DISEASE**
Session Chairs:	*Brett Kaufman, PhD; University of Pittsburgh* *Lianghui Zhang, MD, PhD; University of Pittsburgh*

9:55 – 10:00 AM	**Session Chair Introduction**
10:00 – 10:20 AM	**Alterations to Metabolism as a Driver of Pulmonary Vascular Disease** *Sruti Shiva, PhD* *University of Pittsburgh School of Medicine*
10:20 – 10:25 AM	Q&A
10:25 – 10:45 AM	**Noncoding RNAs Direct Metabolism in Pulmonary Hypertension Physiology** *Stephen Y. Chan, MD, PhD, FAHA* *University of Pittsburgh School of Medicine*
10:45 – 10:50 AM	Q&A
10:50 – 11:05 AM	**Refreshment Break** BALLROOM A, FIRST FLOOR

MAIN MEETING SESSION: BALLROOM B, SECOND FLOOR:

Rapid Fire #1:	**EARLY CAREER ORAL PRESENTATIONS**
Moderators:	*Fernando Holguin, MD; University of Colorado, Denver* *Tomeka Suber, MD, PhD; University of Pittsburgh*

11:05 – 11:10 AM	**Introductions**
11:10 – 11:20 AM	*Abstract Oral Presentation #1:* **Multiomic Mesenchymal Cell Profiling in Systemic Sclerosis-associated Interstitial Lung Disease** *Eleanor B. Valenzi, MD* *University of Pittsburgh School of Medicine*
11:20 – 11:25 AM	Q&A
11:25 – 11:35 AM	*Abstract Oral Presentation #2:* **Pulmonary Vascular Disease in COPD** *Aparna Balasubramanian, MD, MHS* *Johns Hopkins University School of Medicine*
11:35 – 11:40 AM	Q&A

Thursday, September 8, 2022 *(continued)* WiFi Network: **UClub-Guest**
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11:40 – 11:50 AM	*Abstract Oral Presentation #3:* **Airway Immune Pathways in Allergic Asthma** *Jehan W. Alladina, MD* *Massachusetts General Hospital, Harvard Medical School*
11:50 – 11:55 AM	Q&A
12:00 – 12:45 PM	**Lunch (provided)** GOLD ROOM, SECOND FLOOR
12:45 – 2:00 PM	**Poster Session and Refreshments** *(No CME credit awarded)* **BALLROOM A, FIRST FLOOR**

MAIN MEETING SESSION: BALLROOM B, SECOND FLOOR

Session 3:	**STUDYING AIRWAYS DISEASE THROUGH THE LENS OF METABOLISM**
Session Chairs:	*Oliver Eickelberg, MD; University of Pittsburgh* *Frank Sciurba, MD; University of Pittsburgh*
2:00 – 2:10 PM	**Session Chair Introduction**
2:10 – 2:30 PM	**Immunometabolism Changes in COPD Patients** *Suzanne Cloonan, PhD* *Trinity College, Dublin*
2:30 – 2:35 PM	Q&A
2:35 – 2:55 PM	**The Interplay of Metabolism and Regenerative Signaling Pathways in Chronic Lung Disease** *Melanie Königshoff, MD, PhD* *University of Pittsburgh*
2:55 – 3:00 PM	Q&A
3:00 – 3:20 PM	**Airway Neutrophil Metabolism Impacts Cystic Fibrosis Bacterial Colonization** *Prof. Gerry McElvaney* *Royal College of Surgeons in Ireland*
3:20 – 3:25 PM	Q&A
3:25 – 3:45 PM	**Refreshment Break** BALLROOM A, FIRST FLOOR

Thursday, September 8, 2022 *(continued)* WiFi Network: **UClub-Guest**
Password: **PittConferenceGuest**

MAIN MEETING SESSION: BALLROOM B, SECOND FLOOR:

Session 4:	**UNLOCKING THE ROLE OF METABOLISM AND MITOCHONDRIA IN LUNG PARENCHYMAL DISEASE AND CANCER**
Session Chairs:	*Mauricio Rojas, MD; Ohio State University* *Nadia Hansel. MD: Johns Hopkins School of Medicine*

3:50 – 4:10 PM **Mitochondrial Changes in Idiopathic Pulmonary Fibrosis**
Ana Mora, MD
Ohio State University

4:10 – 4:15 PM Q&A

4:15 – 4:35 PM **Diverse Metabolic Signaling in Myeloid Cells as a Driver of Fibrotic Lung Disease**
G.R. Scott Budinger, MD
Northwestern Feinberg School of Medicine

4:35 – 4:40 PM Q&A

4:40 – 5:00 PM **Tumor Immunity and Metabolism in Cancer**
Tullia C. Bruno, PhD
UPMC Hillman Cancer Center

5:00 – 5:05 PM Q&A

5:05 – 5:25 PM **Mitochondria of Alveolar Type 2 Cells Determine Severity of the Lung's Innate Immunity**
M. Naeem Islam, PhD
Columbia University

5:25 – 5:30 PM Q&A

5:45 PM **Adjournment**

5:45 – 6:15 PM **Travel Time to Reception**

MOLLY'S TROLLEYS will arrive in the University Club parking lot circle at approximately 5:30pm to begin loading passengers for Carnegie Science Center. The first trolley will depart around **5:45pm** and subsequent trips will depart in approximate 10-15 minute intervals, with the last trip leaving around 6:15 pm.

6:00 – 9:00 PM **Reception**
CARNEGIE SCIENCE CENTER
(please wear your name badge for admittance)

6:00 – 6:30 PM COCKTAILS/APPETIZERS

6:30 – 7:30 PM DINNER

Thursday, September 8, 2022 ***(continued)***

7:30 – 8:10 PM DESSERT & KEYNOTE PRESENTATION:

"Do you believe in miracles? Yes, at the Monongahela River!"

SPECIAL GUEST SPEAKER:
Augustine M.K. Choi, MD
Stephen and Suzanne Weiss Dean, Weill Cornell Medicine
Provost for Medical Affairs, Cornell University

8:10 – 9:30 PM SOCIAL/EXHIBITS

8:45 - 9:15 PM **Return Transportation to Hotels**

MOLLY'S TROLLEYS WILL BE AVAILABLE TO BEGIN RETURNING PASSENGERS AT APPROXIMATELY **8:45 PM**
Approximate departure times (8:45pm, 9:00pm, 9:10pm, 9:15pm)

Friday, September 9, 2022

WiFi Network: **UClub-Guest**
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7:30 – 8:00 AM **Registration and Refreshments**
LOBBY & BALLROOM A, FIRST FLOOR

MAIN MEETING SESSION: BALLROOM B, SECOND FLOOR:

8:00 – 8:10 AM **WELCOME**

Session 5:	**METABOLISM AS A DRIVER OF IMMUNE RESPONSES AND IN PULMONARY TRANSPLANT**
Session Chairs:	*Chadi Hage, MD; University of Pittsburgh* *Mark Snyder, MD; University of Pittsburgh*

8:10 – 8:15 AM **Session Chair Introduction**

8:15 – 8:35 AM **Mitochondrial ROS Fine-tunes Lung Dendritic Cells to Regulate Allergic Disease**
Anuradha Ray, PhD
University of Pittsburgh

8:35 – 8:40 AM Q&A

8:40 – 9:00 AM **Immunometabolism as a Determinant in Success or Failure of Bone Marrow Transplant**
Craig A. Byersdorfer, MD, PhD
University of Pittsburgh

9:00 – 9:05 AM Q&A

Friday, September 9, 2022 *(continued)* WiFi Network: **UClub-Guest**
Password: **PittConferenceGuest**

9:05 – 9:20 AM **Refreshment Break**
BALLROOM A, FIRST FLOOR

MAIN MEETING SESSION: BALLROOM B, SECOND FLOOR:

Session 6:	**MODULATIONS OF METABOLISM IN IMMUNITY AND INFECTION**
Session Chairs:	*Barbara Methé, PhD; University of Pittsburgh* *Prabir Ray, PhD; University of Pittsburgh*

9:20 – 9:25 AM **Session Chair Introduction**

9:25 – 9:45 AM **Persistence of Klebsiella and Pseudomonas in the Respiratory Tract by Metabolite Adaptation and Implications in Pathogenicity**
Alice Prince, MD
Columbia University

9:45 – 9:50 AM Q&A

9:50 – 10:10 AM **Metabolic Determinants in the Pathogenesis of Legionella Infection**
Sunny Shin, PhD
University of Pennsylvania

10:10 – 10:15 AM Q&A

10:15 – 10:35 AM **Pseudomonas Microbial Metabolism and Adaptation in the CF Microenvironment**
Jennifer M. Bomberger, PhD
Geisel School of Medicine at Dartmouth

10:35 – 10:40 AM Q&A

10:40 – 11:00 AM **Refreshment Break**
BALLROOM A, FIRST FLOOR

MAIN MEETING SESSION: BALLROOM B, SECOND FLOOR:

Rapid Fire #2:	**EARLY CAREER ORAL PRESENTATIONS**
Moderator:	*Jessica Bon, MD, MS; University of Pittsburgh* *Anna Zemke, MD, PhD; University of Pittsburgh*

11:00 – 11:05 AM **Introductions**

11:05 – 11:15 AM *Abstract Oral Presentation #4:*
Immune Pathways in Severe Asthma
Marc C. Gauthier, MD
University of Pittsburgh

11:15 – 11:20 AM Q&A

Friday, September 9, 2022 *(continued)* WiFi Network: **UClub-Guest**
Password: **PittConferenceGuest**

11:20 – 11:30 AM *Abstract Oral Presentation #5:*
Metabolism and the Lung Microbiome after Lung Transplantation
John E. McGinniss, MD
University of Pennsylvania

11:30 – 11:35 AM Q&A

11:35 – 11:45 AM *Abstract Oral Presentation #6:*
Maresin 1/LGR6 axis in the resolution of Respiratory Syncytial Virus- induced inflammation
Nandini Krishnamoorthy, PhD
Harvard Medical School, Brigham & Women's Hospital

11:45 – 11:50 AM Q&A

11:50 AM – 1:00 PM **Lunch (provided)**
GOLD ROOM, SECOND FLOOR

MAIN MEETING SESSION: BALLROOM B, SECOND FLOOR:

1:00 – 2:00 PM ***Panel Discussion***

CHANGING PATTERNS OF PUBLICATIONS AND ITS IMPACT ON ACADEMIC SUCCESS

- ***Rama Mallampalli, MD****; Associate Editor, American Journal of Respiratory Cell & Molecular Biology*
- ***Lorraine Ware, MD****; Past President, The American Society for Clinical Investigation*
- ***Corinne Williams, PhD****; Senior Science Editor, The Journal of Clinical Investigation and JCI Insight*

2:00 – 2:15 PM **Refreshment Break**
BALLROOM A, FIRST FLOOR

MAIN MEETING SESSION: BALLROOM B, SECOND FLOOR:

Session 7:	**METABOLIC AND PHYSIOLOGIC DETERMINANTS OF COVID PATHOGENESIS**
Session Chairs:	*Georgios Kitsios, MD, PhD; University of Pittsburgh* *John McDyer, MD; University of Pittsburgh*

2:15 – 2:20 PM **Session Chair Introduction**

2:20 – 2:40 PM **Immuno-metabolomes and Immuno-lipidomes in COVID-19**
Charles Dela Cruz, MD, PhD
Yale University

2:40 – 2:45 PM Q&A

2:45 – 3:05 PM **Metabolic Vulnerabilities in COVID-19**
Peter Mullen, PhD
USC Keck School of Medicine

Friday, September 9, 2022 *(continued)* WiFi Network: **UClub-Guest**
Password: **PittConferenceGuest**

3:05 – 3:10 PM Q&A

3:10 – 3:35 PM **Refreshment Break**
BALLROOM A, FIRST FLOOR

MAIN MEETING SESSION: BALLROOM B, SECOND FLOOR:

Session 8:	**TARGETING METABOLISM FOR NOVEL THERAPIES**
Session Chairs:	*Faraaz Shah, MD, MPH; University of Pittsburgh*
	Alison Morris, MD, MS; University of Pittsburgh

3:35 – 3:40 PM **Session Chair Introduction**

3:40 – 4:00 PM **Understanding Metabolic Changes in Patients with Sepsis**
Matthew Rosengart, MD, MPH
University of Pittsburgh

4:00 – 4:05 PM Q&A

4:05 – 4:25 PM **The Interplay of Metabolism and Sleep Physiology**
Vsevolod Y. Polotsky, MD, PhD
Johns Hopkins University

4:25 – 4:30 PM Q&A

4:30 – 4:45 PM **Poster Recognitions**
(No CME credit awarded)

4:45 – 5:00 PM **Concluding Remarks**
Alison Morris, MD, MS

5:00 PM **Adjournment**

Educational Objectives

The educational objectives of this conference are to describe and discuss the latest clinical and research advances in Pulmonary Medicine.

Upon completion of this conference, the attendees should be able to:

- Describe the role of metabolism and the inflammasome on Cystic Fibrosis patients with pseudomonas colonization; consider novel therapies targeting the inflammasome;
- Understand the changes to lung immune cell metabolism in patients with asthma;
- Understand the changes to lung immune cell metabolism in patients with COPD;
- Recognize the implications of beta agonist and inhaled steroid therapy on immune function and weigh the risks and benefits of therapy for asthmatic and COPD patients;
- Recognize metabolism of immune cells in the containment and elimination of cancer as new immunotherapy for cancer is becoming widely used.

Target Audience

The target audience for this conference is practicing physicians, nurses, fellows-in-training, allied health personnel, basic and translational researchers, public health experts, industry scientists, and any other health care or academic professional with a major clinical or research interest in pulmonary medicine.

Further, because the University of Pittsburgh and UPMC are internationally recognized leaders in pulmonary and critical care and research, the conference will also enable providers on a treatment team to contribute specialized knowledge of metabolic and immune processes happening in specific disease states to inform their team and bring consensus to therapeutic strategy for patients with these diseases.

