



P A R K E R B . F R A N C I S
F E L L O W S H I P
P R O G R A M

Class of 2015

The Parker B. Francis Fellowship Program provides career development support to M.D. and Ph.D. scientists embarking on careers in clinical, laboratory or translational science related to Pulmonary, Critical Care and Sleep Medicine. Funding is awarded for three years to fellows working with experienced mentors in diverse areas of research related to lung disease.

Since 1976 the Francis Family Foundation through the PBF Fellowship Program has supported more than 815 new investigators. Many of the individuals who have received Parker B. Francis Fellowships have become prominent investigators with highly productive careers based at universities in North America and throughout the world. They have published their work in the leading scientific and medical journals and their research has improved patient care and identified preventive strategies to decrease the incidence of pulmonary disease, disability and death.

We are pleased to provide support for the following new investigators who make up the Parker B. Francis Fellowship Class of 2015.

Class of 2015

Hitesh S. Deshmukh, M.D., Ph.D.

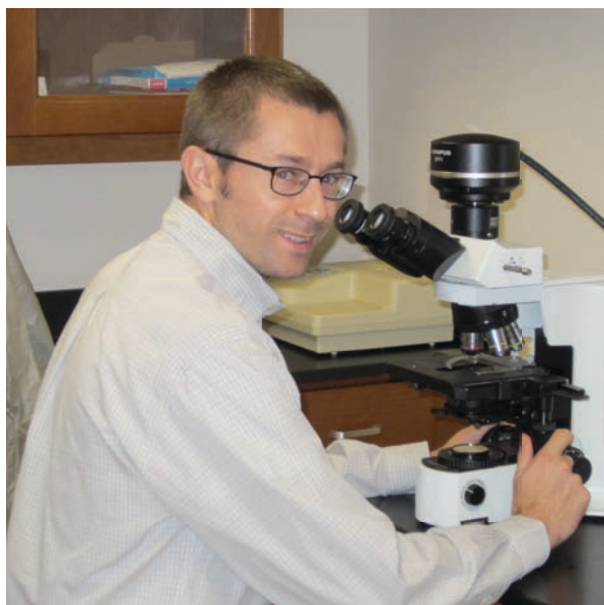


Mentor: Jeffrey A. Whitsett, M.D.
Institution: Cincinnati Children's Hospital

Role of commensal bacteria in regulating neutrophil-mediated host defense in neonates

Pneumonia is responsible for more than one million infant deaths around the world each year. Recent studies demonstrate that increased use of antibiotics disrupts the commensal gut bacteria and leads to increased risk of pneumonia in newborn infants. Neutrophils, a group of white blood cells play an important role in protecting newborn infants against pneumonia. But the role of commensal gut bacteria in controlling neutrophil numbers and thus protecting the newborn infant against pneumonia is unclear. Our studies will clarify the role of commensal bacteria in regulation of neutrophil mediated lung defense against pneumonia. Uncovering the mechanism by which alteration of commensal bacteria contributes to pneumonia in newborn infants will lead to new therapeutic approaches for immune support of infants receiving antibiotics and will help us devise better strategies to restore the normal commensal bacteria, which is altered by antibiotic use.

Jonathan A. Kropski, M.D.



Mentor: Timothy S. Blackwell, M.D.
Institution: Vanderbilt University

Regulator of telomere elongation helicase (RTEL1) in pulmonary fibrosis

Genetic mutations in genes related to telomere biology have been linked to pulmonary fibrosis, however the mechanisms through which these mutations cause disease are not yet known. We have recently identified mutations in a telomere-related gene (RTEL1) that appear to confer increased susceptibility to DNA-damage. In our studies, using cell, stem cell and animal models, we will investigate the hypothesis that mutations in RTEL1 impair the ability of epithelial cells in the lung to repair DNA-damage, leading to ineffective repair of the lung epithelium following injury, promoting instead scar formation and progressive fibrosis. These studies should provide new insights into how these DNA-damage response pathways may play a more general role in driving lung fibrosis.

Class of 2015

Merry-Lynn McDonald, Ph.D.

