Pulmonary Center Newsletter:

June—August 2021

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Welcome to the Newsletter!

We made it through the summer!!! In these days, I think it’s important to be thankful for everything we’ve accomplished, and WOW have we accomplished a lot this summer! We are happy to announce that our Pulmonary Center survived the heat, rain, hurricane, Delta emergence, and rising Covid numbers. As always, our remarkable Trainees continue to astonish us with their accomplishments, receiving awards, publishing papers, and receiving exciting Grants! Our faculty continue with research, training, and have produced an astounding number of publications this past quarter. Lab and Administrative staff, still effectively communicate and support projects and keep the Center running as a well-oiled machine. Only together were we able to accomplish all these wonderful successes, so thank you for helping to keep this Center running!

I hope you Enjoy!

Lindsey Stein
Administrative Assistant
Pulmonary Center
New Faces

Daniel Peterson
Research Data Analyst
Walkey Group

David Boamah
Temporary Research Assistant
Maglione Group

Kara Farquharson
Microbiology/PIBS student
Bosmann Group

Melissa Pesta
Research Technician
Bosmann Group

Kayleigh Berthiaume
MS Student
A. Wilson Group

Carly Merritt
MD/PhD Student
A. Wilson Group

Danielle Zimmerman
Lab Manager
A. Wilson Group
Welcome!

New First Year Fellows

Aaron Dobie
Lauren Kearney
Jennifer Maccarone
Brandon Pang
Jeffrey Sellman
Jingzhou Zhang

Allergy:

Christopher Chu
Baby Updates

Jessica Gereige's little boy

Elliot

getting so big!
2021 Summer Events

Mary Williams Lecture
July 7, 2021

Nicholas Heaton, PhD

Duke University School of Medicine
Assistant Professor of Molecular Genetics and Microbiology
Member of the Duke Cancer Institute

Sue Kim Hanson Lecture
September 10, 2021

Kate A. Fitzgerald PhD, MRIA

University of Massachusetts Medical School
Professor of Medicine, Vice Chair of Research, Department of Medicine
Director, Program in Innate Immunity
Division of Infectious Diseases and Immunology
Jerry Brody Professorship

We are so pleased to announce that in August of 2021 we learned that the Jerome S. Brody, MD, Professor of Pulmonary Medicine has been endowed! The professorship will honor in perpetuity Dr. Jerry Brody, our former Director. The installation of the first Brody Professor will come in September (to be highlighted in our winter newsletter), but now we celebrate the establishment of this endowment. For 23 years, Jerry’s leadership and vision of multidisciplinary biological research in pulmonary medicine drove our growth and achievement, while he also served as a valued mentor to faculty, fellows, and students. Jerry established foundations for our current knowledge about lung cell and molecular biology, and he made seminal contributions relating to cigarette smoke-induced lung diseases including lung cancer and COPD. He helped establish the American Journal of Respiratory Cell and Molecular Biology, the ATS’s red journal. He began our T32-funded training program in 1975, now funded through fifty years based on the principles of research training that he initially outlined. The professorship has been endowed thanks to commitments (donations and pledges) from the Department of Medicine, the friends and family of Dr. Brody, and the members and supporters of the Pulmonary Center, including the following:

Anonymous
Ansell, Jack, M.D. and Ansell, Beth
Babayan, Richard K., M.D. and Nersessian, Sonya, Esq.
Barkin, Peter, M.D.
Baron, Michael, M.D. and Baron, Sonya, Esq.
Bosch, Nicholas, M.D. and Modzelewski, Katherine
Bosmann, Markus, M.D.
Brody, Alan J.
Brody, Karen L.
Brody, Lisa R., M.D. and Ernsberger, Daniel L.
Brody, Marion L., and Ziegler, Donald
Brody, Michael and Brody, Anne
Carter, Robert
Center, David, M.D. and Rabbett, Patricia
Chen, Felicia, M.D.
Chmielinski, Kasia
Chobanian, Aram V., M.D.
Clark, John and Clark, Mia
d’Avenas, Anne, M.D. and Brody, Jerome, M.D.
Dagneau, Lucy and Dagneau, Zack
Desai, Tushar, M.D.
Dickey, Burton, M.D. and Dickey, Yean
Doerschuk, Claire M., M.D.
Evans, John
Evans Medical Foundation, Inc.
Fechheimer, Jean, M.D. and Schur, Peter, M.D.
Fine, Alan, M.D. and Rosenberg, Carol, M.D.
Fox, Pamel
Fredberg, Jeffrey, Ph.D. and Fredberg, Ellen
Gaynor, Robert and Gaynor, Lynne
Glassroth, Jeffrey, M.D. and Glassroth, Carol
Glenn, Vicki Jean
Goodenberger, Daniel, M.D.
Green, David, M.D.
Gruenberg, Lisa, M.D. and Carmichael, Martin
Hammond, Terese, M.D.
Hillman, Aline and Hillman, Scott
Hollingsworth, Helen, M.D. and Reed, John
Hunt, Christine
Jin, Yang, M.D.
Jones, Matthew Robert, Ph.D.
Joyce-Brady. Martin, M.D. and Joyce-Brady, Jean
Kagan, Herbert, Ph.D. and Kagan, Elinore
Kathuria, Hasmeena, M.D. and Singh, Karan
Kirchgasler, Christopher and Kirchgasler, Kathryn
Kotton, Darrell, M.D. and Kotton, Camille, M.D.
Lee, Eun-Hyung, M.D.
Masuyama, Junichi
Mizgerd, Joseph B., M.D. and Mizgerd, Ann M.D.
Mizgerd, Joseph P., Sc.D. and Mizgerd, Louise Mogayzel, Peter and Mogayzel, Cyndra
Najarian, Carolann S., M.D. and Najarian, George K.
O’Connor, George, M.D. and O’Connell, Rosemary
Powell, Charles, M.D.
Quinton, Lee J., Ph.D. and Quinton, Maria Ravid, Katya, Ph.D. and Ravid, Shmuel, M.D., M.P.H.
Reardon, Christine, M.D. and Reardon, Michael Rindler, Bruce Harvey
Roberts, Janis
Rounds, Sharon, M.D.
Salant, David J., M.D. and Salant, Anne
Sales, Leila
Samet, Jeffrey, M.D. and Marram, Michele Schwartz, David, M.D., M.P.H.
Senior, Robert, M.D.
Smith, Lewis J., M.D.
Spira, Avrum, M.D. and Pruyn, Susan
Steiling, Katrina Ann, M.D.
Swartz, Harold and Flood, Ann
Theodore, Arthur, M.D. and Theodore, Dawn
Traber, Katrina, M.D., Ph.D.
Weintraub, Leah
Wilson, Andrew, M.D.
Antibodies Produced in the Lung Can Prevent Respiratory Infections from Becoming Severe

Wednesday, June 2nd, 2021

Only a small subset of people who get a lung infection go on to become very sick yet who will become severely ill or why is unclear. This is now widely recognized in the context of COVID-19, where most people have mild or no illness while others with the same infection become extremely sick or even die.

Researchers now have discovered that after recovering from a respiratory infection, new cells get deposited in lung tissue, persist there and then become antibody secreting cells very quickly if the lungs later get re-infected by something similar.

“It is increasingly clear that our lungs contain their own specialized immune system, different from the immune system throughout the rest of the body,” explained corresponding author Joseph Mizgerd, ScD, professor of medicine, microbiology and biochemistry.

Mizgerd and his team studied a combination of infections in experimental models and analyses of cells collected from human lungs. “We found lungs that had recovered from infections had new cells that were not there before infection, capable of quickly producing antibodies when stimulated. We showed that antibodies in the lungs helped fight microbes and removing the cells making these antibodies compromised lung defense against respiratory pathogens,” Mizgerd said.

According to the researchers, differences in lung-specific antibodies and antibody-secreting cells may be one of the important factors determining who will become very ill or instead experience mild or even no symptoms when infected by a respiratory pathogen. “With a better understanding of the components of lung immunity that prevent severe infections, we will be able to identify who is prone to severe disease when infected,” he added.

