PARKER B. FRANCIS
FELLOWSHIP
PROGRAM

Class of 2009

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 760 new investigators. These fellows have made remarkable discoveries working in laboratories and clinics in North America and throughout the world. They have published their work in the best-known 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.

Many of the individuals who have received Parker B. Francis Fellowships have become prominent investigators and international leaders in pulmonary research.

We are pleased to provide support for the following new investigators who make up the Parker B. Francis Fellowship Class of 2009.

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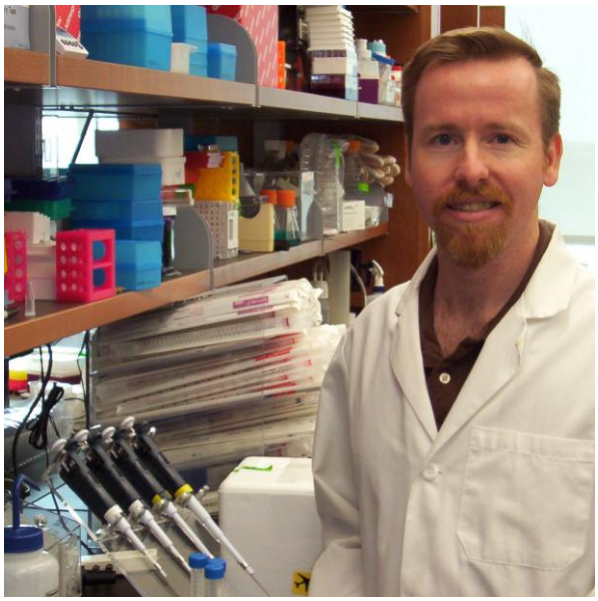
John F. Alcorn, Ph.D.

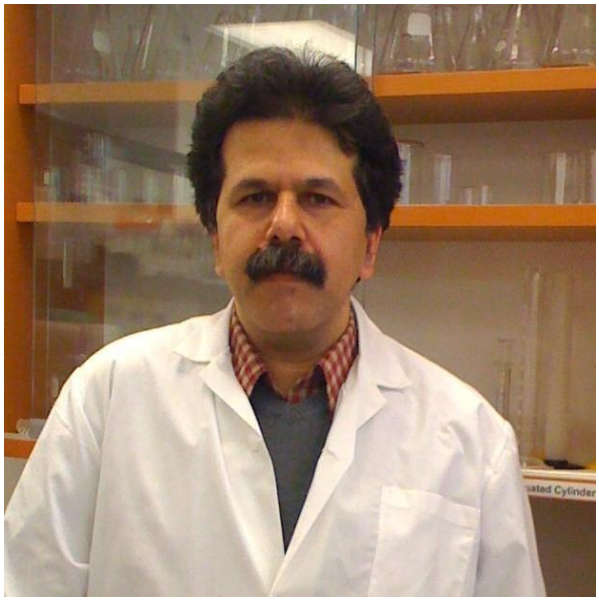


Mentor: Jay K. Kolls, M.D.
Institution: Children's Hospital of Pittsburgh

The JNK/IL-17 signaling axis and pneumonia

The lung is exposed to many potential external pathogens, including bacteria, with every breath. In spite of a vast amount of research, the disease mechanisms of pneumonia are unclear. The work proposed in this study will identify roles for novel immune regulators and help to define the molecular pathways involved in pneumonia. Specifically, this study will address the role of helper T cells and their downstream signaling pathways involved in host defense. To do this, we will employ mouse models of disease and utilize genetically altered mouse strains to dissect these signaling networks. The goal of the current study is to define novel therapeutic targets in the lung and promote our understanding of pneumonia pathogenesis. These studies will identify novel mechanisms of innate and adaptive immunity that promote the resolution of pneumonia.

Saeid Ghavami, Ph.D.



Mentor: Andrew J. Halayko, Ph.D.
Institution: University of Manitoba

S100A8/A9 and airway mesenchymal cell function in allergic airway inflammation

Asthma is a chronic inflammatory airway disease that affects ~12% of children and ~6% of adults in North America. In most patients symptoms can be controlled by common therapies such as steroids. However, 20% of patients are resistant to steroid control. This patient subpopulation accounts for ~80% of asthma health care costs. Our project examines a unique protein complex called S100A8/A9 released by neutrophils, which are inflammatory cells that characterize steroid-resistant asthmatics. We will study the effects of S100A8/A9 on human airway cells that contribute progressive disease worsening over time. Ours will be the first studies examining these proteins in allergic airway inflammation, thus they have potential to uncover new means for future treatment of asthma.