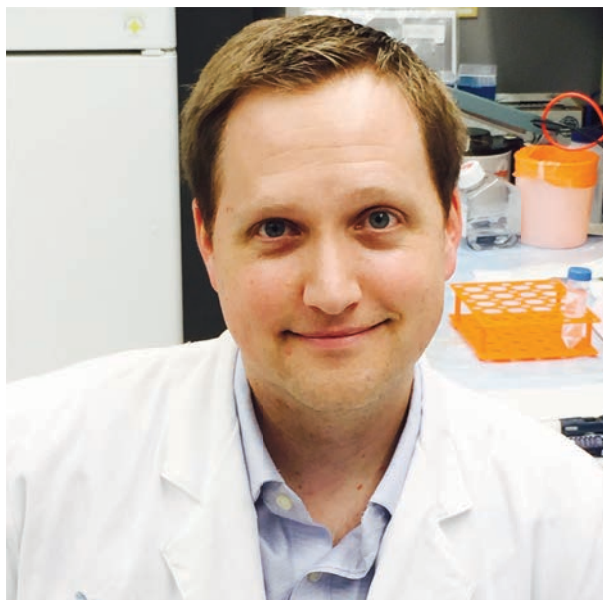


Mentor: Edwin K. Silverman, M.D., Ph.D.
Institution: Brigham and Women's Hospital

Network medicine approaches to cachexia in COPD

Chronic Obstructive Pulmonary Disease (COPD) is the third leading cause of death in the U.S. Muscle wasting in COPD cases, frequently termed cachexia, is an indicator of poor prognosis. Studying muscle wasting requires measuring muscle and not just body mass index (BMI). Most COPD studies only collect BMI data. Our group has developed a measure of pectoralis (pec) muscle that correlates with overall body muscle and a measure of fat from chest scans already collected in large COPD studies. We will assess whether genetics and metabolite levels influence muscle, fat and cachexia in COPD. This research can lead to new ways for identifying people who are at risk of developing cachexia in COPD cases and also lead to insight for targeting drug therapy to help them.

Jason R. Mock, M.D., Ph.D.



Mentor: Claire M. Doerschuk, M.D.
Institution: University of North Carolina

Regulatory T cells promote alveolar epithelial repair

Acute Respiratory Distress Syndrome (ARDS) is a common pulmonary disease with high morbidity and mortality. One type of white blood cells, the regulatory T cells (Tregs), appears important in the resolution of ARDS, but how Tregs interact with the cells lining the lungs (the AT2 cells) to aid lung repair is unknown. Our studies will examine the effects of Tregs on AT2 cells during resolution of the injury, particularly looking at approaches to increase the numbers of Tregs and the effects of the molecule CD103 on Tregs when it binds to its receptor E-cadherin on AT2 cells. We anticipate that these studies of Treg-AT2 cell interactions will identify targets for potential drugs that will hasten lung repair and improve patient outcomes in this often fatal disease.

Class of 2015

Victor E. Ortega, M.D.



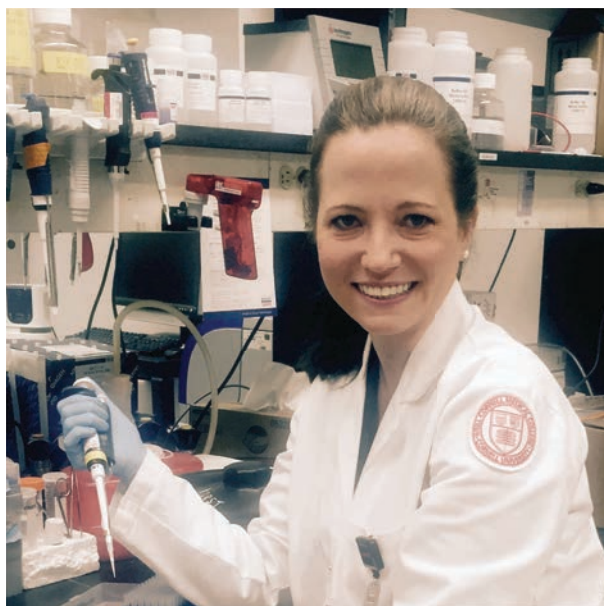
Mentor: Eugene R. Bleecker, M.D.

Institution: Wake Forest University

Effects of rare variants and ancestry on beta agonist response in asthma

Although several drugs are available to treat asthma, long-acting beta agonists (LABAs) are commonly used and work well for most people. However, for a small subgroup with asthma, LABA can cause life threatening side effects and carries a boxed safety warning from the U.S. Food and Drug Administration (FDA). Negative responses to LABA appear to be more frequent in African Americans compared to Whites and is currently being evaluated in an FDA-mandated safety study. Due to rarity of these negative responses and differences between ethnic groups, we will study rare mutations and ancestry in over 3,000 asthmatics to find mutations which influence inhaled beta agonist response. Mutations from these studies could constitute personalized treatment strategies for asthma and prevent negative responses in an important subgroup.