Mizgerd believes that immunity that is lung-localized differs from more conventional types of immunity in that it tends to prevent severe disease instead of preventing infection altogether and it tends to be effective against a wider range of microbes instead of against only one single virus or bacteria. “Leveraging this knowledge may provide opportunities to develop novel types of vaccines that prevent severe disease caused by a broader spectrum of microbes, such as for all coronaviruses or all influenza viruses.”

These findings appear online in the Journal of Clinical Investigation.

This work was supported by funding from National Institutes of Health grants including: R35 HL135756, R01 AI115053, R33 HL137081, and F31 HL142199.
BUSM Awarded $4.1M to Support the Next Generation of Trail-blazers in Multidisciplinary Lung Science | School of Medicine

Thursday, July 1st, 2021

BUSM’s longest NIH-funded research training program, “Biology of the Lung: A Multi-Disciplinary Program,” has been awarded a five-year, T32 grant to provide multidisciplinary training and exposure to collaborative lung biology in three scientific areas that are special strengths at Boston University: Development and Regenerative Medicine; Immunology and Infection; and Biomedical Data Sciences.

This renewal means that the NIH has continuously funded this program for 50 years. The award provides federal support for BU faculty members to mentor research trainees in lung biology and pulmonary sciences, as well as in professional skills like grant writing, science communication and career development.

This $4.1 million award from the NIH’s National Heart, Lung and Blood Institute will be led by Co-Principal Investigators Joseph Mizgerd, ScD, professor of medicine, microbiology and biochemistry, and Darrell Kotton, MD, the David C. Seldin Professor of Medicine. During each year of the grant, six pre-doctoral trainees who are PhD or MD/PhD students and six post-doctoral trainees who are MD, PhD, or MD/PhD fellows will participate in the program.

According to the principal investigators, the science of health and disease has become increasingly complex, requiring highly coordinated research efforts to ask and answer relevant questions and sophisticated environments to train the individuals who will make tomorrow’s most important discoveries. “This T32 program offers training for pre-doctoral PhD students and postdoctoral MD and PhD fellows in the most advanced areas of lung science in an integrated fashion, concentrating on providing high quality mentorship in the scientific disciplines most likely to make advancements in the diagnosis and treatment of lung diseases,” explained Mizgerd, who also directs the University’s Pulmonary Center.

Kotton, who also is Director of the Center for Regenerative Medicine (CReM) at BU and Boston Medical Center, believes the keystone principle of the training is bi-directional translation of ideas between basic and clinical spheres. “That is why we train MD fellows together with PhD students and fellows in a unified program. Our structure ensures that postdoctoral MD physician-scientists train side-by-side with PhD pre-doctoral students and postdoctoral fellows, learning from each other as well as their mentors, in Scientific Focus Groups integrating basic science with clinical science as applied to lung disease,” he said.
Lottery-Based Incentives Do Not Increase COVID-19 Vaccination Rates

Friday, July 2nd, 2021

Would you be more willing to get vaccinated against the COVID-19 virus if you could participate in a lottery for cash and prizes? The answer was surprisingly no, according to BUSM researchers who found that Ohio’s “Vax-a-Million” lottery-based incentive system, intended to increase COVID-19 vaccination rates, was not associated with an increase in COVID-19 vaccinations.

Prior reports in the media had suggested that the Ohio lottery increased COVID-19 vaccinations, leading other states to use COVID-19 vaccine incentive lotteries in an attempt to increase slowing vaccination rates. “However, prior evaluations of the Ohio vaccine incentive lottery did not account for other changes in COVID-19 vaccination rates in the United States, such as those that may have been due to expansion of vaccination to ages 12-15,” explained corresponding author Allan J. Walkey, MD, MSc, professor of medicine.

Using data from the U.S. Centers of Disease Control to evaluate trends in vaccination rates among adults 18 and older, the researchers compared vaccination rates before and after the Ohio lottery versus other states in the U.S. that did not yet have vaccine incentive lottery programs. Vaccination rates in other states served as a “control” for vaccination trends measured in Ohio, allowing the researchers to account for factors besides the Ohio lottery (such expanding vaccine eligibility to adolescents) throughout the country.