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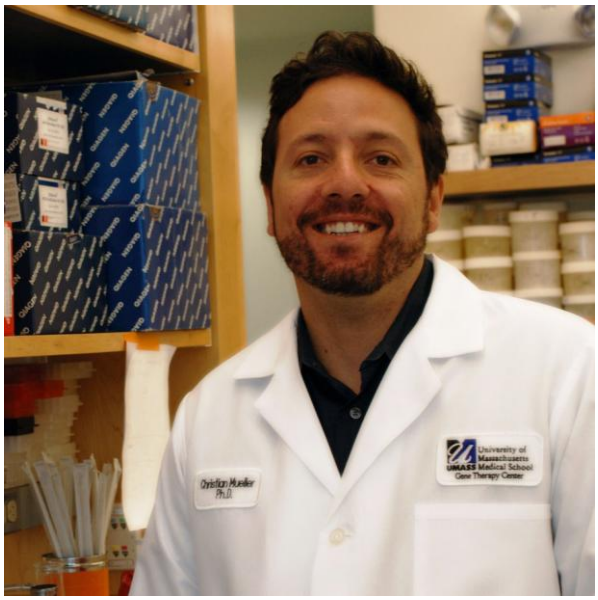
Christian Mueller, Ph.D.



Mentor: Terrence Flotte, M.D.
Institution: University of Massachusetts

Lymphocyte abnormalities in a CF mouse model

Cystic fibrosis (CF), the most common lethal, single-gene disorder affecting North Americans. We have developed a novel mouse model which shows that some of the inflammatory problems with CF disease may be inherent to immune cells and as a consequence the CF defect may be causing CF immune systems to be dysfunctional. This model not only suggests that the CF defect also plays a role in the immune system but correction of the immune cells via gene therapy with viral vectors may also serve to help the pathology associated with lung disease. These studies will focus on determining exactly what cells in the immune system are malfunctioning in CF and by what mechanism the malfunction is caused. This research will lead to new insights into the inflammatory mechanism in CF and will serve to test novel therapies aimed at regulating these responses.

Silvia Pagliardini, Ph.D.

Mentor: John J. Greer, Ph.D.
Institution: University of Alberta

Identification of an active expiratory rhythm generator in brainstem respiratory circuits

Understanding the brain networks responsible for the cyclical and coordinated contraction of respiratory muscles in breathing is a fundamental first step in order to treat disorders such as apnea and several diseases associated with respiratory problems such as Parkinson's and Alzheimer's. For the past decade, a single unique network of neurons in the brainstem (preBötzingerComplex) was generally regarded as the principal source of the respiratory cycle, resulting in a pattern where inspiration is an active process and expiration at rest is passive. However, might be responsible for active expiratory activity (parafacial respiratory group). We will study how each center generates rhythmic activity and how the two centers interact with each other in order to maintain coordinated respiratory activity.

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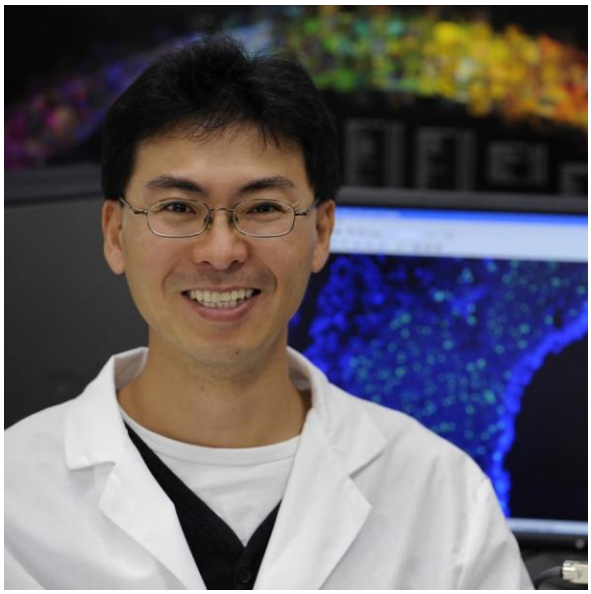
Kwon-Sik Park, Ph.D.

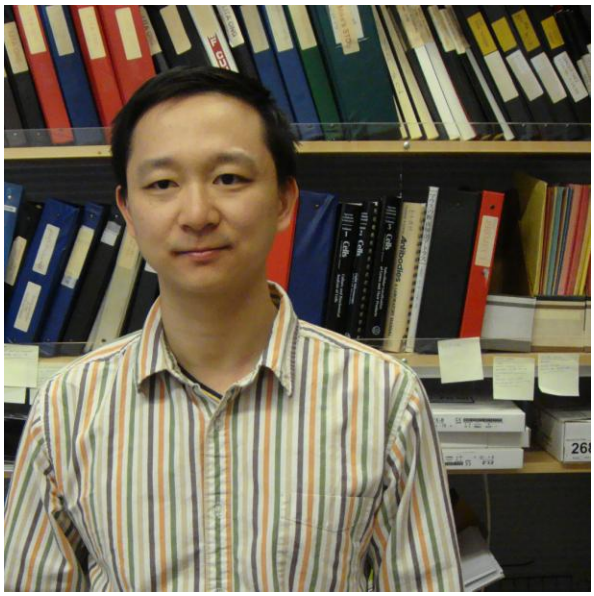


Mentor: Julien Sage, Ph.D.
Institution: Stanford University

Cellular and molecular mechanisms of small cell lung cancer development

Every year in the US, more than 25,000 new cases are diagnosed. These patients have a dismal 5-year survival rate of about 5%. While SCLC responds well to initial chemo-/radiation therapy, the tumor cells become rapidly resistant to treatment. To better understand the mechanisms of SCLC development, and as a first step to identify novel therapeutic modalities against SCLC, we generated a mouse model of human SCLC. Our first goal is to identify the cell of origin of SCLC in the lung of these mutant mice. Our second goal is to identify signaling pathways that may drive the proliferation of SCLC cells. A better knowledge of the mechanisms underlying lung cancer initiation may ultimately lead to the development of novel means to diagnose and treat SCLC patients before their disease has spread to other organs.

Liming Pei, Ph.D.



Mentor: Ronald Evans, Ph.D.
Institution: The Salk Institute for Biological Studies

SMRT regulates type I pneumocyte and embryonic lung development

Using an elegant program during embryonic development, the lung branches into millions of airways for the air exchange that is required immediately after birth. These airways are lined by cells called pneumocytes. The transition from complete dependence on the mother to breathing on one's own at birth is a critical turning point in life. However, the details of this transition remain to be understood. I have recently created an animal model that dies right after birth due to lung immaturity. This animal model recapitulates many features of some human infant respiratory diseases. Using this unique model, I propose to elucidate the details of pneumocyte and embryonic lung development. This work will bring novel insight and may ultimately lead to new prevention and treatment methodologies for infant respiratory diseases.

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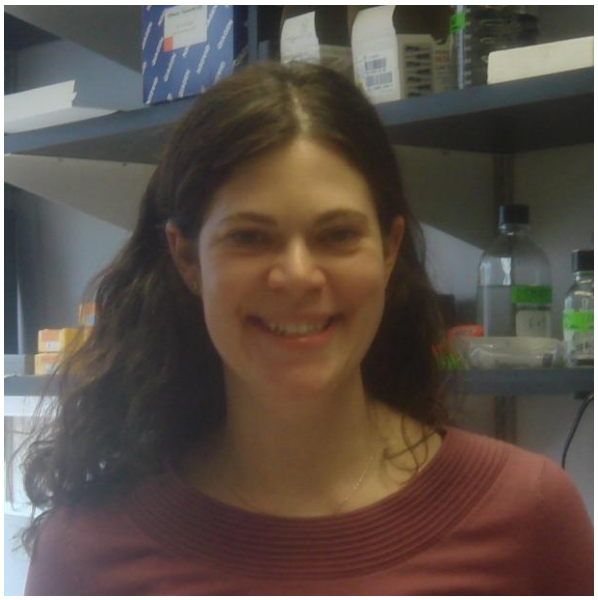
Miera H. Rechtschaffen, M.D., Ph.D.

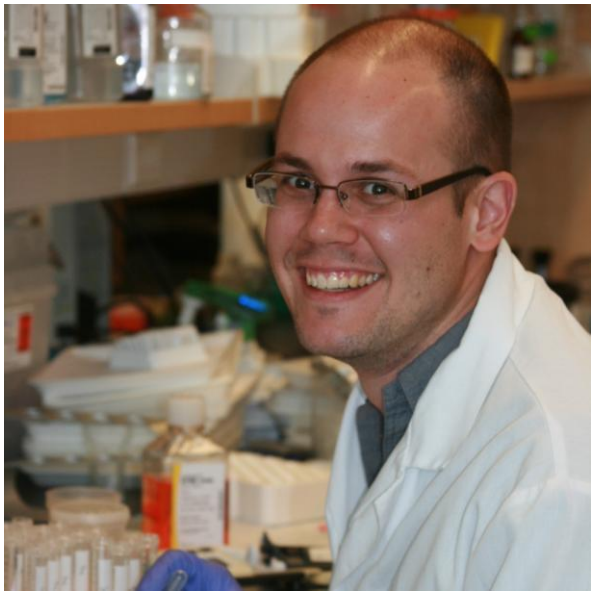


Mentor: Boris V. Reizis, Ph.D.
Institution: Columbia University

Zfx in the lung: its role in stem cell maintenance and tumorigenesis

Stem cells are long-lived cells critical for the maintenance of tissue integrity in both normal turnover and injury. They have been identified in many adult organs, including the lung. One recently identified lung stem cell is the bronchioalveolar stem cell, or BASC. In addition to repairing the lung after injury, the BASC appears to be involved in the initiation of lung adenocarcinoma in a mouse model of the disease. An exciting candidate that may link stem cell survival and cancer is Zfx, a transcription factor that has been shown in our lab to be indispensable for the self-renewal of both embryonic and hematopoeitic stem cells. These studies are designed to determine if Zfx is important in regulating the survival of lung stem cells, and to define its role in the development of lung cancer.

Matthew Schaller, Ph.D.

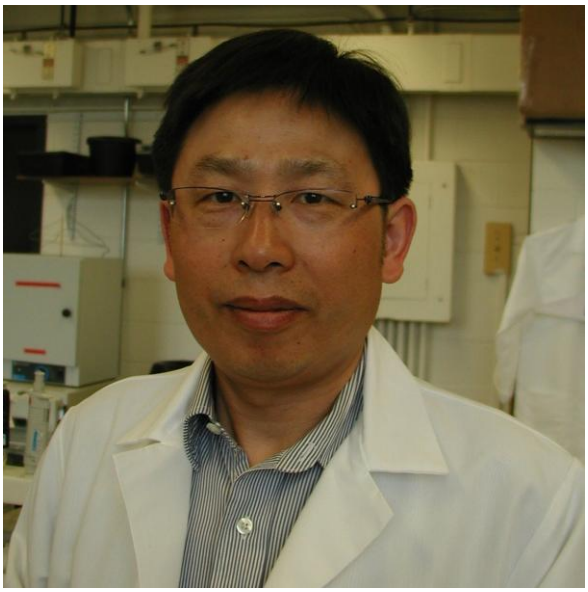


Mentor: Steven Kunkel, Ph.D.
Institution: University of Michigan

SSEA4 marks a novel stem cell in the lung

It is known that inflammation can cause improper tissue buildup in the lung. In the case of asthma, the tissue is fibrotic and it leads to a further shortness of breath. In the case of smoking the inflammation leads to chronic obstructive pulmonary disorder (COPD). A consequence of COPD is pulmonary hypertension, a disease where the heart becomes overworked because of difficulty pumping blood to the lungs. We will assess the role of adult stem cells in contributing to pulmonary hypertension and lung fibrosis. We believe that inflammatory events, caused by allergic asthma or smoking, may lead to pulmonary hypertension and lung remodeling by triggering stem cells to differentiate in a way that is detrimental to the patient. Understanding these problems could lead to an improvement in the quality of life for patients with these diseases.

Xiao Su, M.D., Ph.D.



Mentor: Asrar B. Malik, Ph.D.
Institution: University of Illinois at Chicago

Activation of Î±7 nAChR mobilizes hematopoietic stem cells to repair acute lung injury

In the US approximately 200,000 patients develop acute lung injury (ALI) annually. Despite the best supportive care, mortality remains high and new treatments are needed. ALI is a complex of excessive inflammatory response, neutrophil infiltration, and disruption of endothelial and epithelial barriers. An anti-inflammatory mechanism (such as cholinergic anti-inflammatory pathway) functions to control the inflammatory response and prevent injury. Recently, stem cell-based therapies have shown the protective effects on acute lung injury. Our studies will examine whether stimulation of cholinergic anti-inflammatory pathway is a potential novel therapy to reduce lung injury by regulating the function of bone marrow hematopoietic stem cells. Ultimately, we hope the discovery will lead to an effective treatment of acute lung injury.

Rachel Zemans, M.D.

Mentor: Gregory P. Downey, M.D.
Institution: National Jewish Health

The synergistic effects of PMN proteinases and LPS on epithelial injury in ALI

Acute Lung Injury (ALI) has many causes, including bacterial infections. It is characterized by an accumulation of fluid in the lungs, which impedes the absorption of oxygen from the air. In ALI, the accumulation of fluid in the lungs is due to a breakdown of the lining of the lungs, or “epithelium,” which normally functions as a barrier to prevent movement of fluid from the bloodstream into the lungs. In ALI, inflammatory cells called polymorphonuclear neutrophils (PMN) injure the lung epithelium in part through the release of substances called “proteinases”. In addition, bacterial products such as lipopolysaccharide (LPS) directly damage the lung. We propose to study the mechanisms by which PMN proteinases and LPS act synergistically to injure lung epithelium. By determining how proteinases and LPS act in synergy to damage the lungs, we hope to identify novel targets for therapies aimed at preventing tissue destruction in ALI.