Odelya E. Pagovich, M.D.



Mentor: Ronald G. Crystal, M.D.

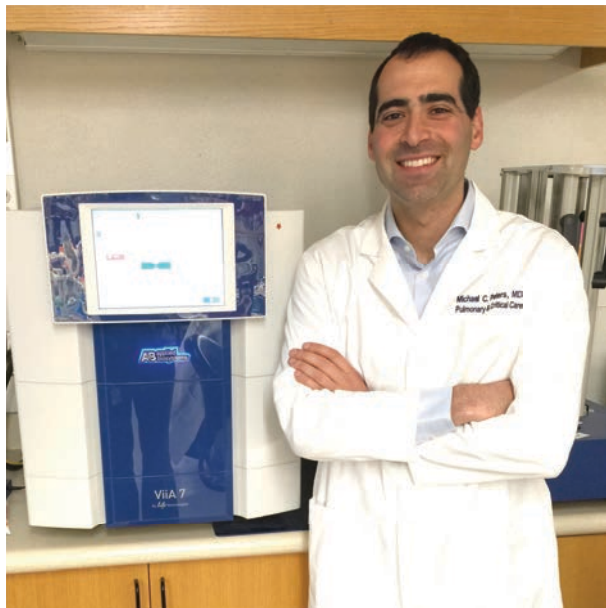
Institution: Weill Cornell Medical College

One-time gene therapy to prevent peanut-induced anaphylaxis

Peanuts are the most common food that provoke fatal or near fatal reactions. There are currently no therapies to treat peanut allergy. Prior studies suggest that therapy with anti-IgE antibodies may be effective for the treatment of food allergy, but the main limiting factor is the inconvenience and the high cost for frequent administration of a monoclonal antibody. To overcome this issue, we hypothesize that a one-time administration of an adeno-associated virus gene transfer coding for anti-IgE, the antibody that modulates peanut allergy, will be sufficient to protect against repeated peanut exposure in the peanut allergic host. We will test this in a peanut-allergic humanized mouse model sensitive to peanut using immune cells from peanut allergic subjects compared to controls.

Class of 2015

Michael C. Peters, M.D.



Mentor: John V. Fahy, M.D.

Institution: U of California, San Francisco

Role of type-2 cytokines and IL-6 in severe asthma

The economic and public health burden of severe asthma is substantial, but very little is known regarding factors that modify asthma severity, why some subjects are steroid resistant, or why some subjects experience recurrent asthma exacerbations. Our studies will attempt to answer these questions with a focus on two specific molecular pathways. The first pathway is increased airway type-2 inflammation, an allergic pathway known to be associated with airway dysfunction in asthma. The second pathway is increased IL-6 driven inflammation, and preliminary data implies that this pathway could be a driver of severe asthma. Thus, in a cohort of severe asthma subjects recruited through the Severe Asthma Research Program we will determine the role of type-2 inflammation and IL-6 in driving asthma severity.

Russell Ray, Ph.D.



Mentor: Huda Y. Zoghbi, M.D.

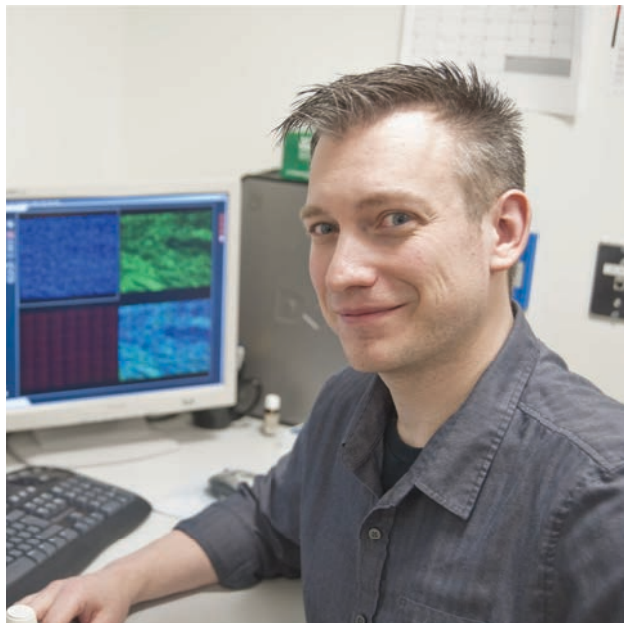
Institution: Baylor College of Medicine

Mapping developmental, genetic and functional organization of respiratory neural circuits