“Our results suggest that state-based lotteries are of limited value in increasing vaccine uptake. Therefore, the resources devoted to vaccine lotteries may be more successfully invested in programs that target underlying reasons for vaccine hesitancy and low vaccine uptake,” said Walkey, a physician at Boston Medical Center.

The researchers believe identifying interventions that can successfully increase COVID-19 vaccination rates is a critical public health issue necessary to curb the pandemic. “It is important to rigorously evaluate strategies designed to increase vaccine uptake, rapidly deploy successful strategies, and phase out those that do not work,” Walkey said.

Although Walkey and his colleagues were sorry to see that state lottery incentives were not associated with an increase COVID-19 vaccinations, they hope their findings will lead to a shift in focus away from ineffective and expensive lotteries, and on to further study of other programs that may more successfully increase vaccine uptake.

These findings appear online in the Journal of the American Medical Association.

Allan J Walkey was funded by NIH R01HL139751, NIH R01HL151607, NIH R01HL136660, and NIH OT2HL156812-01. Anica C Law was funded by NIH K23HL 153482. Nicholas A Bosch was funded by NIH 1F32GM133061-01.
New Research Identifies Key Set of Signals that Control Mucus Production in the Lung

Thursday, July 15th, 2021

Proper lung function relies on the precise balance of specialized epithelial cells (cells that line the surfaces of the body) that coordinate functions to maintain homeostasis. One important lung cell type is the goblet cell, which secretes mucus that helps protect the lining of the bronchus (major air passages of the lung) and trap microorganisms. Goblet cells are often increased in lung diseases, but signals that lead to their dysregulation are not well understood.

Researchers have now discovered a new set of signals that control the production of goblet cells in the lung. “By altering the proteins that control these signals we are able to either increase or decrease the production of goblet cells which offers potential new avenues for therapeutically targeting goblet cells in lung disease,” explained corresponding author Bob (Xaralabos) Varelas, PhD, associate professor of biochemistry.

The researchers used an experimental model carrying a genetic deletion of Yap and Taz, which are genes that encode proteins that control an important signaling network in the lung. They compared the genetic deletion model with a “control” model and found that the Yap/Taz deletion model had severe lung damage and elevated goblet cell number that was associated with increased mucin production.

In order to understand how loss of Yap/Taz led to increased goblet cell numbers, the researchers isolated cells from the experimental model and human lungs and cultured them in the lab. They then used gene expression and chromatin binding analyses to discover how these proteins control a network of genes important for mucus production. Finally, they used these cells in the lab to test inhibitors of goblet cell differentiation and mucus production.

According to the researchers, several lung diseases exhibit an expansion of goblet cells including asthma, COPD, Cystic Fibrosis and chronic bronchitis. “By identifying new regulators of goblet cell production, we offer insight into mechanisms that may contribute to these diseases. By targeting these signals we can repress the production and maintenance of goblet cells and therefore may offer therapeutic directions for limiting the expansion of these cells in lung disease,” said Varelas.

These findings appear online in the journal Cell Reports.

This work was supported by the Boston University Sequencing Core and Flow Cytometry Core and by BU-CTSI grant UL1TR001430. XV was funded by NIH/NHLBI R01HL124392 and NIH/NICHD R21HD094012 and by an ACS Research Scholar Grant (RSG-17-138-01-CSM). J.H.-B. was funded Q12 by NIH/NHLBI grants F31HL132506 and T32 HL007035. S.M. was in part funded by Find the Cause Breast Cancer Foundation. A.F. and B.N. were funded by Moorman-Simon Fellowships in Computational Biomedicine.
August 31, 2021

August Idiopathic pulmonary fibrosis (IPF) is the most common and severe form of lung disease characterized by relentless scarring leading to death within an average of four years from the time of diagnosis. The poorly understood pathogenesis of IPF, in part due to the lack of human disease models, has been a major hurdle in developing effective therapies.

