



P A R K E R B . F R A N C I S  
F E L L O W S H I P  
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## **Class of 2017**

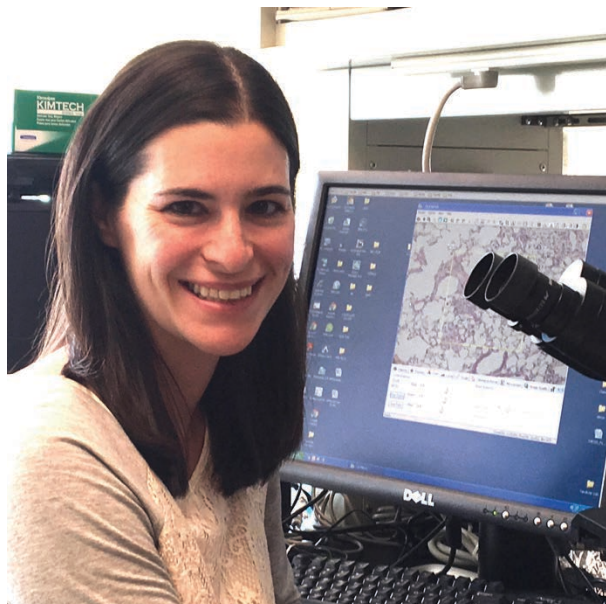
The Parker B. Francis Fellowship Program provides career development support to M.D. and Ph.D. scientists embarking on careers in clinical, laboratory or translational science related to Pulmonary, Critical Care and Sleep Medicine. Funding is awarded for three years to fellows working with experienced 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 850 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 2017.

## Class of 2017

### Yael Aschner, M.D.

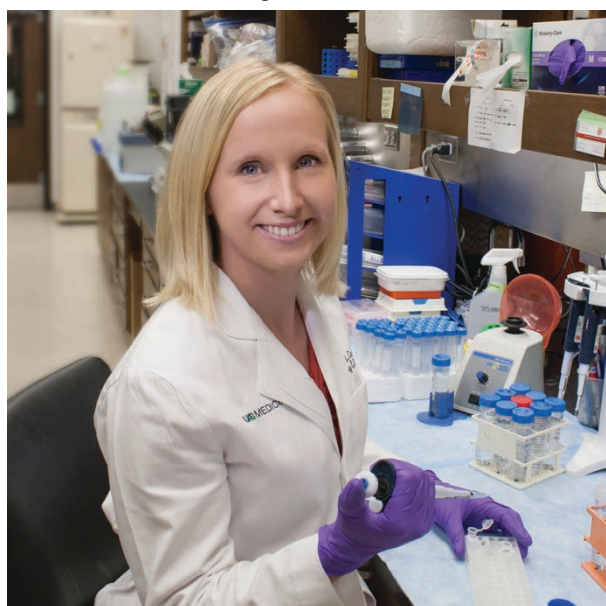


**Mentor:** Gregory P. Downey, M.D.  
**Inst:** University of Colorado Denver

#### Mechanisms of fibroproliferation

The acute respiratory distress syndrome (ARDS) represents a major healthcare problem, and is a source of significant mortality in ICUs, a large burden of healthcare expenditures, and long-term consequences for many survivors, including impaired health-related quality of life. Residual changes from excessive fibroproliferative activity (FP-ARDS) affect approximately 25% of ARDS patients six months after their acute illness. Understanding the clinical relevance of fibroproliferation and its relationship to long-term outcomes may aid in the development of novel interventions for a sizable subset of patients with ARDS. Our research aims to evaluate the role of a novel tyrosine phosphatase, PTPa, in the pathogenesis of FP-ARDS and its potential inhibition as a therapeutic approach to the treatment of FP-ARDS.

### Jennifer L. Casey, Ph.D.



**Mentor:** A. Brent Carter, M.D.  
**Inst:** University of Alabama at Birmingham

#### Cigarette smoke impairs innate immunity in alveolar macrophages

It is estimated that 1 in 6 adult Americans currently smoke cigarettes. One of the most prevalent complications of smoking is an increase in lower respiratory tract infections (LRTI). LRTIs are the most common infection that results in hospitalization. Alveolar macrophages are an important cell type within the lung and play an integral role in host defense from respiratory pathogens. Cigarette smoke (CS) contains more than 4,500 compounds some of which are carcinogens, toxins, and metals. Our studies indicate that cadmium, one of the metals present in CS, inhibits alveolar macrophage function preventing the ability of macrophages to fight lung infections. The proposed studies are designed to determine the mechanism(s) by which cadmium from CS alters the clearance and killing of pathogens by alveolar macrophages.

## Class of 2017

### Lauren E. Ferrante, M.D., M.P.H.



#### **Prediction of post-ICU disability among critically ill older adults**

Over 1 million older adults survive an ICU stay every year, and most will have greater difficulty in activities essential to independent living (such as bathing, walking, or taking medications), a problem known as "disability." For older adults, new or worsening disability can mean dependence on caregivers, admission to a nursing home, and/or increased mortality. Currently, there is no way to know which patients are at greatest risk of post-ICU disability. We plan to create a tool that ICU providers can use to identify older adults at greatest risk of post-ICU disability. This tool will provide prognostic information to patients and families, identify patients for interventions to improve function, and inform future research to reduce disability after an ICU stay.

**Mentor:** Thomas M. Gill, M.D.

**Inst:** Yale University

### Sarah E. Gilpin, Ph.D.



#### **Regenerative potential of airway stem cells in lung engineering for transplant**

We have developed a procedure to remove all the cells from an organ, leaving only the protein scaffold behind. This protein matrix, like the framework of a house, can be used as the foundation to rebuild organs on-demand, using new cells derived from the intended recipient. These lungs can then be custom-made for the person who needs them, therefore reducing wait times and avoiding negative immune responses following the transplant. In order to create new lungs, this project will first develop methods to make all the required cell types using adult stem cells, and then tests ways to culture and mature the reassembled lungs outside the body, to ensure they can function properly again before transplantation.

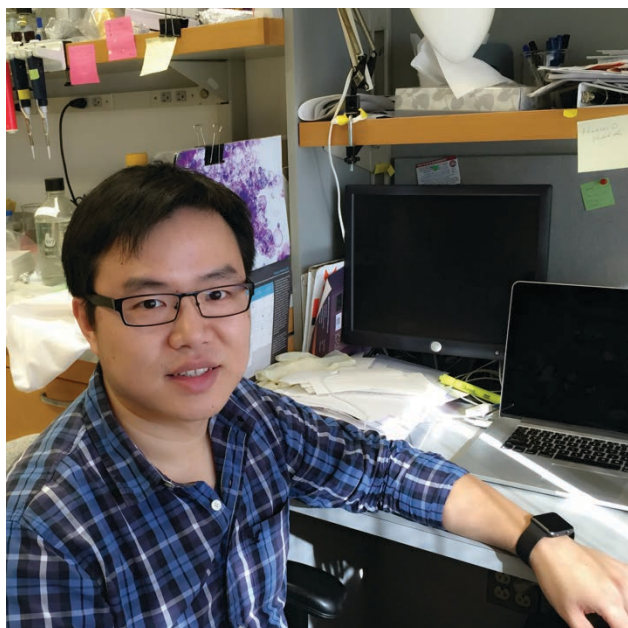
**Mentor:** Harald C. Ott, M.D.

**Inst:** Massachusetts General Hospital



## Class of 2017

### Peng Li, Ph.D.



**Mentor:** Mark A. Krasnow, M.D., Ph.D.

**Inst:** Stanford University

#### Functional dissection of a sigh integration center

The rate and pattern of breathing is constantly changing, powerfully regulated by our physiology and emotions. This regulation is critical for optimal physiology, and for pulmonary and cardiovascular health. Our research is aimed at understanding how physiological signals, such as oxygen, carbon dioxide and sleep, control breathing rhythm and pattern. We recently discovered a neural circuit that controls sighing, the deep breaths that plays critical roles in maintaining lung and cardiovascular health. This is the first control circuit identified for any breathing rhythm variant, and provides an opportunity to understand how changes in physiology switch breathing patterns, how this contributes to lung and cardiovascular health, and how this control goes awry in conditions such as sleep apnea and sudden infant death syndrome.

### Sydney B. Montesi, M.D.



**Mentor:** Andrew M. Tager, M.D.

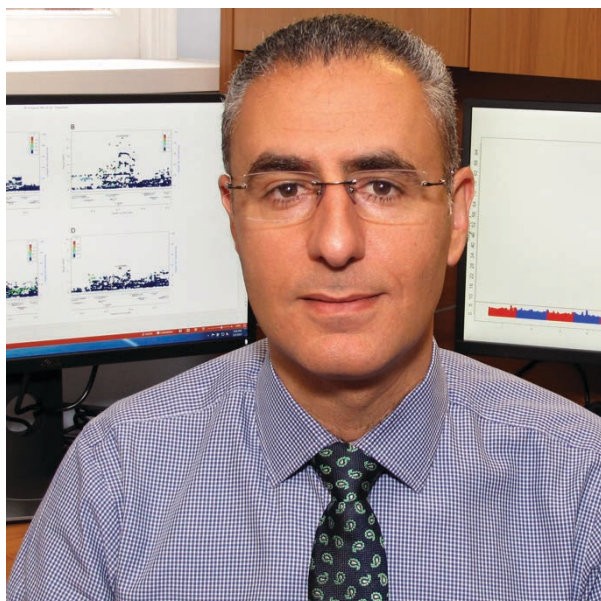
**Inst:** Massachusetts General Hospital

#### Novel imaging and biomarker measures of injury to assess IPF disease activity

Idiopathic pulmonary fibrosis (IPF) is a progressive and ultimately fatal disease. Despite major advances in our understanding of this disease, there has been little change in its poor prognosis, with patients on average surviving only three years from the time that they are diagnosed. There are marked differences in the course of IPF in different patients, however, with some progressing rapidly while others may remain stable for long periods. The ability to predict how rapidly or slowly individual patients will progress would help clinicians take care of them, and help clinical researchers perform studies to find better treatments. This project aims to develop new ways to predict how individual patients with IPF will fare, using combinations of new lung imaging and blood tests.

## Class of 2017

### Ma'en Obeidat, Ph.D.



**Mentor:** Don D. Sin, M.D. M.P.H.

**Inst:** University of British Columbia

#### **Integrative genomics to identify novel therapeutics and biomarkers for COPD**

Our research will identify which genes in our genome cause some people to get COPD or lead to disease worsening over time and will allow us to understand these processes more and to develop new drugs to treat the disease. Our research will use a sophisticated analysis tool called integrative genomics that will enable us to translate COPD genes into clinically useful information. We will identify and test the actual genes and their products that are responsible for some individuals developing COPD. The goal is to use this information on genes and gene products to monitor disease and will additionally allow us to interfere with these gene products to treat disease. Findings from this project will be immensely helpful in managing patients with COPD and in preventing its progression."

### Andrew J. Paris, M.D.



**Mentor:** George S. Worthen, M.D.

**Inst:** University of Pennsylvania

#### **Neutrophil-derived oncostatin M promotes alveolar epithelial repair**

The acute respiratory distress syndrome (ARDS) is a common and devastating inflammatory lung injury that affects approximately 200,000 people annually in the United States and has a 34-46% mortality rate. We have developed a murine model of acid-induced lung injury that closely resembles human ARDS and can be used to delineate how inflammation influences alveolar epithelial repair. This project will incorporate a scientific approach and a unique training plan encompassing experts from the fields of developmental biology and immunology that will generate novel insights into a model of ARDS treatment that seeks to promote alveolar epithelial repair.



## Class of 2017

### Alejandro A. Pezzulo, M.D.



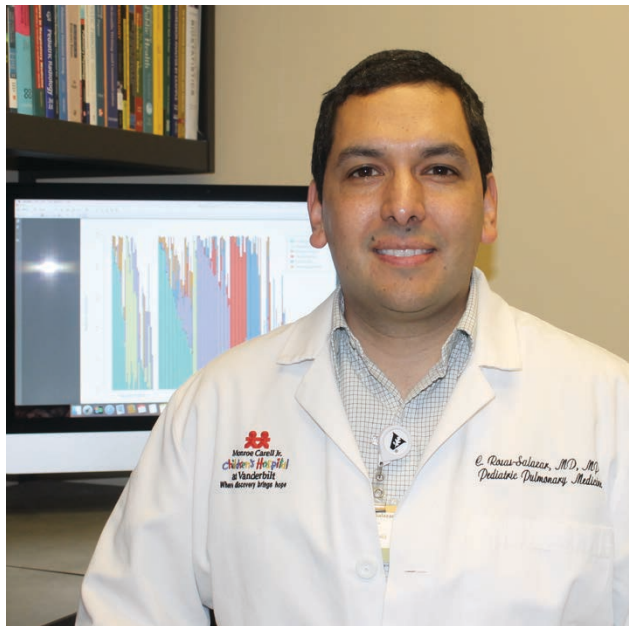
**Mentor:** Joseph Zabner, M.D.

**Inst:** University of Iowa

#### **Role of HDAC6 and HSP90 in airway goblet cell metaplasia**

People with lung diseases such as smoking-related chronic bronchitis, or the genetic disease cystic fibrosis, suffer due to excessive amounts of mucus produced by their lungs. While new treatments for excessive mucus have become available for a sub-group of patients with asthma, most other people with chronic lung diseases have no available treatment options. Our research will: a) study two drugs previously identified with computer-based biology methods. These drugs may decrease the number of mucus-producing cells within human lungs, and b) determine how these mucus-decreasing drugs work. Findings from this work have the potential to improve the lives of people with excessive mucus production due to lung disease.

### Christian Rosas-Salazar, M.D., M.P.H.



**Mentor:** Tina V. Hartert, M.D., M.P.H.

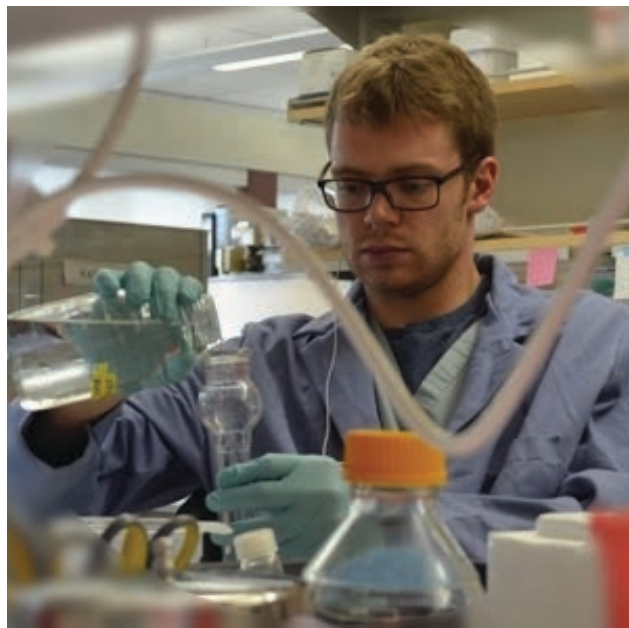
**Inst:** Vanderbilt University

#### **Infant RSV Infection, the airway microbiome, and childhood respiratory outcomes**

Early-life infection with respiratory syncytial virus (RSV) is the leading cause of hospitalizations in infancy and is strongly associated with the development of childhood wheezing illnesses, including recurrent wheeze and asthma. One of the mechanisms through which RSV leads to worse long-term respiratory problems is through modification of the airway bacteriome (i.e., the community of bacteria that lives in our airways). This project will elucidate how the airway bacteriome changes over the first few years of life, how it changes in response to RSV infection in infancy, and how it impacts the development of childhood wheezing illnesses after this infection. Our study could help to identify novel interventions (such as manipulation of the airway bacteriome) aimed to prevent the development of childhood wheezing illnesses.

## Class of 2017

### Jason J. Rose, M.D.



#### Developing an antidotal therapy for carbon monoxide poisoning

CO exposure is the leading cause of human poisoning in the United States, with 50,000 cases every year. While 2,000 of these patients will die, mostly from cardiovascular collapse, there is still no antidote. The harmful effects of CO are from CO binding to red blood cells and mitochondria to severely lower the delivery of oxygen throughout the body. We have developed rNgb, a CO scavenging agent, that directly binds CO from poisoned mitochondria and red blood cells, reversing the likely cause behind CO toxicity. We propose studies to: 1) investigate the basis of the cardiovascular toxicity of CO poisoning; 2) demonstrate the efficacy and safety of rNgb as an antidotal therapy and 3) identify and develop a second generation CO scavenging small molecule.

**Mentor:** Mark T. Gladwin, M.D.

**Inst:** University of Pittsburgh

### Priya B. Shete, M.D.



#### From poverty to cure: overcoming socioeconomic barriers to tuberculosis care

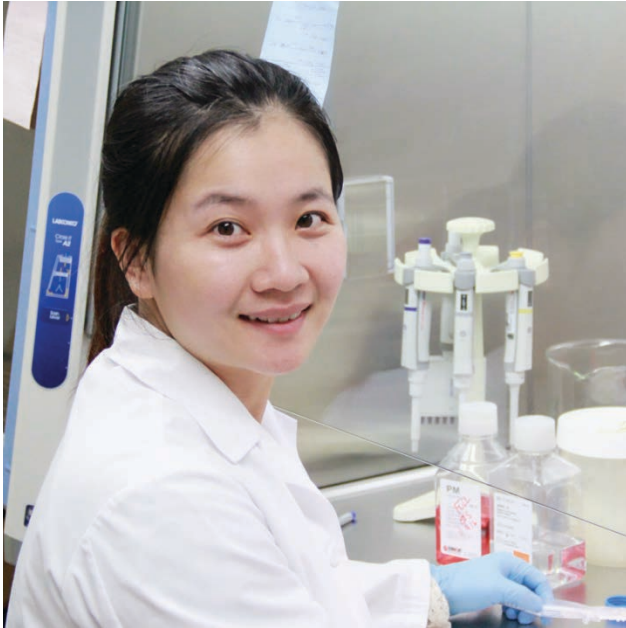
Tuberculosis (TB), the leading infectious cause of death worldwide, is ultimately a disease of poverty. TB more commonly affects patients of low socioeconomic status who face exceptional barriers in accessing quality care. This is particularly tragic given that TB is a treatable, curable disease. It is known that the risks for TB and the risk of poor outcomes of disease are linked to social and economic vulnerabilities that make it difficult for even the most cutting edge interventions to improve outcomes. This proposal seeks to understand the social and economic barriers that inhibit patient access to quality TB diagnostic care and to further design and test interventions that overcome those barriers.

**Mentor:** Adithya Cattamanchi, M.D.

**Inst:** University of California, San Francisco

## Class of 2017

**Ke Yuan, Ph.D.**



### **Lung pericytes: a novel source of pathogenic smooth muscle cells in PAH**

Pulmonary arterial hypertension (PAH) is a life-threatening disorder associated with an abnormal increase in pulmonary pressures that, if untreated, leads to heart failure and premature death. While the cause is unknown, progressive distal vessel loss and muscularization due to uncontrolled growth of smooth muscle cells (SMCs) are major pathological features of PAH. The source of these SMCs remains poorly understood. No study to date has shown whether pericytes give rise to SMCs or if pericytes contribute to muscularization. We will study for the first time the critical role of pericytes in assembling vessel networks and how this process is severely disrupted. My project will result in innovative insights into pulmonary vascular biology and facilitate the discovery of novel therapeutic approaches to treat PAH.

**Mentor:** Mark R. Nicolls, M.D.

**Inst:** Stanford University