CME Accreditation & Credit Designation Statement

In support of improving patient care, the University of Pittsburgh is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

Physician (CME)

The University of Pittsburgh designates this live activity for a maximum of 13.0 *AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Nursing (CNE)

The maximum number of hours awarded for this Continuing Nursing Education activity is 13.0 contact hours.

Physician Assistant (AAPA)

The University of Pittsburgh has been authorized by the American Academy of PAs (AAPA) to award AAPA Category 1 CME credit for activities planned in accordance with AAPA CME Criteria. This activity is designated for 13.0 AAPA Category 1 CME credits. PAs should only claim credit commensurate with the extent of their participation.

Other health care professionals will receive a certificate of attendance confirming the number of contact hours commensurate with the extent of participation in this activity.

UPMC
University of Pittsburgh School of Medicine
Center for Continuing Education in the Health Sciences

2022 Pittsburgh International Lung Conference: Metabolism and the Lung: Homeostasis, Immunity, and Disease
September 8 – 9, 2022
123 The University Club
Pittsburgh, PA

This is not your official certificate.

How to receive your continuing education credit?

https://cce.upmc.com/2022-pittsburgh-international-lung-conference

This activity is approved for the following credit: *AMA PRA Category 1 Credit™,* ANCC, and AAPA Category 1 CME. Other health care professionals will receive a certificate of attendance confirming the number of contact hours commensurate with the extent of participation in this activity.

To receive credit, you will be required to login, complete the course evaluation, and claim credit. If you are a new user, click "Register" to create a new account. The activity will be added to your Pending Activities and accessible on the first day of the activity. You will have 30 days to complete the evaluation before the activity is closed. Upon completion, certificates will be available to download and stored for future reference in your Completed Activities.

How to receive your official certificate?

To receive credit, login to the UPMC Center for Continuing Education in the Health Sciences (CCEHS) continuing education learning portal, http://cce.upmc.com. If you are a new user, choose "Register" to create an account. **Note, records are matched to users by email address.**

- Go to **My Account**, **My Courses**
- Choose **Pending Activities**
- Click on the **course title** to complete the course evaluation and claim credit

FACULTY DISCLOSURE

All individuals in a position to control the content of this education activity have disclosed all financial relationships with any companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

All of the relevant financial relationships for the individuals listed below have been mitigated:

Jehan Alladina, MD	Grant/Research Support: AstraZeneca
Stephen Chan, MD, PhD	Grant/Research Support: Actelion; Bayer; Pfizer Consultant: Acceleron Pharma; United Therapeutics Stockholder: Synhale Therapeutics Other: (Patent) Targeting PH Metabolism
Augustine M.K. Choi, MD	Other: (Stockholder) Proterris; (Patents) CO and COPD
Oliver Eickelberg, MD	Grant/Research Support: Bristol-Meyers-Squibb; Pieris Pharmaceuticals Consultant: Pieris Pharmaceuticals; Blade Therapeutics; Yap Therapeutics Stockholder: Blade Therapeutics
Toren Finkel, MD, PhD	Grant/Research Support: Generian Other: (Stockholder) Generian
Nadia Hansel, MD, MPH	Grant/Research Support: AstraZeneca; Boehringer Ingelheim Other: (Advisory Board) AstraZeneca
Fernando Holguin, MD	Grant/Research Support: AstraZeneca; GSK; Sanofi; Imara
Janet Lee, MD	Consultant: Janssen R&D
Ana Mora, MD	Grant/Research Support: Boehringer Ingelheim
Anuradha Ray, PhD	Grant/Research Support: Pieris Pharmaceuticals

Lorraine Ware, MD	Grant/Research Support: Genentech; Boehringer Ingelheim Consultant: Boehringer Ingelheim; Global Blood Therapeutics

No other members of the planning committee, speakers, presenters, authors, content reviewers and/or anyone else in a position to control the content of this education activity have relevant financial relationships with any companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

DISCLAIMER STATEMENT

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ACKNOWLEDGEMENTS

SPONSORS

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Division of Pulmonary, Allergy, and Critical Care Medicine

UPMC LIFE CHANGING MEDICINE

University of Pittsburgh McGowan Institute for Regenerative Medicine

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE – NATIONAL INSTITUTES OF HEALTH:

Funding for this conference was made possible by the National Institutes of Health by R13 HL156271 from the National Heart, Lung, And Blood Institute. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government.

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- Boehringer-Ingelheim
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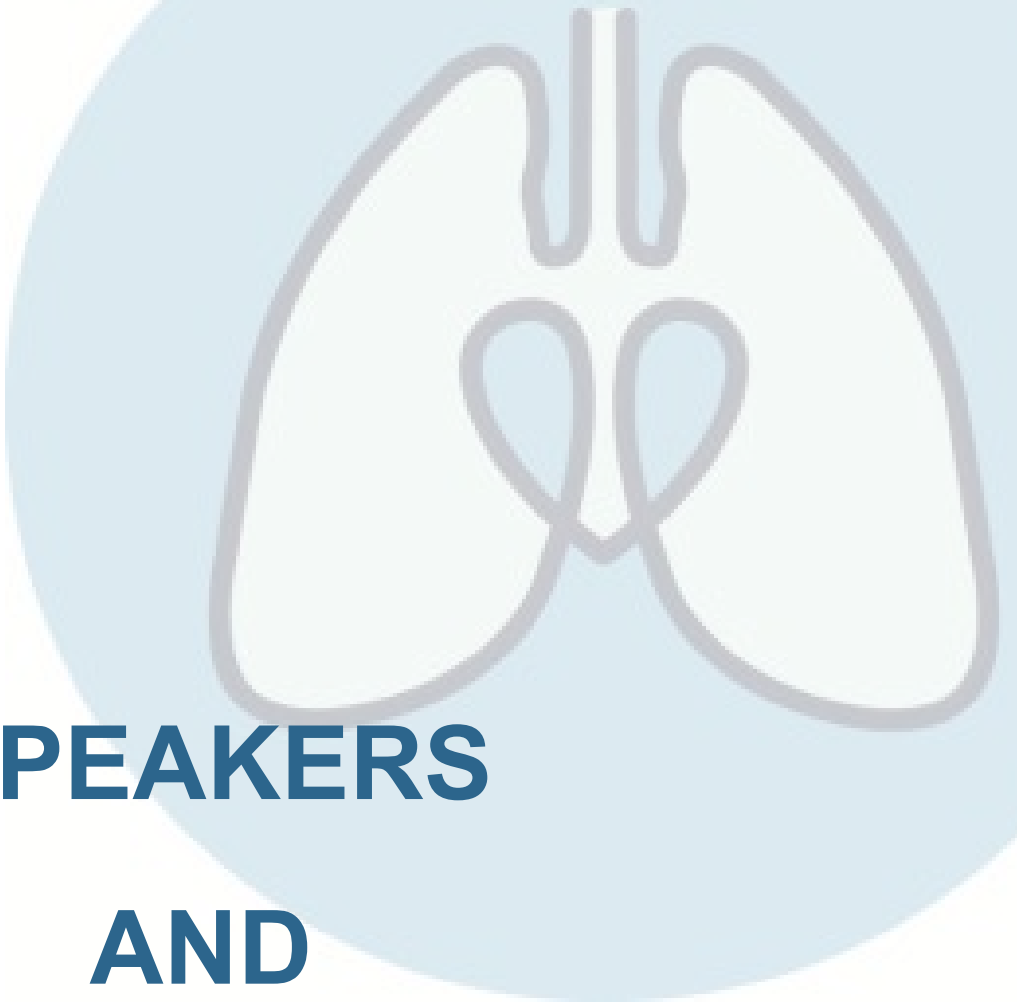


SPEAKERS AND SESSION CHAIRS

(in order of presentation)

COURSE DIRECTORS

Alison Morris, MD, MS

Professor of Medicine, Immunology, and Clinical and Translational Research Division
Chief, Division of Pulmonary, Allergy and Critical Care Medicine
Director, Center for Medicine and the Microbiome
UPMC Chair in Translational Pulmonary and Critical Care Medicine
University of Pittsburgh School of Medicine

Alison Morris, MD, MS is a UPMC Chair in Translational Pulmonary and Critical Care Medicine and Professor of Medicine, Immunology, and Clinical and Translational Science in the Division of Pulmonary, Allergy, and Critical Care Medicine at the University of Pittsburgh. She is also the founder and director of the University of Pittsburgh Center for Medicine and the Microbiome. She attended medical school at Duke University followed by residency and fellowship at the University of California, San Francisco. She moved to the University of Pittsburgh from 2000 to 2003, joined the faculty at University of Southern California from 2003-2006, then returned to Pittsburgh in 2006. Dr. Morris' research interests focus on the pulmonary complications of HIV infections and on the lung microbiome; however, she has recently begun work on COVID-19 pathogenesis and outcomes. She has established the University of Pittsburgh COVID-19 biorepository, is on the Steering Committee and site PI for the Healthcare Worker Exposure Response and Outcomes of Hydroxychloroquine Trial (HERO HCQ) and has worked on the ACTIV-4 anticoagulation studies. She is one of the founding physicians and clinical leaders of the UPMC Post-COVID Recovery Clinic.

Janet S. Lee, MD

Professor of Medicine
Director, Acute Lung Injury Center of Excellence
UPMC Chair in Acute Lung Injury
Division of Pulmonary, Allergy, and Critical Care Medicine
Member, Pittsburgh Heart, Lung, Blood and Vascular Medicine Institute
University of Pittsburgh School of Medicine

Dr. Janet S. Lee is a UPMC Chair in Acute Lung Injury, a Professor of Medicine, Member of the Pittsburgh Heart, Lung, and Blood Vascular Medicine Institute, and Director of the Acute Lung Injury Center of Excellence at the University of Pittsburgh. She received her medical degree at Georgetown University and completed her internship and residency at the University of Alabama at Birmingham. Dr. Lee went on to complete her fellowship at the University of Washington before joining the faculty at the University of Pittsburgh. Her clinical interest is acute respiratory distress syndrome, severe pneumonia, sepsis-related immunosuppression and hospital-acquired infections in the critically ill. Dr. Lee's laboratory studies pulmonary host defense and molecular pathogenesis of acute lung injury. Her expertise is effector function of myeloid cells at mucosal sites such as the lower respiratory tract, and immune regulation of local and systemic inflammation during severe infection. Dr. Lee is an elected member of the American Society for Clinical Investigation and Association of American Physicians.

Tomeka L. Suber, MD, PhD

Assistant Professor of Medicine
Division of Pulmonary, Allergy & Critical Care Medicine
University of Pittsburgh School of Medicine

Dr. Tomeka Suber is an Assistant Professor of Medicine in the Division of Pulmonary, Allergy, and Critical Care Medicine at the University of Pittsburgh. She earned both her MD and PhD at Johns Hopkins University School of Medicine and completed her residency at Johns Hopkins Hospital. She then moved to the University of Pittsburgh for her fellowship training. Dr. Suber's clinical interests include acute respiratory distress syndrome, sepsis, and bacterial pulmonary infections. Her research focuses on how metabolism regulates host defense mechanisms in intrapulmonary bacterial infections that lead to acute lung injury. She is currently funded by a K08 Career Development Award and the Harold Amos Medical Faculty Development Program.

SESSION 1: THE STATE OF METABOLISM RESEARCH IN HEALTH SCIENCES: METABOLISM, BIOENERGETICS, AND THE TOOLS OF THE TRADE

SESSION CHAIRS:

Janet S. Lee, MD

Professor of Medicine
Director, Acute Lung Injury Center of Excellence
UPMC Chair in Acute Lung Injury
Division of Pulmonary, Allergy, and Critical Care Medicine
Member, Pittsburgh Heart, Lung, Blood and Vascular Medicine Institute
University of Pittsburgh School of Medicine

Dr. Janet S. Lee is a UPMC Chair in Acute Lung Injury, a Professor of Medicine, Member of the Pittsburgh Heart, Lung, and Blood Vascular Medicine Institute, and Director of the Acute Lung Injury Center of Excellence at the University of Pittsburgh. She received her medical degree at Georgetown University and completed her internship and residency at the University of Alabama at Birmingham. Dr. Lee went on to complete her fellowship at the University of Washington before joining the faculty at the University of Pittsburgh. Her clinical interest is acute respiratory distress syndrome, severe pneumonia, sepsis-related immunosuppression and hospital-acquired infections in the critically ill. Dr. Lee's laboratory studies pulmonary host defense and molecular pathogenesis of acute lung injury. Her expertise is effector function of myeloid cells at mucosal sites such as the lower respiratory tract, and immune regulation of local and systemic inflammation during severe infection. Dr. Lee is an elected member of the American Society for Clinical Investigation and Association of American Physicians.

Anuradha Ray, PhD

Lung Immunology Endowed Chair, Department of Medicine
Professor of Medicine and Immunology
Division of Pulmonary, Allergy & Critical Care Medicine
University of Pittsburgh School of Medicine

Dr. Anuradha Ray is a Professor of Medicine and Immunology and Endowed Chair of Lung Immunology in Medicine at the University of Pittsburgh School of Medicine. She received her Ph.D. from Calcutta University in India. She underwent postdoctoral training at Cornell University, Ithaca, NY and at Rockefeller University in New York. She was on the faculty at Rockefeller University and at Yale University between the years 1990 and 2001 before moving to the University of Pittsburgh. Dr. Ray's early research led to the first identification of NF-κB as a target for the anti-inflammatory actions of corticosteroids and the discovery of GATA-3 as the master regulator of Th2 cells which promote asthma and allergic diseases. In ongoing research, she and her colleagues are investigating immune dysfunction in severe asthma that unlike milder asthma is refractory to corticosteroid treatment. One novel finding in these studies is a dominant Type 1/IFN-γ response in CD4+ and CD8+ T cells that includes tissue resident memory (TRM) cells in the airways of a subset of severe asthma patients. In studies of immune homeostasis, her studies have implicated mitochondrial H2O2 in dendritic cells as a regulator of immune tolerance in the airways. Her research has been continuously funded by grants from the National Institutes of Health (NIH). She currently serves on the Advisory Council of the National Institute of Allergy and Infectious Diseases (NIAID).

Nate Weathington, MD, PhD

Pulmonary Consultants, UPMC

Dr. Nathaniel Weathington is a graduate of the University of Alabama in Birmingham MD/PhD program, where he investigated tissue breakdown and inflammatory cell recruitment. After residency at UAB, he joined the Division of Pulmonary, Allergy & Critical Care Medicine at the University of Pittsburgh as a fellow in 2011. He later joined the Division faculty in 2014 as a member of the Acute Lung Injury Center, where he conducted research on cytokine receptor regulation in lung inflammatory responses, ubiquitin biology in lung inflammation, and the preclinical testing of novel small molecule anti-inflammatory agents. Dr. Weathington is currently focusing on patient care at several UPMC facilities.

SESSION SPEAKERS:

Toren Finkel, MD, PhD
Distinguished Professor of Medicine
Director of Aging Institute
G. Nicholas Beckwith III and Dorothy B. Beckwith Endowed Chair of Translational Medicine
University of Pittsburgh/UPMC

Dr. Toren Finkel received his undergraduate degree in Physics and his MD and PhD degree from Harvard Medical School. Following a residency in Internal Medicine at the Massachusetts General Hospital, he completed a fellowship in Cardiology at Johns Hopkins Medical School. In 1992, after completing his clinical training, he came to the NIH as an Investigator within the Intramural Research Program of the National Heart, Lung and Blood Institute (NHLBI). Over the next 25 years at the NIH, he held various positions including Chief of the Cardiology Branch and Chief of the Center for Molecular Medicine within the NHLBI. He is a member of the American Society for Clinical Investigation (ASCI) and the Association of American Physicians (AAP). He has also been inducted as a Fellow of the American Association for the Advancement of Science (AAAS) and is an elected member of the National Academy of Medicine. He serves on numerous editorial boards including currently serving on the Board of Reviewing Editors for Science. As of September 1, 2017, Dr. Finkel assumed the role of the Director of the Aging Institute, and the G. Nicholas Beckwith III and Dorothy B. Beckwith Endowed Chair of Translational Medicine at the University of Pittsburgh/UPMC. Over the last three decades, his laboratory has made fundamental contributions in our understanding of the role of reactive oxygen species and mitochondrial function in aging and age-related diseases. He also has recently helped co-develop several small molecules which are anticipated to be in Phase I testing within 12 months and may be of potential benefit for a range of age-related disorders.

AGING, METABOLISM AND AUTOPHAGY

I plan to review the current understanding of the molecular regulators of mammalian aging. I will pay particular concern to how changes in metabolism and nutrient sensing regulate the aging process. I will also discuss how a decline in mitochondria function and quality control might contribute to aging. In particular, I will discuss our genetic models to measure in vivo mitophagy and other models that modulate mTOR function. Finally, I will provide an overview of how these metabolic and autophagic pathways might be therapeutically approached with the development of novel small molecules.

Stacy Wendell, PhD
Associate Professor, Pharmacology and Chemical Biology and Clinical Translational Science
Scientific Director, Health Sciences Mass Spectrometry Core
University of Pittsburgh

Dr. Stacy Wendell is an Associate Professor of Pharmacology and Chemical Biology and Clinical Translational Science. Dr. Wendell is the Scientific Director for the Health Sciences Mass Spectrometry Core at the University of Pittsburgh. Dr. Wendell received her PhD in chemistry from the University of Maryland, Baltimore County and was an NRSA postdoctoral fellow in the lab of Ian Blair at the University of Pennsylvania. Her research focuses on the formation and signaling actions of bioactive lipids in asthma and other inflammatory diseases, where she uses mass spectrometry-based approaches to look at global changes in disease pathophysiology. Dr. Wendell has over 20 years of liquid chromatography mass spectrometry experience and is internationally recognized for her work in lipid signaling and small molecule mass spectrometry.

OVERVIEW OF METABOLOMICS ANALYSIS

Metabolomics is the broad analysis of metabolites found in a biological specimen. Metabolomics analyses, including lipidomics, has been widely used in basic research and is increasingly utilized in the analysis of clinical samples including the investigation of acute and chronic lung disease. Current methodologies of biological samples are primarily performed using high resolution mass spectrometry coupled to either gas or liquid chromatography separation modalities. Using these analytical platforms both targeted, hypothesis-guided and untargeted, global profiling strategies are possible. Global profiling analyses provide great promise for the discovery of novel biomarkers of disease and the discovery of dysregulated metabolic pathways; however, untargeted metabolomics is still in its infancy compared to genomics and proteomics. The diversity of chemical structures that comprise the same chemical formula and therefore the same mass leads to complications in data analysis and interpretation. Improvements in databases containing both full scan and product ion fragmentation spectra are an ongoing push, but the future also holds promise for advanced techniques including both spatial `omics strategies and single cell metabolomics, which will provide more specific insight into both acute and chronic lung disease.

William M. Oldham, MD, PhD
Associate Physician, Pulmonary and Critical Care Medicine Division
Brigham and Women's Hospital
Assistant Professor, Harvard Medical School

William Oldham, M.D., Ph.D. is an Associate Physician in the Pulmonary and Critical Care Medicine Division at Brigham and Women's Hospital and Assistant Professor at Harvard Medical School. His laboratory studies the cellular metabolic responses to hypoxia and the metabolic pathobiology of lung diseases leveraging the power of metabolomics, stable isotope tracing, extracellular flux analyses, and network medicine.

CELLULAR MEASUREMENTS AND METABOLISM

This presentation will cover various approaches to investigating the metabolism of cultured cells with a particular focus on the Seahorse bioanalyzer. We will review the basic measurements of cellular oxygen consumption and extracellular acidification rates, the molecular drivers of these rates, and how these rates can be perturbed to provide insights into cellular energy metabolism. The use of stable isotope tracing and metabolic flux analyses as complementary approaches will be described. Our lab's work to understand the metabolic response of pulmonary vascular and fibroblast cells to hypoxia will serve as motivating examples of this experimental approach.

SESSION 2: ALTERATIONS TO METABOLISM AS A DRIVER OF PULMONARY VASCULAR DISEASE

SESSION CHAIRS:

Brett A. Kaufman, PhD
Associate Professor of Medicine
Division of Cardiology
Associate Professor of Bioengineering
Pittsburgh Heart, Lung, and Blood Vascular Medicine Institute
University of Pittsburgh School of Medicine

Dr. Kaufman's long-standing research interest is to understand the contribution of mtDNA metabolism to disease progression. For 20 years he has been uncovering the fundamental processes that underlie mitochondrial respiratory deficiency with a focus on mtDNA stability and copy number control – processes essential for respiratory function and viability. Dr. Kaufman's major research goals are 1) to define the biochemical events responsible for the maintenance of mtDNA content, 2) to understand how distinct pathways influence mtDNA maintenance, and 3) to understand mechanisms of mtDNA damage and resistance to damage in the context of disease.

Lianghui (Lucy) Zhang, MD, PhD
Assistant Professor of Medicine
Division of Pulmonary, Allergy and Critical Care Medicine
University of Pittsburgh School of Medicine

Dr. Lianghui Zhang received her M.D. from the Medical School of Fudan University and Ph.D. in Pharmacology from the University of Rochester. Dr. Zhang is an Assistant Professor of Medicine in the Division of Pulmonary, Allergy, Critical Care Medicine at the University of Pittsburgh. Her research interests have been focused on exploring the mechanisms of inflammatory endothelial injury and repair using viral lung injury mouse model and developing novel mechanism-based regenerative strategies. She has published in high impact journals such as Nature Chemical Biology, Nature Communications, Circulation, Cell, etc.

SESSION SPEAKERS:

Sruti Shiva, PhD
Professor & Vice Chair of Academics and Equity
Department of Pharmacology & Chemical Biology
Principle Investigator, Heart, Lung, Blood, and Vascular Medicine Institute
Director, Center for Metabolism and Mitochondrial Medicine
University of Pittsburgh School of Medicine

Dr. Sruti Shiva obtained her PhD at the University of Alabama in Birmingham in 2004 after studying the mechanisms by which nitric oxide regulates mitochondrial function. She completed her post-doctoral training at the National Heart Lung and Blood Institute at the National Institutes of Health. She joined the faculty at the University of Pittsburgh in 2008 as an Assistant Professor and is currently a tenured Professor of Pharmacology & Chemical Biology and a Principal Investigator in the Vascular Medicine Institute. Dr. Shiva also is Director of the University of Pittsburgh Center for Metabolism and Mitochondrial Medicine (C3M). Dr. Shiva's research focuses on understanding the mechanisms by which mitochondrial function is regulated, particularly by reactive oxygen and nitrogen species and the contribution of these mechanisms to cardiovascular health and disease pathogenesis.

ALTERATIONS TO METABOLISM AS A DRIVER OF PULMONARY VASCULAR DISEASE

Pulmonary hypertension is characterized by increased mean pulmonary artery pressure, that leads to vascular remodeling and right heart failure. Accumulating evidence suggests that altered cellular metabolism is systemic in PH and contributes to disease pathogenesis. However, the exact nature of bioenergetic changes in PH patients and their contribution to disease pathogenesis remains unclear. Circulating platelets are integral to vascular signaling and are highly metabolically active. Notably, platelet bioenergetic measurements have been proposed as a surrogate for systemic mitochondrial function. Here we measure bioenergetics in platelets isolated from PH patients and demonstrate that these platelets display a metabolic dysfunction characterized by increased glycolysis and fatty acid oxidation, which is accompanied by a concomitant production of mitochondrial reactive oxygen species. These parameters of altered metabolism were highly correlated with clinical parameters of disease severity such as mean pulmonary artery pressure, pulmonary vascular resistance, and right ventricular stroke work index. At a mechanistic level the platelet metabolic changes observed were associated with augmented enzymatic activity of carnitine palmitoyltransferase-1 and electron transport chain complex II, as well as the upregulation of the mitochondrial GTPase mitofusin-1 (MFN-1). We present data in novel murine models exploring the role of platelet MFN-1 in regulating fatty acid oxidation and its contribution to PH pathogenesis. These studies advance the understanding of metabolic dysfunction in PH patients and elucidate a mechanistic role for platelet mitochondria in PH pathogenesis.

Stephen Y. Chan, MD, PhD, FAHA
Vitalant Chair in Vascular Medicine
Professor of Medicine, Division of Cardiology
Director, Vascular Medicine Institute
Director, Center for Pulmonary Vascular Biology and Medicine
University of Pittsburgh School of Medicine and UPMC

Dr. Stephen Chan serves as the Vitalant Chair in Vascular Medicine, Professor of Medicine, and Director of the Vascular Medicine Institute (VMI) at the University of Pittsburgh School of Medicine. Dr. Chan has devoted his career as a physician-scientist and cardiologist to leading a basic and translational research program and clinical center investigating the mechanisms of pulmonary hypertension (PH). He uses computational theory to study gene network architecture and couple these insights with unique experimental reagents derived from genetically altered rodent and human subjects. Dr. Chan's work was among the first (1) to introduce -omics-wide discovery in PH focusing on vascular mechanosignaling; (2) to identify the network biology of non-coding RNAs in PH; (3) to define the regulation of mitochondrial and metabolic dysfunction in PH; and (4) to clarify the regulation of inflammatory cell recruitment to pulmonary vessels. Dr. Chan has published >100 peer-reviewed publications. He has carried grants as PI, including NIH R-level and U-level grants as well as the AHA Established Investigator Award. He is an elected Fellow of the AHA and ASCI; he serves on the AHA 3CPR Council Leadership Committee and recently served as Chair of the NIH RIBT study section.

NONCODING RNAS DIRECT METABOLISM IN PULMONARY HYPERTENSION PHYSIOLOGY

Hypoxic reprogramming of vasculature relies upon genomic, epigenetic, and metabolic circuitry, but the control points are unknown. In pulmonary arterial hypertension (PAH), a disease driven by HIF-dependent vascular dysfunction, we found that the master transcription factor of hypoxia, HIF-2α, promoted expression of a long non-coding RNA (lncRNA) and a neighboring protein-coding gene. This lncRNA stabilized its neighboring protein binding partner to alter epigenetic histone methylation, driving metabolic and pathogenic endothelial activity. We identified a significant association between a single nucleotide variant (SNV) within this gene tandem and disease risk in PAH discovery (N=694 vs. 1,560 controls) and replication (N=96 vs. 401 controls) patient cohorts and in a global meta-analysis (N=2,181 vs. N=10,060 controls). Mechanistically underlying this association, this SNV displayed allele specific association with HIF-2, engaging in long-range chromatin interactions and inducing the lncRNA gene tandem in hypoxic cells. In vivo, deficiency of this lncRNA protected against PAH, as did pharmacologic inhibition of histone methylation. Thus, combining insights of genetic epidemiology with molecular mechanism, we identified a lncRNA-protein complex that controls multi-omic reprogramming in PAH and represents a fundamental molecular hierarchy driving hypoxic signaling as well as endothelial pathobiology. Moreover, this work offers a roadmap toward more effective diagnostic and therapeutic opportunities focused on genome editing, RNA-based, and epigenetic platforms.

RAPID FIRE #1: EARLY CAREER ORAL PRESENTATIONS

MODERATORS:

Fernando Holguin, MD, MPH

James C. Campbell Professor of Pulmonary Medicine
Division of Pulmonary Sciences and Critical Care Medicine
University of Colorado Anschutz Medical Campus

Dr. Fernando Holguin is the James C. Campbell Professor of Pulmonary Medicine in the Division of Pulmonary Sciences and Critical Care Medicine at the University of Colorado Anschutz Medical Campus. He grew up in Mexico City, where he went to school. He subsequently trained at Emory University where he also served as faculty and also joined the Respiratory Health Branch at the CDC. He was later recruited to the University of Pittsburgh where he worked in the Asthma Institute until 2016. Throughout his academic career he has focused much on his work on research and patient care. He has been in practice for more than 25 years and has many clinical interests including severe asthma, obesity and asthma and air pollution. Dr. Holguin is current Director of the Clinical & Research Asthma Program and the former Executive Director of CU School of Public Health's Latino Research and Policy Center (LRPC). He also served as the co-chair of the American Thoracic Society and European Respiratory Society Task Force on severe asthma. He is currently funded by the NIH & DOD for the implementation of clinical & translational studies related to obesity and asthma. His work initially focused on epidemiology of disease and lung physiology, but more recently, he has been studying mechanisms by which metabolic dysregulations cause airway inflammation and dysfunction. Dr. Holguin has authored or co-authored more than 170 papers and is internationally known for his work in asthma, COPD and air pollution. Dr. Holguin enjoys spending time with his family (wife Shanta, and sons Mateo and Diego), skiing, reading, and traveling to new places.

Tomeka L. Suber, MD, PhD

Assistant Professor of Medicine
Division of Pulmonary, Allergy and Critical Care Medicine
University of Pittsburgh School of Medicine

Dr. Tomeka Suber is an Assistant Professor of Medicine in the Division of Pulmonary, Allergy, and Critical Care Medicine at the University of Pittsburgh. She earned both her MD and PhD at Johns Hopkins University School of Medicine and completed her residency at Johns Hopkins Hospital. She then moved to the University of Pittsburgh for her fellowship training. Dr. Suber's clinical interests include acute respiratory distress syndrome, sepsis, and bacterial pulmonary infections. Her research focuses on how metabolism regulates host defense mechanisms in intrapulmonary bacterial infections that lead to acute lung injury. She is currently funded by a K08 Career Development Award and the Harold Amos Medical Faculty Development Program.

LUNG CELL PROFILING IN MULTIOMIC MESENCHYMAL CELL PROFILING IN SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

Eleanor B. Valenzi, MD
University of Pittsburgh School of Medicine

Dr. Eleanor Valenzi is an Assistant Professor Medicine at the University of Pittsburgh, and member of the Dorothy P. and Richard P. Simmons Center for Interstitial Lung Disease and the Scleroderma Center. She completed her undergraduate education at the University of Pennsylvania followed by medical school at the UAB School of Medicine. She completed residency at the University of Chicago, then pulmonary /critical care fellowship at the University of Pittsburgh. With the mentorship of Dr. Robert Lafyatis, her translational research program focuses on determining the molecular mechanisms and transcription factor regulation underlying systemic sclerosis and other chronic fibrotic lung diseases, utilizing single-cell based technologies, genomic, and explant culture models.

PULMONARY VASCULAR DISEASE IN COPD

Aparna Balasubramanian, MD, MHS
Johns Hopkins University School of Medicine

Aparna Balasubramanian received her B.A in Molecular Biology from Princeton University in 2008. She went on to obtain her MD from St. George's University School of Medicine in 2013, followed by a residency in Internal Medicine at Georgetown University which she completed in 2016. She subsequently pursued fellowship in Pulmonary and Critical Care Medicine from Johns Hopkins University, after which she was appointed to a faculty position as Assistant Professor of Medicine. Her clinical and research interests are focused on pulmonary vascular disease and pulmonary hypertension in COPD under the mentorship of Dr. Meredith McCormack and Dr. Stephen Mathai. Her work focuses on developing and examining noninvasive biomarkers to define subgroups of COPD patients who may benefit from therapies targeting the pulmonary vasculature.

AIRWAY IMMUNE PATHWAYS IN ALLERGIC ASTHMA

Jehan W. Alladina, MD
Massachusetts General Hospital, Harvard Medical School

Dr. Alladina is a physician-scientist in the Division of Pulmonary and Critical Care Medicine at Massachusetts General Hospital. She is a researcher in the laboratory of Dr. Benjamin Medoff in the Center for Immunology and Inflammatory Diseases at MGH and her research prioritizes the use of human biospecimens and translational methods to understand the innate immune programs underlying pulmonary inflammatory disease. Dr. Alladina leverages human models of lung inflammation and detailed immunophenotyping to identify novel cellular and molecular signaling pathways that govern acute pulmonary inflammation and its resolution.

SESSION 3: STUDYING AIRWAYS DISEASE THROUGH THE LENS OF METABOLISM

SESSION CHAIRS:

Oliver Eickelberg, MD, FERS, ATSF
Visiting Professor of Medicine
Division of Pulmonary, Allergy, and Critical Care Medicine
Vice Chair for Basic and Translational Science
Department of Medicine
University of Pittsburgh School of Medicine

Dr. Oliver Eickelberg is a Visiting Professor in the Division of Pulmonary, Allergy, and Critical Care Medicine as well as a Vice Chair for Basic and Translational Science in the Department of Medicine at the University of Pittsburgh School of Medicine. Dr. Eickelberg studied at the medical schools of the Universities of Lübeck (Germany), Vienna (Austria) and Basel (Switzerland) and obtained his doctorate in medicine (MD) at Basel University. He worked as a Postdoctoral Fellow at the Department of Medicine in Basel and went to Yale University, Connecticut (USA), before returning to Germany in 2002 as assistant professor at the Justus-Liebig-University in Giessen. Dr. Eickelberg's research focus centers on deciphering the mechanisms of tissue fibrosis, particularly in idiopathic pulmonary fibrosis (IPF) and chronic lung allograft dysfunction (CLAD) after transplantation. His team seeks to investigate disease pathobiology, identify biomarkers to stratify patient subgroups, and develop novel treatment options for patients with the above-mentioned diseases. His research mechanistically interrogates profibrotic signaling pathways that control the dynamics of extracellular matrix (ECM) composition during tissue injury, repair, and fibrosis. Dr. Eickelberg has contributed significantly to provide the entire proteome during lung injury, repair, fibrosis, and regeneration, in animal models as well as human disease. He has extensive expertise in interpreting large datasets of tissue samples, as well as using complex phenotypic in vitro models that recapitulate aspects of human disease.

Frank C. Sciurba, MD, FCCP
Professor of Medicine and Education
Director, Emphysema and COPD Research Center
Director, Pulmonary Function Exercise Physiology Laboratory
Division of Pulmonary, Allergy & Critical Care Medicine
University of Pittsburgh School of Medicine

Dr. Frank Sciurba, M.D. is a Professor at the University of Pittsburgh School of Medicine, Director of the Emphysema/COPD research center, and director of the clinical pulmonary physiology laboratories and pulmonary rehabilitation program. He received his undergraduate degree in Biochemistry from the University of Illinois and attended medical school at the University of Chicago Pritzker School of Medicine. Dr. Sciurba's research has been inspired by real clinical problems facing his patients. He has co-authored over 200 manuscripts and has had continuous NIH funding for 20 years. Dr. Sciurba's current leadership positions include: His role as a Principle Investigator of the Network Management Core of the new NHLBI sponsored Pulmonary Trials Consortium (PTC) which manages the execution of pragmatic, "real world" studies in a variety of chronic pulmonary conditions; and his role as academic chair of the COPD Biomarker Qualification Committee (CBQC), a group that works with the FDA to address the need for new biomarkers to facilitate development of drugs and devices for chronic pulmonary conditions. He is also past chair of the American Thoracic Society Clinical Problems Program Committee.

SESSION SPEAKERS:

Suzanne Cloonan, PhD
Associate Professor in Respiratory Biochemistry
School of Medicine, Trinity College Dublin (Ireland)
Adjunct Professor of Biochemistry, Weill Cornell Medical College

Dr. Cloonan is an Associate Professor in Respiratory Biochemistry in the School of Medicine at Trinity College Dublin as well as an Adjunct Assistant Professor of Biochemistry in Medicine at Weill Cornell Medical College. Dr. Cloonan received her PhD in Biochemistry in 2010 from Trinity College Dublin Ireland. She carried out her Post-Doctoral training in the lab of Dr. Augustine MK Choi in The Division of Pulmonary and Critical Care Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston. In 2014, she became faculty at Weill Cornell Medicine having obtained funding from the National Institute of Health (K99/R00 award) and the American Lung Association to understand the role of mitochondrial dysfunction and iron metabolism in the development of Chronic Obstructive Pulmonary Disease (COPD). After obtaining Science Foundation Ireland Future Research Leaders Award, she relocated her lab to Trinity College Dublin as an Associate Professor in 2020. Her lab is focused on applying cutting edge techniques and concepts to aid in understanding the molecular mechanisms behind iron metabolism in normal and diseased lung; related to inflammation, alveolar epithelial cell biology, host-pathogen interactions in the lung microenvironment and subsequent systemic implications.

IMMUNOMETABOLISM CHANGES IN COPD PATIENTS

This presentation will cover the concept of nutritional immunity as well as metabolic changes in immune cells of the lung in COPD. Dr. Cloonan will give an up-to-date synopsis of the literature on how nutrient utilization and flux plays a role in immune cell dysfunction in the COPD lung. She will also review the current data from her lab on the role of iron metabolism in macrophage function in smoking and COPD.

Melanie Königshoff, MD, PhD, ATSF, FERS
Professor of Medicine
Division of Pulmonary, Allergy & Critical Care Medicine
Associate Chief of Research
University of Pittsburgh School of Medicine

Dr. Melanie Königshoff is a Professor of Medicine and Associate Chief of Research at the University of Pittsburgh School of Medicine. She received her medical degree and PhD degree at Justus-Liebig University, Germany. She underwent postdoctoral training at the University of Giessen Lung Center, Germany and completed her residency in the Department of Medicine at University Hospital Giessen. Dr. Königshoff's research focuses on deciphering mechanisms involved in lung repair and regeneration, with the aim to identify novel therapeutic targets relevant for age-related chronic lung diseases, such as idiopathic pulmonary fibrosis (IPF) and chronic obstructive pulmonary disease (COPD).

THE INTERPLAY OF METABOLISM AND REGENERATIVE SIGNALING PATHWAYS IN CHRONIC LUNG DISEASE

Chronic lung disease, such as chronic obstructive pulmonary disease (COPD), are diseases of aging and impaired regeneration. While once thought to be a quiescent organ, research findings over the last decades have revealed a remarkable regenerative capacity of the lung. Thus, emerging anti-aging and regenerative medicine approaches hold therapeutic promise to be able to reverse disease. Within this presentation the basic concepts of lung aging and regeneration will be summarized and the current knowledge on (impaired) lung stem cell function and regenerative signaling pathways involved in chronic lung disease will be discussed. The presentation will outline how aging mechanisms, such as cellular senescence or impaired mitochondrial metabolism, contribute to chronic lung disease and impact endogenous lung regeneration.

Prof. Gerard (Gerry) McElvaney
Professor of Medicine
Royal College of Surgeons in Ireland
Director of the Irish Centre for Genetic Lung Disease
RCSI - University of Medicine and Health Sciences
Dublin, Ireland

Prof. Gerry McElvaney (MB, FRCPI, FRCPC, DSc) is Professor of Medicine, Royal College of Surgeons in Ireland (RCSI) and the Director of the Irish Centre for Genetic Lung Disease. He has worked in the area of inflammatory lung disease over the past 30 years and has extensive experience in protease-anti-protease interactions in the lung and their effects on innate anti-microbial proteins. He has also significant experience in neutrophil biology and how inflammation affects neutrophil proteomics, metabolomics and degranulation pathways. He has published some of the seminal papers on neutrophil/monocyte activation in AATD/COPD/CF along with significant research into the role of protease/anti-proteases, oxidants/anti-oxidants and ER stress in lung disease. He has performed the two largest trials to date on the risk for COPD in mild (MZ) and moderate (SZ) AATD and was lead investigator on the two biggest trials to date of augmentation therapy in people with severe (ZZ) AATD. More recently, he has evaluated the inflammatory manifestations of SARS-CoV-2 infection and how these might be ameliorated.

AIRWAY NEUTROPHIL METABOLISM IMPACTS CYSTIC FIBROSIS BACTERIAL COLONIZATION

Cystic fibrosis (CF) pulmonary disease is characterized by chronic infection with Peudomonas aeruginosa and sustained neutrophil-dominated inflammation. Despite the advent of successful modulator therapy the lack of more specific anti-inflammatory therapies for people with CF (PWCF) remains a significant challenge. In this study we show that CF neutrophil immunmetabolism is altered in response to inflammation, independent of CFTR (cystic fibrosis transmembrane conductance regulator) modulation and is shifted towards increased aerobic glycolysis with increased production of IL-1β, whose processing in the lung is controlled by the NLRP3 (NOD-,LRR-, and pyrin domain containing protein 3) inflammasome. We further show that inhibition of the NLRP3 inflammasome in vivo via small molecule inhibition with MCC950 results in a significant reduction in IL-1β in the lung and improved clearance of Pseudomonas, thus identifying a new potential therapeutic approach to neutrophil dominated lung disease with both anti-inflammatory and anti-infective effects.

SESSION 4: UNLOCKING THE ROLE OF METABOLISM AND MITOCHONDRIA IN LUNG PARENCHYMAL DISEASE AND CANCER

SESSION CHAIRS:

Mauricio Rojas, MD

Scientific Director, Comprehensive Transplant Center Biorepository
Associate Vice-Chair for Research
Tenure Professor, Department of Internal Medicine
The Ohio State University

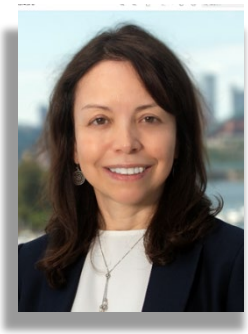
Dr. Mauricio Rojas is a physician-scientist committed to basic-to-translational research. For 30 years, his goal has been to understand the physiological mechanisms of the response of the lung to injury and how resilience is regulated at the cellular, tissue, and organ level. Dr. Rojas did his medical training at the National University of Colombia in Bogota. He did his postdoctoral training at Vanderbilt University and has been faculty at Emory University and the University of Pittsburgh. Dr. Rojas's research lab has been characterized as an international, multicultural, and inclusive environment, where developing a diverse future generation of biomedical scientists is an explicit goal. As an independent researcher, Dr. Rojas pioneered studies of the role of mesenchymal stem cells (MSCs) in repairing the lung after injury and the effects of age on the intrinsic reparative capacity of these progenitor cells. He recently participated in an international consortium demonstrating the positive impact of the systemic infusion of MSCs in patients with ALI/ARDS in a phase I-II clinical trial. In 2009, in collaboration with Dr. Mora, they published the first studies in animal models showing that senescence was a relevant factor in the pathogenesis of chronic lung diseases such as IPF and COPD and that fibroblasts and epithelial cells from fibrotic sites have a senescence phenotype. His continuing research aims to define how resilience can be maintained in the face of aging and stress and how reparative capacity can be enhanced. We are currently using multimodal technologies like single cell and spatial transcriptomics, proteomics, and metabolomics to generate longitudinal maps of cell senescence over the lifetime of human lungs. He has more than 170 peer-reviewed publications, and his research has been supported by NIH, the Department of Defense, private foundations, and partnerships with industry. He is currently the Scientific Director of the Comprehensive Transplant Center Biorepository and the Associate Vice-Chair for Research and Tenure Professor in the Department of Internal Medicine at the Ohio State University.

Nadia N. Hansel, MD, MPH

David Marine Professor of Medicine
Director, Pulmonary and Critical Care Medicine
Associate Dean of Research, Johns Hopkins Bayview
Chair, Bayview Scientific Advisory Board
The Johns Hopkins School of Medicine

Dr. Nadia Hansel is a Professor of Medicine and Director of the Division of Pulmonary and Critical Care Medicine at Johns Hopkins with joint appointments in the Division of Allergy and Clinical Immunology at the Johns Hopkins School of Medicine and the Department of Environmental Health Sciences at the Johns Hopkins Bloomberg School of Public Health. She assumed the position of the Associate Dean of Research for the Bayview Campus, Johns Hopkins University School of Medicine in July 2014. Dr. Hansel received her undergraduate degree magna cum laude in biology from Harvard College and her medical degree from Harvard Medical School. She completed her internal medicine residency at the University of Pennsylvania and came to Johns Hopkins University to complete her Pulmonary and Critical Care fellowship. She subsequently completed her Masters of Public Health Degree from the Johns Hopkins Bloomberg School of Public Health. Dr. Hansel's research is focused on environmental determinants of obstructive lung diseases. She is widely recognized as an international expert in defining the indoor air quality on asthma and chronic obstructive pulmonary disease (COPD) health. Her work is funded by the National Institutes of Health, Housing of Urban Development and the Environmental Protection Agency. Dr. Hansel is the Director of the Johns Hopkins Center for the Study of the Childhood Asthma in the Urban Environment (CCAUE) and the Director of the Johns Hopkins Center of Excellence on Environmental Health Disparities Research. Dr. Hansel serves on numerous editorial boards and professional organizations, is frequently an invited speaker nationally and internationally to present her research and has published over 150 peer reviewed publications. She received the David M. Levine Excellence in Mentoring Award in recognition of her dedication to training future physician scientists.

SESSION SPEAKERS:



Ana L. Mora, MD
Associate Director of Lung Research DHLRI
Professor, Department of Internal Medicine
Division of Pulmonary, Critical Care & Sleep Medicine
The Ohio State University

Dr. Mora is a Professor at the Division of Pulmonary, Critical Care and Sleep Medicine at the Ohio State University and Director for Pulmonary Research of the Davis Heart Lung Research Institute. She received her MD degree from Universidad Nacional de Colombia in Bogotá, Colombia. She did postdoctoral training at Vanderbilt University and moved in 2002 as independent investigator to Emory University. In 2010, she joined the Division of Pulmonary at the University of Pittsburgh, where she was member of the Vascular Medicine Institute and Director of Education of the Aging Institute. Dr. Mora is one of the pioneers of the study the molecular aspects of the aging lung and the pathogenesis of age-related lung diseases, such as IPF. Her studies have elucidated a critical role of mitochondrial homeostasis in the vulnerability to lung injury and activation of fibrotic responses. She has received awards by the American Association of Immunologists, the Pulmonary Fibrosis Foundation, and by the Helmholtz Zentrum München in Germany. She is elected chair of the ATS RCMB Assembly Program Committee, and member of the Editorial Board of the American Journal of Respiratory Cell and Molecular Biology. She has been an ad hoc reviewer of several NIH study sections and is permanent member of the Lung Injury Repair and Remodeling (LIRR) study section. Dr. Mora has received support for her research from ALA, AHA, and the NIH. Her work has been published in more than 100 peer review publications, several book chapters, and editorial comments.

MITOCHONDRIAL CHANGES IN IDIOPATHIC PULMONARY FIBROSIS

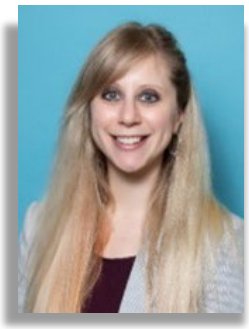
Idiopathic Pulmonary Fibrosis (IPF) is a lethal chronic age-related lung disease characterized by progressive scarring of the lung. Age-related perturbations are increasingly found in epithelial cells and fibroblasts from IPF lungs and are believed to play a critical role in the predisposition to lung injury, disrepair, and fibrosis. Our studies show that mitochondrial dysfunction and metabolic distress potentiate maladaptation to stress and susceptibility to lung fibrosis. Our lab is focused on the elucidation of mechanistic insights of the aging process of the lung and the mitochondrial and metabolic adaptations to aging, injury and repair that contributes to the pathogenesis of IPF with the goal to define potential therapeutic approaches that target aging processes and might be beneficial for halting the progression of the disease.

G.R. Scott Budinger, MD
Ernest S. Bazley Professor of Airway Diseases
Chief, Division of Pulmonary and Critical Care
Professor of Cell and Molecular Biology
Northwestern University Feinberg School of Medicine

Dr. G.R. Scott Budinger is a leading investigator in lung disease and is internationally recognized for his research to understand how aging biology affects the function of macrophages, resident immune cells in multiple tissues. His laboratory is particularly interested in how an age-related loss of function in macrophages prevents recovery in patients with viral pneumonia, including patients infected with SARS-CoV-2, the virus responsible for COVID-19. As Chief, Dr. Budinger seeks to apply the novel tools and molecular discoveries Feinberg scientists have made and continue to make to the care of patients with lung disease at Northwestern Medicine in a bench to bedside to bench approach that blurs historic distinctions between clinical and basic research. He has led a team that is combining advanced flow cytometry techniques with transcriptomic, epigenomic and proteomic approaches to better understand the complex intercellular interactions in the lung that drive the development of lung disease. The goal of this multidisciplinary and multi-specialty research program is to identify molecular pathways active in during disease that might be targeted in a personalized approach to therapy for chronic lung diseases. This work draws on the skills and expertise of the outstanding clinical and research faculty in the Division of Pulmonary and Critical Care Medicine and the larger FSM, NM and NU research communities.

DIVERSE METABOLIC SIGNALING IN MYELOID CELLS AS A DRIVER OF FIBROTIC LUNG DISEASE

Alveolar macrophages play important roles in maintaining lung homeostasis, responding to acute injury and participating in lung repair. We sought to determine the role of alveolar macrophages in the response to severe SARS-CoV-2 pneumonia in humans. As part of the Successful Clinical Response in Pneumonia Therapy SCRIPT systems biology center at Northwestern supported by the National Institute of Allergy and Infectious Disease of the NIH, we collected serial bronchoalveolar lavage samples from 600 patients with severe pneumonia, including 200 patients with severe SARS-CoV-2 pneumonia and analyzed them using multiple "omic" approaches. We developed a model of SARS-CoV-2 pathobiology that explains the unique clinical features observed in patients with COVID-19. We used this model to predict a novel therapy for SARS-CoV-2 pneumonia that shows promise in early studies.



Tullia C. Bruno, PhD
Assistant Professor, Department of Immunology
University of Pittsburgh School of Medicine
Faculty member, Tumor Microenvironment Center and Cancer Immunology and Immunotherapy Program
UPMC Hillman Cancer Center

Tullia C. Bruno, PhD, is an Assistant Professor in the Department of Immunology at the University of Pittsburgh and a faculty member in the Tumor Microenvironment Center and the Cancer Immunology and Immunotherapy Program at the UPMC Hillman Cancer Center. She obtained her Ph.D. in Immunology from Johns Hopkins in 2010 and completed her postdoctoral fellowship at the University of Colorado in 2015—both with a focus in tumor immunology. While Dr. Bruno's PhD training focused on inhibitory receptors on intratumoral T cells, she became interested in the role of B cells and tertiary lymphoid structures (TLS) in the tumor microenvironment (TME) during her postdoctoral fellowship and has built her independent research program around understanding intratumoral B cell and TLS function in multiple human cancers, in particular, lung head and neck, and ovarian cancer. Dr. Bruno's research lab has an overt focus on studying immunity within cancer patients, which makes her research highly translational with the potential for future clinical trials targeting B cells. Thus, Dr. Bruno's overall research objective is to develop a B cell-specific immunotherapy in the next five to ten years.

TUMOR IMMUNITY AND METABOLISM IN CANCER

Tertiary lymphoid structures (TLS) are lymphoid aggregates that often form locally in tissues with chronic infection, autoimmune disease, and cancer. As such, TLS correlate with favorable prognosis in patients with solid tumors, including non-small-cell lung cancer (NSCLC). Further, TLS have recently been associated with superior response to immune checkpoint blockade (ICB). B cells are predominantly located within TLS and correlate with improved survival and ICB response. Despite the therapeutic promise of B cells and TLS, they have not been investigated as immunotherapeutic targets. Moreover, a mechanistic understanding of TLS formation and function in cancer is lacking. Our studies in NSCLC include investigation of human cancer for unique factors that promote or inhibit TLS formation paired with a physiologically relevant, carcinogen induced murine model of lung cancer that spontaneously forms TLS. Specifically, we utilized multispectral imaging (Vectra Polaris) with spatial transcriptomics (Nanostring Digital Spatial Profiler) to interrogate TLS in NSCLC patients. Tumor-associated TLS have decreased TLS-initiating and maturation factors such as CXCL13, IL-21, CD40, and LT/LIGHT in comparison to normal lymphoid tissues. We also utilized these state-of-the-art platforms to uncover new pathways to improve TLS formation and B and T cell function. We paired these studies with our mouse model and other subcutaneous mouse models to test if TLS induction and maturation was increased with an oncolytic virus that targets CXCL13, IL-21, CD40 and LTR/LIGHT. We interrogated TLS formation over time with or without oncolytic virus treatment. B cell infiltration was increased, and tumor burden was decreased even in tolerogenic mouse models. These studies will increase our understanding of TLS formation for improved immunotherapies in NSCLC patients and will potentially provide therapeutic interventions that could be administered prior to cancer progression.

M. Naeem Islam, PhD
Associate Research Scientist, Lung Biology Lab
Department of Medicine
Division of Pulmonary, Allergy and Critical Care Medicine
Columbia University

Mohammad N. Islam, PhD, is an Associate Research Scientist in the Division of Pulmonary, Allergy, and Critical Care Medicine at the Columbia University, New York. Dr. Islam received his PhD from St. John's University in New York. Dr. Islam is interested in defining the fundamental mechanisms responsible for acute respiratory distress syndrome (ARDS) related to alveolar and organ injury. He is trained in live-lung optical imaging methods in mouse and human alveoli and microvessels for measurements of cell calcium, bioenergetics, mitochondrial mechanisms, and genetic approaches for protein expression and knockdown in intact animals. His research on bone marrow-derived stromal cells (BMSCs) showed mitochondrial transfer from BMSCs to alveolar epithelial cells, increasing alveolar ATP. His recent works aim to understand interactions between SARS-CoV2 and the alveolar epithelium in two genetic mouse models.

MITOCHONDRIA OF ALVEOLAR TYPE 2 CELLS DETERMINE SEVERITY OF THE LUNG'S INNATE IMMUNITY

Acute Lung Injury (ALI) due to inhaled pathogens causes high mortality. Underlying mechanisms are inadequately understood. Here, by optical imaging of live mouse lungs we show that a key mechanism is the viability of cytosolic Ca^{2+} buffering by the mitochondrial Ca^{2+} uniporter (MCU) in the lung's surfactant-secreting, alveolar type 2 cells (AT2). The buffering increased mitochondrial Ca^{2+} and induced surfactant secretion in wild-type mice, but not in mice with AT2-specific MCU knockout. In the knockout mice, ALI due to intranasal LPS instillation caused severe pulmonary edema and mortality, which were mitigated by surfactant replenishment prior to LPS instillation, indicating surfactant's protective effect against alveolar edema. In wild-type mice, intranasal LPS, or *Pseudomonas aeruginosa* decreased AT2 MCU. Loss of MCU abrogated buffering. The resulting mortality was reduced by spontaneous recovery of MCU expression, or by MCU replenishment. Enhancement of AT2 mitochondrial buffering, hence endogenous surfactant secretion, through MCU replenishment might be a novel therapy against ALI.

BANQUET DINNER

Thursday, September 8

Carnegie Science Center
One Allegheny Avenue
Pittsburgh, PA 15212

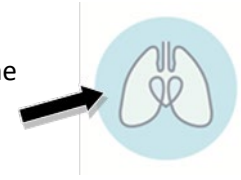
Adobe photostock image

Located in the heart of Pittsburgh's North Shore between *Acrisure Stadium* and *Rivers Casino*, the *Carnegie Science Center* is a family attraction close to downtown and sits along the Three Rivers Heritage Trail. The conference banquet dinner will be held in *PointView Hall*, a modern event space with a stunning view of the Pittsburgh skyline. After dinner, guests will have the opportunity to explore two floors of the museum's interactive exhibits.

Image from www.mollystrolleyspgh.com

Transportation to the Carnegie Science Center will be provided by **Molly's Trolleys of Pittsburgh**

Molly's Trolleys is a trolley transportation company with vehicles that are elegant, charming, immaculate and reminiscent of 1920's-style trolleys. The trolley's feature air conditioning and heat and offer panoramic window views of our city.



Please look for the distinctive red trolley with the Lung Conference Logo displayed in the window. Please wear your name when boarding from the University Club and throughout arrival at the venue for admittance. A member of our staff will be available and be happy to assist you.

The trolleys will pick up our banquet dinner guests on the Thackeray Street side of the University Club (parking lot side).

The first trolley will depart around **5:45pm** and subsequent trips will depart in approximate 10-15 minute intervals, with the last trolley departing at 6:15pm to transport guests to the dinner.

The trolleys will be available to begin returning passengers at approximately **8:45pm**.

Approximate departure times from the Carnegie Science Center: 8:45pm, 9:00pm, 9:10pm, and the last trolley departing around **9:15pm**.

For the convenience of our guests, the trolleys will return to the *Wyndham Hotel University Center*, with stops at the *Hilton Garden Inn* and *The Oaklander*, as needed.

BANQUET DINNER SPEAKER

Augustine M.K. Choi, MD

Stephen and Suzanne Weiss Dean, Weill Cornell Medicine
Provost for Medical Affairs, Cornell University
Weill Cornell Medicine

Dr. Augustine M.K. Choi is the Stephen and Suzanne Weiss Dean of Weill Cornell Medicine and Provost for Medical Affairs of Cornell University. An internationally renowned physician-scientist in the field of lung disease, Dr. Choi has focused his research on understanding how chronic and acute lung diseases develop in response to molecular, cellular and genetic triggers. He has published more than 350 peer-reviewed articles and is a member of the National Academy of Medicine, American Society of Clinical Investigation, and the Association of American Physicians. Among his many awards and honors are the 2011 Ho-Am Prize in Medicine, which is often referred to as the Korean Nobel Prize, and the 2015 J. Burns Amberson Lecture, which recognizes a career of major lifetime contributions to pulmonary research. He has a longstanding commitment to the training of postdoctoral fellows and physician-scientists in lung diseases.

Dr. Choi is also the founder of the **Pittsburgh International Lung Conference**, launched during his tenure as Division Chief (2000-2007) of Pulmonary, Allergy and Critical Care Medicine at the University of Pittsburgh.

SESSION 5: METABOLISM AS A DRIVER OF IMMUNE RESPONSES AND IN PULMONARY TRANSPLANT

SESSION CHAIRS:

Chadi A. Hage, MD
Professor of Medicine
Division of Pulmonary, Allergy, and Critical Care Medicine
University of Pittsburgh School of Medicine
Medical Director, Lung Transplant
University of Pittsburgh Medical Center

Chadi A. Hage, MD, is the Medical Director of Lung Transplant at UPMC. Dr. Hage specializes in lung transplant, ECMO, transplant critical care, and fungal infections. He is board certified in infectious diseases, pulmonary medicine, and critical care medicine by the American Board of Internal Medicine. Dr. Hage received his medical degree from the Lebanese University School of Medicine, followed by a residency in internal medicine and fellowships in pulmonary medicine, infectious diseases, and critical care medicine at Indiana University School of Medicine. His research interest is in fungal diagnostics, endemic mycoses, lung transplant outcomes and translational immunology.

Mark Snyder, MD
Assistant Professor of Medicine and Immunology
Member, Starzl Transplantation Institute
Co-director, Pitt Ex-vivo Research Core (PERC)
Division of Pulmonary, Allergy and Critical Care Medicine
University of Pittsburgh School of Medicine

After finishing his post-doctorate in transplant immunology at the Columbia Center for Translational Immunology, Dr. Snyder established his laboratory at the University Pittsburgh in 2018. Dr. Snyder's laboratory uses translational approaches to study the development and maintenance of human lung tissue resident memory T cells in both health and disease. Utilizing single cell RNA and T cell receptor (TCR) sequencing, Dr. Snyder's lab can track both donor and recipient T cell clones in the lungs of transplant recipients to study the molecular drivers of T cell migration, maturation, and activation in the human lung. Using ex-vivo lung perfusion of human lungs rejected for transplantation, Dr. Snyder's lab can test the impact of inhaled and systemic immune modulators on tissue resident immune populations. His long-term goal is to develop new therapeutics to promote helpful mucosal T cells and eradicate alloreactive or proinflammatory tissue resident memory T cells.

SESSION SPEAKERS:

Anuradha Ray, PhD
Lung Immunology Endowed Chair, Department of Medicine
Professor of Medicine and Immunology
Division of Pulmonary, Allergy & Critical Care Medicine
University of Pittsburgh School of Medicine

Dr. Anuradha Ray is a Professor of Medicine and Immunology and Endowed Chair of Lung Immunology in Medicine at the University of Pittsburgh School of Medicine. She received her Ph.D. from Calcutta University in India. She underwent postdoctoral training at Cornell University, Ithaca, NY and at Rockefeller University in New York. She was on the faculty at Rockefeller University and at Yale University between the years 1990 and 2001 before moving to the University of Pittsburgh. Dr. Ray's early research led to the first identification of NF-κB as a target for the anti-inflammatory actions of corticosteroids and the discovery of GATA-3 as the master regulator of Th2 cells which promote asthma and allergic diseases. In ongoing research, she and her colleagues are investigating immune dysfunction in severe asthma that unlike milder asthma is refractory to corticosteroid treatment. One novel finding in these studies is a dominant Type 1/IFN-γ response in CD4+ and CD8+ T cells that includes tissue resident memory (TRM) cells in the airways of a subset of severe asthma patients. In studies of immune homeostasis, her studies have implicated mitochondrial H2O2 in dendritic cells as a regulator of immune tolerance in the airways. Her research has been continuously funded by grants from the National Institutes of Health (NIH). She currently serves on the Advisory Council of the National Institute of Allergy and Infectious Diseases (NIAID).

MITOCHONDRIAL ROS FINE-TUNES LUNG DENDRITIC CELLS TO REGULATE ALLERGIC DISEASE

Many studies suggest a critical time window in early life for achieving immune tolerance to prevent development of allergic disease. While early introduction of allergen immunotherapy (AIT) for common food allergens such as peanuts has been shown to result in sustained desensitization to the allergen, such attempts are rare in the treatment of asthma due to safety concerns and lack of useful pre-clinical models. To address this limitation, we have developed a mouse model of airway tolerance to the allergen, house dust mite (HDM), commonly associated with allergic asthma, by exposing newborn mice repeatedly to a low-dose of HDM. Our earlier work on tolerance induced by inhaled allergen in adult mice and our ongoing work with young mice demonstrate an important role of mitochondrial H^2O^2 (mt H^2O^2), a reactive oxygen species (ROS), in tolerance establishment in the airways as tolerance fails in transgenic mice with mitochondrion-targeted overexpression of the H^2O^2-scavenging enzyme, catalase (MCAT mice). ROS is more commonly associated with oxidative stress. However, the beneficial effects of ROS, especially of H^2O^2, are increasingly being recognized although the underlying mechanisms are not well understood. Towards this end, our phenotypic and molecular assessment of DCs in WT vs MCAT mice subjected to the model of tolerance (WT Tol vs MCAT Tol) have provided novel insights. Low dose HDM-induced mt H^2O^2 constrains lung DC numbers that includes both cDC1s and cDC2s. scRNA-seq studies of cDCs from WT Tol and MCAT Tol mice show that mt H2O2 controls expression of genes associated with DC apoptosis, migration and activation. Our scRNA-seq data in conjunction with ongoing studies of conditional gene knockout mice will help link mt H^2O^2 with specific genes and biological pathways in the context of allergen-induced immune tolerance. Harnessing the potential of mt H^2O^2 in early life may reduce the incidence of allergic disease in later life.

Craig A. Byersdorfer, MD, PhD
Associate Professor, Department of Pediatrics
Division of Blood and Marrow Transplantation and Cellular Therapies
UPMC Children's Hospital of Pittsburgh
Associate Professor of Immunology
University of Pittsburgh School of Medicine

Dr. Byersdorfer is an Associate Professor in the Department of Pediatrics and holds a secondary appointment in the Department of Immunology at the University of Pittsburgh School of Medicine. He also serves as an attending physician in the Division of Blood and Marrow Transplantation and Cellular Therapies at UPMC Children's Hospital of Pittsburgh. He was named a Scholar by the American Society of Hematology (ASH) and received the Junior Scholar Award from the UPMC Hillman Cancer Center in 2017. His research focuses on understanding the metabolic pathways utilized by immune cells during pathogenic disorders such as graft-versus-host disease and in elucidating ways to reshape cellular metabolism to improve cancer-directed immunotherapies. He currently serves as a member on the ASH Scientific Committee on Transplantation Biology and Cellular Therapies.

IMMUNOMETABOLISM AS A DETERMINANT IN SUCCESS OR FAILURE OF BONE MARROW TRANSPLANT

Hematopoietic stem cell transplantation from allogeneic donors (alloHSCT) is a curative treatment for numerous hematologic disorders and can be used to induce tolerance following solid organ transplantation. However, the application of alloHSCT is often limited by graft-versus-host disease (GVHD), where T cells from the donor attack host tissues in the skin, liver, and gastrointestinal tract. New therapies to prevent GVHD, while still preserving immune reconstitution and beneficial immunity, are urgently needed. We have discovered that the cellular energy sensor AMP-activated protein kinase (AMPK) plays a fundamental role in alloreactive T cells during the development of GVHD. AMPK activity increased >15-fold early post-transplant in allogeneic T cells and transplantation of T cells lacking the kinase subunit of AMPK (and therefore AMPK signaling) exhibited decreased GVHD severity in multiple disease models. Importantly, a lack of AMPK signaling in T cells mitigated GVHD without compromising anti-leukemia responses or impairing lymphopenia-driven immune reconstitution. Mechanistically, absence of AMPK decreased both CD4+ and CD8+ effector T cell numbers as early as day 3 post-transplant, while simultaneously increasing regulatory T cell percentages. Metabolically, AMPK deficient T cells decreased oxygen consumption rates and were incapable of adopting alternative metabolic pathways following inhibition of the electron transport chain, revealing the significant metabolic inflexibility of these cells. In addition, AMPK KO T cells produced much less interferon-gamma upon re-stimulation, a finding that both supports their inability to induce severe GVHD and reflects a possible consequence of their compromised metabolic phenotype. Together, these results highlight a specific role for AMPK in effector T cells following alloHSCT and suggest AMPK inhibition as an innovative approach to mitigate GVHD while still preserving graft-versus-leukemia responses and maintaining robust immune reconstitution.

SESSION 6: MODULATIONS OF METABOLISM IN IMMUNITY AND INFECTION

SESSION CHAIRS:

Barbara Methé, PhD
Professor of Medicine
Director, Center for Medicine and the Microbiome
Division of Pulmonary, Allergy and Critical Care Medicine
University of Pittsburgh School of Medicine

Dr. Methé is a Professor in the Department of Medicine at the University of Pittsburgh and a Director of the University of Pittsburgh Center for Medicine and the Microbiome (CMM). She has extensive experience in microbial ecology, computational biology and the application of 'omics technologies to study whole microbial communities. She has led studies of microbial communities in diverse environments including the terrestrial subsurface and the deep subseafloor and was a leader of the NIH supported Human Microbiome Project (HMP). Among current projects, she is studying the role of the microbiome in HIV-associated COPD to identify novel biomarkers of lung disease and test new therapeutics. This work is also supporting the development of new laboratory and computational methods to generate, analyze and integrate multi-omics data from low microbiome biomass samples. She is also working on a project for improvement of personalized medicine by integrating microbiome and human genome data with medical electronic health records from individuals representing multiple health and disease phenotypes.

Prabir Ray, PhD
Lung Immunology Endowed Chair, Department of Medicine
Professor of Medicine and Immunology
Division of Pulmonary, Allergy & Critical Care Medicine
University of Pittsburgh School of Medicine

Dr. Prabir Ray is a Professor of Medicine and Immunology and Endowed Chair of Lung Immunology in Medicine at the University of Pittsburgh School of Medicine. He received his Ph.D. from Calcutta University in India. He underwent postdoctoral training at Cornell University and Memorial Sloan-Kettering Cancer Center. He pioneered the development of inducible cell-specific transgenic mice in the early years of his career at Yale University using which he demonstrated an important role of the growth factor KGF in protection from lung injury. Dr. Ray is interested in immunoregulatory mechanisms of lung inflammation as they relate to disease inception and resolution. A highlight of this investigation in the context of infection by respiratory syncytial virus (RSV) is breaching of immune tolerance by RSV infection in early life resulting in disabling of Tregs increasing the risk for asthma in later life. His recent studies have examined cellular and molecular processes that help resolve inflammation and acute lung injury (ALI) after bacterial pneumonia. This research first identified regulatory myeloid cells resembling myeloid derived suppressor cells (MDSCs) in the lung playing an important role in efferocytosis of apoptotic neutrophils during bacterial infection. His ongoing research is devoted to understanding innate immune dysfunction during bacterial pneumonia, a common cause of sepsis that can precipitate ARDS. Using scRNA-seq methods his group recently described a gene signature in peripheral blood monocytes that can discriminate between sepsis patients who develop ARDS vs those who do not. His research utilizes human samples and mouse models employing state-of-the-art techniques in immunology, molecular biology, and imaging in conjunction with advanced bioinformatic tools. His research has been continuously supported by grants from the National Institutes of Health (NIH).

Session Speakers:

Alice S. Prince, MD
John M. Driscoll Professor of Pediatrics
Chief, Division of Infectious Diseases
Columbia University Medical Center

Dr. Prince received her MD and post graduate training in Pediatrics and in Infectious Diseases at Columbia University in New York. Following post-doctoral fellowships in Microbiology and in ID at Columbia and Massachusetts General Hospital she returned to Columbia as an Assistant Professor, where she is now the John M. Driscoll Professor of Pediatrics and Chief of the Division of Infectious Diseases. Her laboratory has focused upon host-pathogen interactions in the lung, specifically addressing the consequences of CFTR dysfunction on the pathogenesis of P. aeruginosa infection in patients with cystic fibrosis. These studies identified specific airway metabolites as major substrates for bacterial proliferation and adaptation. The lab is now studying several health care associated pathogens using a combination of bacterial mutants and murine models to examine how host and bacterial metabolic activity shapes the airway microenvironment resulting in an immuno-tolerant host response.