Now, a team of regenerative medicine researchers at Boston University and the University of Pennsylvania have created a model (using pluripotent stem cells) to show how dysfunction of a highly specialized cell of the air sacs, the type 2 pneumocyte, initiates the fibrotic cascade that characterizes a number of adult and pediatric lung diseases, including IPF and childhood interstitial lung disease (chILD).

“Understanding how dysfunction of the highly specialized cells of the air sacs initiates the fibrotic cascade can result in development of novel targeted therapies for this devastating disease. Furthermore, this model has the potential to serve as a platform for testing new therapeutics,” explains first author, Kontantinos Alysandratos, MD, PhD, assistant professor of medicine.

The researchers used two groups of patient-specific cells. The first group had an altered gene that made them dysfunctional. The second group consisted of normal cells which were engineered by gene editing to correct the altered gene. When both sets of cells were examined using a number of different methods, the cells with the altered gene displayed abnormal proliferation, aberrant recycling of unnecessary cellular components, altered metabolic profiles, and inflammatory activation. When both sets of cells were exposed to hydroxychloroquine, a medication commonly used in pediatric patients carrying this altered gene, aggravation of the observed disturbances occurred in the cells with the altered gene, while no changes were seen in the normal cells.

According to the researchers, studying lung diseases in children, particularly those diseases that affect the air sac cells that reside deep in the lung, is very difficult since it is hard to access those cells for biological studies. “Generating stem cell-based in vitro models of lung disease, using easily accessible blood or skin cells from these children that are then reprogrammed into induced pluripotent stem cells, remains a very attractive approach for studying pediatric lung disease because it avoids risky biopsies of the deep lung, yet provides a simulation in the laboratory dish of the same processes that we think are occurring in the in vivo lung tissue itself,” says corresponding author Darrell Kotton, MD, the David C. Seldin Professor of Medicine at BUSM and Director of the BU/Boston Medical Center’s Center for Regenerative Medicine (CReM).

The researchers believe it should now be possible to take similar approaches to study many other types of interstitial lung diseases that arise from dysfunction in the air sacs and affect both children and adults. “In this way, these in vitro models should really expand drug development efforts to treat these diseases that until now have suffered from a lack of access to living cells from patients,” Alysandratos says. The work was led by co-senior authors, Kotton and Michael F. Beers, MD, the Robert L. Mayock and David A. Cooper Professor in Pulmonary Medicine at the University of Pennsylvania Perelman School of Medicine.

These findings appear online in the journal Cell Reports.
Awards and Accomplishments

**Nick Bosch MD, MSc & Kari Gillmeyer MD,**
Assistant Professors, Pulmonary Center

**Good News:**
The Epidemiology, Clinical, Health services, and Outcomes (ECHO) Research group has had a productive start to 2021, with 66 distinct publications among ECHO faculty and fellows for the first 6 months of 2021.

**Justin Lui MD**
Assistant Professor, Pulmonary, Allergy, Sleep & Critical Care Medicine

**Leadership Committees:**
Elected to serve on the Committee on Continuing Education Review of the Massachusetts Medical Society

**Awards/ Honors:**
Invited to present at the 17th Annual Respiratory Disease Young Investigators’ Forum as a top 30 Abstract Finalist

**Arjun Sharma PhD**
Lab Technician Bosmann Lab, Pulmonary Center

**Travel Award** to attend the 44th Annual Conference on Shock to be held in Portland, OR, October 12-15, 2021.

**Saravanan Subramaniam PhD**
Research Assistant Professor, Pulmonary Center

**Early career award,** International Society on Thrombosis and Haemostasis-2021, USA

**Conference:**
Subramaniam S, Hekman RM, Jayaraman A, O’Connell KA, Montanaro P, Ravid K, Crossland NA, Douam F, Emili A, Bosmann M. SARS-CoV-2 infection of K18-hACE2 transgenic mice induces an early hyperactive phenotype in circulating platelets. – ISTH 2020 (July 16-18, USA) – Talk

**Allan J. Walkey MD, MSc**
Professor, Pulmonary, Allergy, Sleep & Critical Care Medicine
Associate Professor, Health Law, Policy & Management

**Promotion to Professor**
Gilead Sciences/BMC subaward - LINC: Leveraging Informatics for NAFLD Care
Kevin C. Wilson MD
Professor, Pulmonary, Allergy, Sleep & Critical Care Medicine
Received ATS Presidential Commendation, for the third time.