To understand how central NA neurons are organized to help regulate breathing and the role they play in respiratory disorders, we are using advanced genetic techniques to target specific subsets of central NA neurons that we hypothesize to be important in respiratory control. Once targeted, we can turn these neuron subsets on and off at will to test their requirement in breathing under a number of respiratory conditions, examine their gene expression profiles and characterize their anatomy. This multifaceted approach will enable us to develop a comprehensive model of how these neurons fit into the broader brainstem respiratory circuitry and to understand more clearly the cellular, genetic and molecular mechanisms of poor respiratory function associated with several childhood developmental syndromes.

Class of 2015

Stephen R. Reeves, M.D., Ph.D.



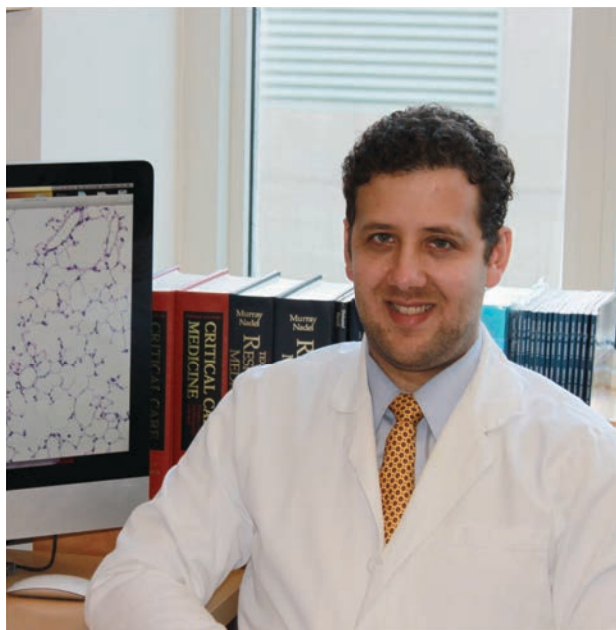
Mentor: Thomas N. Wight, Ph.D.

Institution: Seattle Children's Hospital

Airway epithelial cell regulation of extracellular matrix in asthmatic airway inflammation

Childhood asthma is a significant public health burden that impacts the lives of nearly 10 million American children and leads to a huge impact on their health, families, and communities. Increased deposition of extracellular matrix (ECM) and recruitment of inflammatory cells in the airway is a hallmark of asthma. Our recent work has demonstrated that primary airway epithelial cells obtained from asthmatic children do not regulate the activity of fibroblasts, the cells that produce ECM, as tightly as those obtained from healthy children. This may have important implications for the recruitment of inflammatory cells to the airway. To study this further, we will carefully examine the differences in the ECM produced by fibroblasts co-cultured with airway epithelial cells obtained from either healthy or asthmatic children.

Maor Sauler, M.D.



Mentor: Richard Bucala, M.D., Ph.D.

Institution: Yale University

MIF-CD74 signaling mitigates DNA damage in COPD

Our body has a natural response to stress. Similarly, our lungs have a response to cigarette smoke that try to mitigate the harm. For unknown reasons, that response is lost in COPD. We study a protein, MIF that is important in that stress response. We have found that MIF is decreased in COPD. We have also discovered that MIF can protect against cigarette smoke. We think that MIF can activate antioxidants during stress and promote repair following the damage from cigarette smoke. We hope to understand how MIF protects the lungs against the consequences of cigarette smoke.

Class of 2015

Lauren J. Van Scoy, M.D.



Mentor: Michael J. Green, M.D.

Institution: Pennsylvania State University

Evaluating the impact of a conversation game on advance care planning activities

Despite known health benefits of advance care planning (ACP), approximately 75% of adults do not participate in important ACP activities (e.g., completing an advance directive or discussing end-of-life wishes with family members). While advance directives are key, many experts believe that the most valuable part of the ACP process is having candid conversations about the values and priorities that inform treatment choices. Studies show that a significant barrier to these conversations is people's perceptions of the unpleasantness of the topic. Our studies evaluate whether a game activity designed to engage individuals in such discussions can facilitate high-quality, enjoyable conversations and initiate subsequent actions towards documenting participants' preferences. We hope to demonstrate that this novel approach can help engage individuals in needed ACP activities.