METABOLIC RESPONSES TO KLEBSIELLA PNEUMONIAE DRIVE PERSISTENT INFECTION

ST258 *K. pneumoniae* are health care associated pathogens, often multiply antibiotic resistant, that are associated with pneumonia, blood stream and urinary tract infection worldwide. As pulmonary pathogens, especially in the setting of ventilator associated pneumonia or post Covid-19, they are difficult to eradicate and associated with persistent and often fatal pneumonia. Although the LPS expressed by these organisms does not differ significantly from that of other *K. pneumoniae* strains that cause fulminant sepsis, the immune response to the ST258 strains is very different. These K. pneumoniae strains elicit MDSCs, (Myeloid Derived Suppressor Cells) that are ANTI-inflammatory monocytes. Using a combination of metabolomic and scRNA-Seq data we demonstrate that ST258 strains activate fatty acid oxidation and glutaminolysis, metabolic pathways that skew the host immune response towards MDSCs and M2-like macrophages that enable persistent infection. In this setting of inflammation and oxidant stress, the ST258 K. pneumoniae respond by expressing the type 6 secretion system, which further contributes to their ability to survive in the lung. Immunometabolic responses to the ST258 Klebsiellae contribute substantially to their success as pathogens.

Sunny Shin, PhD
Associate Professor and Vice-Chair of Diversity and Inclusion
Department of Microbiology
University of Pennsylvania Perelman School of Medicine

Sunny Shin, Ph.D. is an Associate Professor and Vice-Chair of Diversity and Inclusion in the Department of Microbiology at the University of Pennsylvania Perelman School of Medicine. Dr. Shin received her B.S. degree from the Massachusetts Institute of Technology, her Ph.D. from Stanford University School of Medicine, and her postdoctoral training from Yale University School of Medicine. Her research is focused on understanding molecular and cellular mechanisms of innate immune defense against bacterial pathogens at mucosal surfaces and in turn, how pathogens subvert host immunity to cause disease. Dr. Shin has received several honors including the Burroughs-Wellcome Fund Investigator in the Pathogenesis of Infectious Diseases Award and the Penn Medicine Michael S. Brown New Investigator Award. She is highly committed to mentoring the next generation of scientists and promoting diversity, equity, and inclusion in academia and science, and she recently received the Penn Medicine Michael P. Nusbaum Graduate Student Mentoring Award. Dr. Shin is Chair of the Cellular and Molecular Biology Graduate Group's Microbiology, Virology, and Parasitology Program, directs and teaches in graduate and medical courses, and mentors postdoctoral fellows, graduate students, and undergraduate students. Dr. Shin is a standing member on the NIH Host Interactions with Bacterial Pathogens study section (2020-2024), serves on the editorial board of Infection and Immunity, and is the Division E: Immunology councilor for ASM.

METABOLIC DETERMINANTS IN THE PATHOGENESIS OF LEGIONELLA INFECTION

Alveolar macrophages are among the first immune cells that respond to inhaled pathogens, such as *Legionella pneumophila*, the causative agent of Legionnaires' disease. Upon entry into the lung, Legionella infects and replicates within alveolar macrophages. *Legionella*-infected macrophages initiate an IL-1-dependent inflammatory cytokine response by recruited monocytes and other cells that allows for successful control of infection in immunocompetent hosts. How IL-1 directs myeloid cells to produce inflammatory cytokines is unknown. We found that collaboration with the alveolar epithelium is critical for control, in that IL-1 induces the alveolar epithelium to produce granulocyte-macrophage colony-stimulating factor (GM-CSF). Intriguingly, GM-CSF signaling amplifies inflammatory cytokine production in recruited monocytes by enhancing TLR-induced glycolysis. Our findings reveal that alveolar macrophages engage alveolar epithelial signals to metabolically reprogram monocytes for antibacterial inflammation.

Jennifer M. Bomberger, PhD
Professor (tenured), Microbiology and Immunology
Geisel School of Medicine at Dartmouth
Adjunct Professor, Microbiology and Molecular Genetics
Clinical and Translational Science, University of Pittsburgh

Dr. Jennifer Bomberger started her independent research program at the University of Pittsburgh in 2011, after receiving her PhD in Cellular and Molecular Physiology at Michigan State University and completing her postdoctoral training at the Geisel School of Medicine at Dartmouth. In the fall of 2022, Dr. Bomberger moved her research program back to Dartmouth in the department of Microbiology and Immunology. Utilizing her training in epithelial cell biology and microbiology as a foundation, the Bomberger 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. Her long-term research goals are to elucidate the cellular and molecular mechanisms whereby cystic fibrosis pathogens and respiratory viruses synergize to impact lung disease and, ultimately, identify new therapeutic approaches to control chronic bacterial infections in people with CF.

PSEUDOMONAS MICROBIAL METABOLISM AND ADAPTATION IN THE CF MICROENVIRONMENT

Viral-bacterial co-infections are becoming increasingly recognized as a cause of morbidity and mortality in chronic lung disease, including cystic fibrosis (CF). Polymicrobial infections frequently occur in the CF respiratory tract, but the underlying mechanisms of how viral-bacterial interactions mediate pathogenesis remain poorly understood. In CF patients, clinical observations link the acquisition of chronic *Pseudomonas aeruginosa* infection with seasonal respiratory virus infections (notably, respiratory syncytial virus (RSV), rhinovirus and influenza A). Recently, we demonstrated that respiratory viral infection, and the subsequent innate immune antiviral interferon (IFN) response, promoted biofilm growth of *P. aeruginosa*, mediated through the disruption of nutritional immunity. We are investigating the underlying innate immune pathways involved in promoting *P. aeruginosa* biofilm growth, with a focus on immunometabolism shifts in the respiratory epithelium. We have identified interferon-regulated genes that promote *P. aeruginosa* biofilm biogenesis by altering the metabolic state of the epithelium and secreted metabolic products. Our research aims to improve our understanding of the mechanisms by which respiratory viral infections alter host immunity to support chronic bacterial infections, with the long-term goal of identifying new therapeutic targets to prevent chronic *P. aeruginosa* infections in the CF respiratory tract.

RAPID FIRE #2: EARLY CAREER ORAL PRESENTATIONS

MODERATORS:

Jessica Bon, MD, MS
Associate Professor of Medicine
Director, Pulmonary and Critical Care Medicine Fellowship Program
Division of Pulmonary, Allergy and Critical Care Medicine
University of Pittsburgh School of Medicine

Jessica Bon, MD, MS is an Associate Professor of Medicine in the Division of Pulmonary, Allergy and Critical Care Medicine at the University of Pittsburgh. Dr. Bon received her medical degree from Jefferson Medical College and completed her internal medicine residency training and a chief residency at Thomas Jefferson University Hospital in Philadelphia. She completed her pulmonary and critical care fellowship training at the University of Pittsburgh. Dr. Bon's area of clinical and research expertise is chronic obstructive pulmonary disease. Her research focuses on understanding mechanisms associated with phenotypic heterogeneity, clinical outcomes, and disease progression in COPD.

Anna Zemke, MD, PhD
Assistant Professor of Medicine
Division of Pulmonary, Allergy and Critical Care Medicine
University of Pittsburgh School of Medicine

Anna Zemke, MD, PhD is an Assistant Professor in Medicine at the University of Pittsburgh, PACCM Division. Her primary research focus is on the pathobiology of Gram-negative airway infections, such as those found in cystic fibrosis and chronically ventilated individuals. She has an ongoing observational cohort study in the LTACH population to better understand the biology and outcomes of tracheobronchitis in people with tracheostomies.

IMMUNE PATHWAYS IN SEVERE ASTHMA

Marc C. Gauthier, MD

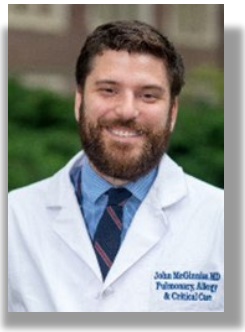
University of Pittsburgh School of Medicine

Dr. Gauthier is an Assistant Professor of Medicine at the University of Pittsburgh. He received his M.D. from Vanderbilt University in 2009 and completed his Internal Medicine residency and Pulmonary and Critical Care fellowships at the University of Pittsburgh. During fellowship he began working with his mentors Dr. Anuradha Ray and Dr. Sally Wenzel studying severe asthma. Dr. Gauthier's research focuses on the role of Type 1 inflammation in asthma, particularly how this inflammatory pathway interacts with other immune mechanisms in asthma and contributes to disease severity and corticosteroid resistance.

METABOLISM AND THE LUNG MICROBIOME AFTER LUNG TRANSPLANTATION

John E. McGinniss, MD

University of Pennsylvania



John McGinniss is an Assistant Professor at the University of Pennsylvania and is interested in host-microbiome interactions in the lung. He received his MD at Rutgers Robert Wood Johnson Medical School, completed medicine residency and chief residency at Yale, and then a pulmonary and critical care fellowship at Penn. He has been mentored by Ron Collman, MD, Rick Bushman, PhD, and Jason Christie, MD, MSCE and developed an interest and expertise in using translational and computational methods to understand the contribution of the respiratory tract microbiome and host responses in lung transplantation complications. His current work is in understanding metabolism alterations at the host-microbiome interface in the lung.

MARESIN 1/LGR6 AXIS IN THE RESOLUTION OF RESPIRATORY SYNCYTIAL VIRUS- INDUCED INFLAMMATION

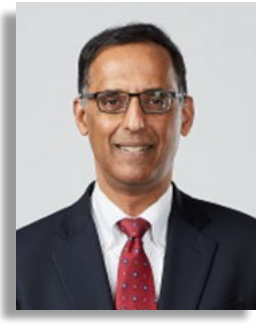
Nandini Krishnamoorthy, PhD

Brigham and Women's Hospital, Harvard Medical School

Dr. Krishnamoorthy obtained her PhD in immunology at the University of Pittsburgh with Dr Prabir Ray and her thesis research focused on dissecting the role of c-kit on dendritic cells in T cell differentiation. She moved to Brigham and Women's Hospital Boston to pursue her post-doctoral fellowship with Dr. Bruce Levy towards understanding the role of specialized pro-resolving mediators in mitigation allergic inflammation and viral infections. The overarching theme of Nandini's research has been the identification of pathways that bridge innate and adaptive immune systems. She is a NIH-funded junior faculty hoping to expand our understanding of resolution of lung inflammation and specifically dissecting mechanism involved in regulatory T cells dysfunction during chronic inflammation.

CHANGING PATTERNS OF PUBLICATIONS AND ITS IMPACT ON ACADEMIC SUCCESS

PANELISTS:



Rama Mallampalli, MD

S. Robert Davis Chair of Medicine
Professor and Chair, Department of Internal Medicine
The Ohio State University Wexner Medical Center

Dr. Rama Mallampalli, is chair for the Department of Internal Medicine and serves as director of OSU's Medical Scientist Training Program. A successful physician-scientist with entrepreneurial experience and numerous leadership roles in academia, Mallampalli was recruited to OSU from the University of Pittsburgh, where he served for nine years in a variety of positions including professor and chief of the Division of Pulmonary, Allergy and Critical Care Medicine (PACCM), inaugural director of the Acute Lung Injury (ALI) of Excellence and vice chair for research in the Department of Medicine. Dr. Mallampalli built his career treating patients with severe pneumonia and acute respiratory distress syndrome (ARDS) – having run an internationally renowned research program in acute lung injury and publishing several high impact articles in top tier journals. Dr. Mallampalli is the principal investigator on several research grants, including serving as PI on 3 NIH R01 awards and a NHLBI P01 on ARDS. Mallampalli is cofounder of a start-up company Koutif Therapeutics, LLC, successfully completing investigational studies for the novel therapy with the goal of treating inflammatory bowel disease, severe pneumonia and rheumatoid arthritis. He is recipient of the American Thoracic Society Recognition Award for Scientific Accomplishment and the Harrington Scholar-Innovator Award. He is a member of the American Society of Clinical Investigation, the Association of American Physicians, and as a permanent member of the National Heart, Lung and Blood Institute Program Project Review Committee.

Lorraine B. Ware, MD

Ralph and Lulu Owen Professor of Medicine
Director, Vanderbilt Medical Scholars Program
Vanderbilt University School of Medicine

Dr. Lorraine Ware is the Ralph and Lulu Owen Professor of Medicine and Professor of Pathology, Microbiology and Immunology at Vanderbilt University School of Medicine. Her research has used a comprehensive bench-to-bedside approach to investigate the pathogenesis of ARDS and sepsis-related organ dysfunction with the goal of developing new therapies. Major research contributions have focused on mechanisms of injury to the lung epithelium in ARDS including studies of alveolar epithelial fluid transport and fibrin deposition in the injured alveolus. Dr. Ware's group also studies the role of oxidized cell-free hemoglobin in the pathogenesis of ARDS and acute kidney injury in sepsis and critical illness. Dr. Ware is a fellow of the American Association for the Advancement of Science, a member of the Association of American Physicians and a member and past President of the American Society for Clinical Investigation.

Corinne Williams, PhD

Senior Science Editor
The Journal of Clinical Investigation | JCI Insight

Corinne Williams, PhD is the Senior Science Editor for the Journal of Clinical Investigation (JCI) and JCI Insight. She joined the editorial staff of the JCI in 2013 and has been involved with JCI Insight since the journal launched in 2016. She earned her PhD in molecular, cellular, and developmental biology from the University of California at Santa Barbara and completed postdoctoral training at the University of North Carolina at Chapel Hill.

SESSION 7: METABOLIC AND PHYSIOLOGIC DETERMINANTS OF COVID PATHOGENESIS

SESSION CHAIRS:

Georgios Kitsios, MD, PhD
Assistant Professor of Medicine
Director, American Board of Internal Medicine (ABIM) Research Pathway
Internal Medicine Residency Program, UPMC
Division of Pulmonary, Allergy and Critical Care Medicine
University of Pittsburgh School of Medicine

Dr. Georgios Kitsios is an Assistant Professor of Medicine in the Division of Pulmonary, Allergy and Critical Care Medicine at the University of Pittsburgh, and the Director of the ABIM Research Pathway of the Internal Medicine Residency Program at UPMC. Dr. Kitsios is a physician-scientist with clinical interest in critical care and research focus on the impact of the human microbiome in critical illness, the use of novel molecular technologies for diagnosis of infections in the ICU, and the study of clinical and biological heterogeneity of acute respiratory failure.

John F. McDyer, MD
Professor of Medicine
Director, Lung Transplantation Translational Research Program
Division of Pulmonary, Allergy & Critical Care Medicine
University of Pittsburgh School of Medicine

Dr. McDyer is a Professor of Medicine and is the Director of the newly launched Lung Transplantation Research Program in the Division of Pulmonary, Allergy, and Critical Care Medicine at the University of Pittsburgh. He has extensive experience as both a transplant pulmonologist and basic immunologist who focuses on mechanisms of Cytomegalovirus (CMV)-specific lung mucosal/systemic immunity and viral control, and allograft rejection/tolerance in lung transplantation. Dr. McDyer has directed the establishment of an extensive lung transplant tissue biorepository/registry (BREATHE-LT) of over 500 patients and 12,000 samples of BAL fluid/cells, plasma/PBMC, bronchial brushes, along with a clinical research database for phenotyping lung transplant recipients and assessing outcomes for translational studies.

Session Speakers:

Charles S. Dela Cruz, MD, PhD
Associate Professor
Vice Chief, Basic and Translational Research
Section of Pulmonary, Critical Care and Sleep Medicine
Department of Internal Medicine and Department of Microbial Pathogenesis
Director, Center of Pulmonary Infection Research and Treatment (CPIRT)
Director, Physician Scientist Training Program (PSTP)
Yale University

Dr. Charles S. Dela Cruz holds dual appointments as associate professor at Yale University's School of Medicine in the departments of internal medicine (pulmonary, critical care, and sleep medicine) and microbial pathogenesis. He is vice chief of basic and translational research and founding director for the Center for Pulmonary Infection Research and Treatment (CPIRT). He directs the physician scientist training program in the department of internal medicine. He completed his education through an MD/PhD program at the and University of Toronto and Yale School of Medicine. He received clinical training at Yale in internal medicine, with a specialization in pulmonary and critical care medicine. His laboratory studies the role of respiratory viral (including SARS-CoV2) and bacterial infection in the pathogenesis of acute and chronic lung diseases such as pneumonia, ARDS, COPD, and fibrosis. Using cell-based approaches, animal modeling and human translational studies, his work focuses on the underlying molecular and cellular mechanisms that help explain how lung infections contribute to the unresolved inflammation, persistent injury, and dysregulated tissue repair in the lung. His group has been pursuing basic, translational, and clinical research related to COVID-19, having established the importance of host responses to SARS-CoV-2 on immune phenotypes and multi-omic signatures, eicosanoid mediators, and immune dysfunctions in disease severity and in its treatment.

IMMUNO-METABOLOMES AND IMMUNO-LIPIDOMES IN COVID-19

The COVID-19 pandemic has led to an unprecedented impact on human health resulting in significant morbidity and mortality in patients with viral pneumonia caused by SARS-CoV-2. Risk factors associated with severe disease and mortality include advanced age, hypertension, diabetes, and obesity. Understanding of how these comorbidities impact SARS-CoV-2's effects on host molecular immune metabolism pathways is important for the discovery of early biomarkers of outcomes of COVID-19 and identification of novel therapeutic targets. The loss of specific regulatory metabolic and lipid mediators, including sex specific responses, are associated pro-inflammatory and immune cytokines and severity of disease. The talk will discuss current data and insights on what is known about the regulatory immune metabolomic and lipidomic pathways in COVID-19.

Peter J. Mullen, PhD
Assistant Professor of Molecular Microbiology and Immunology
Assistant Professor of Gerontology
Keck School of Medicine, Leonard Davis School of Gerontology
University of Southern California

Dr. Peter Mullen is an Assistant Professor at the Keck School of Medicine at the University of Southern California. He earned his Ph.D. from the University of Basel, Switzerland and carried out postdoctoral studies in the lab of Dr. Heather Christofk at the University of California, Los Angeles. He has spent over 10 years studying the regulation and role of metabolism in normal and tumor tissues, and respiratory virus infections. The overall goal of his recently established lab is to understand how whole-body metabolism alters respiratory virus replication and immune cell function.

METABOLIC VULNERABILITIES IN COVID-19

Viruses, such as SARS-CoV-2, hijack host cell metabolism to acquire the building blocks required for replication, and understanding how viruses rewire metabolism may uncover new antiviral strategies. Here, I will show that SARS-CoV-2 and adenovirus increase anabolism by activating mTORC1, and that targeting mTORC1 with inhibitors and nutrient restriction can reduce viral replication. These results suggest that targeting mTORC1 may be a feasible treatment strategy against COVID-19 and other viral infections.

SESSION 8: TARGETING METABOLISM FOR NOVEL THERAPIES

SESSION CHAIRS:

Faraaz Ali Shah, MD, MPH
Assistant Professor of Medicine and Clinical and Translational Science
Division of Pulmonary, Allergy and Critical Care Medicine
University of Pittsburgh School of Medicine

Faraaz Ali Shah, MD, MPH, is an Assistant Professor of Medicine and Clinical and Translational Science in the Division of Pulmonary, Allergy, and Critical Care Medicine. Faraaz is a translational researcher with research interests in sepsis and acute respiratory distress syndrome and with experience with mouse models of critical illness and with clinical trials in critically ill patients. His current research projects are focused on the intersection between precision medicine, nutrition support in sepsis, and long-term outcomes after critical illness.

Alison Morris, MD, MS
Professor of Medicine, Immunology, and Clinical and Translational Research
Division Chief, Pulmonary, Allergy and Critical Care Medicine
Director, Center for Medicine and the Microbiome
UPMC Chair in Translational Pulmonary and Critical Care Medicine
University of Pittsburgh School of Medicine

Alison Morris, MD, MS is a UPMC Chair in Translational Pulmonary and Critical Care Medicine and Professor of Medicine, Immunology, and Clinical and Translational Science in the Division of Pulmonary, Allergy, and Critical Care Medicine at the University of Pittsburgh. Se is also the founder and director of the University of Pittsburgh Center for Medicine and the Microbiome. She attended medical school at Duke University followed by residency and fellowship at the University of California, San Francisco. She moved to the University of Pittsburgh from 2000 to 2003, joined the faculty at University of Southern California from 2003-2006, then returned to Pittsburgh in 2006. Dr. Morris' research interests focus on the pulmonary complications of HIV infections and on the lung microbiome; however, she has recently begun work on COVID-19 pathogenesis and outcomes. She has established the University of Pittsburgh COVID-19 biorepository, is on the Steering Committee and site PI for the Healthcare Worker Exposure Response and Outcomes of Hydroxychloroquine Trial (HERO HCQ) and has worked on the ACTIV-4 anticoagulation studies. She is one of the founding physicians and clinical leaders of the UPMC Post-COVID Recovery Clinic.

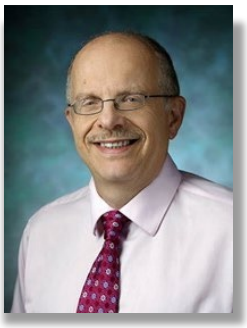
SESSION SPEAKERS:

Matthew R. Rosengart, MD, MPH
Watson Family Chair in Surgery
Professor of Surgery
Critical Care Medicine and Clinical and Translational Science
Vice Chair of Academic Training
Director, University of Pittsburgh Surgical Critical Care Fellowship Program
Director, University of Pittsburgh Department of Surgery
Surgical Outcomes Research Center

Matthew Randall Rosengart, MD, MPH is the Watson Family Chair in Surgery, Professor of Surgery, Critical Care Medicine and Clinical and Translational Science; Vice Chair of Academic Training; Director, University of Pittsburgh Surgical Critical Care Fellowship Program; Director, University of Pittsburgh Department of Surgery, Surgical Outcomes Research Center. He has a long-standing record of examining the systemic response to injury and infection, with particular expertise in phagocyte biology, calcium signaling, autophagy and mitochondrial function, and circadian biology, using clinically relevant models of sepsis and trauma. His collective training in the clinical, biological, and epidemiological sciences enables him to conduct translational studies, particularly those of a T1 nature, that have contributed to advancing our understanding of the cellular and molecular biology of these inflammatory states.

UNDERSTANDING METABOLIC CHANGES IN PATIENTS WITH SEPSIS

Eukaryotic life depends upon ATP and calcium (Ca^{2+}), and the intimacy of this relationship is perhaps best manifested in the mitochondrion. Thus, Ca^{2+} signaling is inherently sensitive to the available cellular free energy (i.e., ATP),[19] and mitochondrial Ca^{2+} homeostasis is intimately linked to many vital cellular processes including the bioenergetics and Ca^{2+} signals that support a phenotype. During sepsis and other shock states, mitochondrial dysfunction occurs that is characterized by a loss in mitochondrial membrane potential ($\Delta\Psi$), the elaboration of toxic reactive oxidant intermediates (ROS), and if progressive, opening of the mitochondrial permeability transition pore (MPTP), release of cytochrome C and apoptosis.[25-30] A concomitant failure of Ca^{2+} homeostatic mechanisms leads to a flood of potentially toxic levels of Ca^{2+} within the cytosol and mitochondrial matrix. These insults are of sufficient magnitude to challenge any cell's adaptive mechanisms and threaten survival. But in the context of evolution, they may also serve as sufficient pressure to select for those cells uniquely able to adapt and restore Ca^{2+} homeostasis. For the cells that survive, these changes may be long-lasting, insofar as evolution selects them to protect against any future threat of overwhelming Ca^{2+} overload. But in the context of the intimate relationship between Ca^{2+} and mitochondria, such changes may also perturb the capacity of a cell to maintain its phenotype; for a multicellular organism this may be poorly tolerated over time. Using murine models of pneumonia and intraabdominal sepsis others and we have elucidated the Ca^{2+}-dependent mechanisms regulating adaptive alterations in mitochondrial dynamics, including fission, fusion, mitophagy and the ramifications of these changes on oxidative metabolism. Furthermore, we will discuss the observation that sepsis imparts durable alterations to mitochondrial structure and function, and consequently the mitochondrial Ca^{2+} homeostasis necessary for metabolism and fundamental to support the phenotype of the cell.



Vsevolod Y. Polotsky, MD, PhD
Professor of Medicine
Director, Sleep Research
Division of Pulmonary and Critical Care Medicine
Department of Medicine
The Johns Hopkins University School of Medicine

Dr. Vsevolod (Seva) Polotsky is a Professor of Medicine and the Director of Sleep Research at the Johns Hopkins University School of Medicine. I received training in molecular biology and biochemistry at the NIH and Yale University. I have also been trained in pulmonary and sleep medicine and have a broad background in animal models and molecular aspects of OSA. My career has been dedicated to extensive studies of the pathogenesis of sleep disordered breathing. We developed a mouse model of intermittent hypoxia mimicking the oxyhemoglobin profile in human OSA. Using this model, we were able to demonstrate that intermittent hypoxia leads to hyperglycemia, dyslipidemia, atherosclerosis and fatty liver and uncovered mechanisms involved, including the carotid body driven activation of the sympathetic nervous system. My overarching career goal is to develop novel therapies for sleep disordered breathing and associated co-morbidities. My current research interests are (1) gene therapy of sleep disordered breathing, (2) the role of leptin in respiratory and cardiovascular physiology; (3) targeting carotid bodies to develop novel therapies of cardiovascular disease; (4) novel treatment of opioid induced respiratory depression. I have trained many fellows and students from many different countries, who since embarked on independent careers. My research received generous support from the National Institutes of Health, American Heart Association. I served as the Chair of the Sleep and Respiratory Neurobiology Assembly of the American Thoracic Society. I am a member of the Editorial Board of several journals including Journal of Applied Physiology, Frontiers in Sleep Medicine, American Journal of Respiratory and Critical Care Medicine, and the European Respiratory Journal.

THE INTERPLAY OF METABOLISM AND SLEEP PHYSIOLOGY

Intermittent hypoxia (IH) is a hallmark manifestation of Obstructive Sleep Apnea (OSA), recurrent obstruction of the upper airway during sleep, which is particularly common in obesity. IH of OSA has been implicated in several metabolic abnormalities, including fasting hyperglycemia, glucose intolerance, insulin resistance, dyslipidemia and fatty liver. In a mouse model IH induced fasting hyperglycemia, glucose intolerance and insulin resistance. Intermittent Hypoxia impairs glucose metabolism and insulin sensitivity in awake human volunteers. The treatment of choice for OSA is continuous positive airway pressure (CPAP). CPAP withdrawal in patients with severe OSA leads to hyperglycemia during sleep. Eight hour of CPAP treatment/night for 2 weeks improved glucose tolerance and insulin resistance in prediabetic patients with OSA. However, a majority of studies in pre-diabetic and diabetic patients with OSA did not show a significant effect of CPAP due to poor adherence to treatment. Animal studies demonstrated that the carotid body chemoreflex and increased sympathetic nervous system output play a key role in IH-induced hyperglycemia. IH causes dyslipidemia selectively increasing fasting free fatty acids and postprandial triglycerides in rodents and men, but CPAP trials failed to show resolution of dyslipidemia. Similarly, IH has been shown to induce hepatic steatosis and liver fibrosis in animal models and is associated with the severity of IH in OSA, but OSA treatment did not show reversal of hepatic abnormalities. In conclusion, experimental evidence implicated IH of OSA in dysmetabolism, but clinical studies did not conclusively demonstrate significant metabolic benefits of IH/OSA treatment.