Grants:

David M. Center MD
Associate Provost of Translational Research
Gordon and Ruth Snider Chair, Pulmonary, Allergy, Sleep & Critical Care Medicine

1 U01CK000632-01-11 CDC for the GeoSentinel Research and Surveillance Network. This is a five year extension of an existing project. I am stepping down as the coPI on September 1st but will be a lead co-investigator for surveillance. We have received $1.5 million in year one between carryover and new funds. This is an emerging infections global surveillance network (68 sites in 28 countries) that uses returning travelers, immigrants, and refugees as sentinel indicators of disease patterns and outbreaks worldwide.

Neelou Etesami MD
PhD Student, Mentor: Jay Mizgerd

NIH NHLBI F30 - Protective lung memory B cell functions and dynamics during respiratory infection

Kari Gillmeyer MD
Assistant Professor, Pulmonary, Allergy, Sleep & Critical Care Medicine

Parker B. Francis - Characterizing Care Coordination in Pulmonary Hypertension: A Mixed Methods Study

Elizabeth S. Klings MD
Associate Professor, Pulmonary, Allergy, Sleep & Critical Care Medicine

Bayer - ROAR: Riociguat Users Registry

Anica Law MD, MS
Assistant Professor, Pulmonary Disease

NIH NHLGI K23 supplement - Prolonged mechanical ventilation: patterns of post-acute care and patient outcomes
Justin Lui MD
Assistant Professor, Pulmonary, Allergy, Sleep & Critical Care Medicine
NIH NHLBI F32 - Left Ventricular Strain in Systemic Sclerosis-related Pulmonary Hypertension

Christine Odom
PhD Student, Mentor: Lee Quinton
NIH NHLBI F31 - Liver-Dependent Lung Remodeling and Pneumonia Susceptibility During Endotoxemia

Paul Maglione MD, PhD
Assistant Professor, Pulmonary, Allergy, Sleep & Critical Care Medicine
Graduate Faculty (Primary Mentor of Grad Students)
Takeda award – Kayla Bell Lecture on Primary Immunodeficiency Disease

Katrina E. Traber MD, PhD
Assistant Professor, Pulmonary, Allergy, Sleep & Critical Care Medicine
NIH NHLBI R01 – Transcriptional Regulation of Migrating Neutrophils during Pneumonia
Also, I moved offices!

Joseph P. Mizgerd ScD
Professor, Pulmonary, Allergy, Sleep & Critical Care Medicine
Director, Pulmonary Center

Darrell Nelson Kotton MD
Professor, Pulmonary, Allergy, Sleep & Critical Care Medicine
Professor, Pathology & Laboratory Medicine

T32 renewal: NIH NHLBI - Biology of the Lung: A Multidisciplinary Program
Upcoming Events

Jerome S. Brody, MD, Lectureship
November 3, 2021

Wellington Cardoso, M.D., PhD
Columbia University School of Medicine
Professor of Medicine and of Genetics and Development; Director of the Columbia Center for Human Development
Publications

Congratulations to the Pulmonary Center members for the following publications this quarter:


during a second wave of the pandemic. *JAMA Network Open* 2021;4:e2116425. PMID: 34170303.


Notable news from Pulmonary Center alumni and former faculty includes...

Scott K. Epstein, MD
Dean for Educational Affairs
Professor of Medicine
Tufts University School of Medicine

I was a fellow from July 1, 1989-June 30, 1992.

After 15 years, I will be stepping down from my position as Dean for Educational Affairs at Tufts at the end of December. I will be staying on at Tufts to teach, oversee continuing education, and work on medical school accreditation.

Antoine Guillon, MD/PhD
Associate Professor of Medicine
University of Tours

Previously a visiting scientist with Dr. Mizgerd in the Pulmonary Center, Antoine reports the following recent publications to share:


