

## KENTUCKY

### JOHN EATON, PhD

University of Louisville Research Foundation, Inc., Louisville, KY

*Lung Cancer Discovery Award* • Funded in partnership between the American Lung Association and the LUNGeivity Foundation

### *Comparing Two Methods To Encourage Home Smoking Bans*

#### **Documenting Child Exposure To Environmental Tobacco Smoke (ETS) Carcinogens: A Novel Approach To Motivate Families To Adopt Home Smoking Bans.**

Exposure to secondhand smoke contributes to about 50,000 deaths in the United States each year and is a recognized cause of respiratory disease in children. Yet 36.1% of children in the U.S. live in a home where people regularly smoke cigarettes. One way to reduce children's secondhand smoke exposure is by limiting or banning smoking in the home. The researchers will evaluate two methods to motivate families to adopt home smoking restrictions. One group will receive a home visit by a counselor who will provide a brochure documenting the health impact of home exposure to secondhand smoke. The second group will receive the same brochure and will be given more education from the counselor about the health risks of home smoking and the importance of a home smoking ban. The second group will also receive the results of a lab test conducted on the urine of a child in the home that will document cotinine (a byproduct of nicotine use) and NNAL, a known cancer-causing agent found only in tobacco. Three months later, the researchers will return to see if the method the smokers received changed their home smoking policies and if the treatment had any effect on their smoking behaviors

## **MICHIGAN**

### **MICHAEL A. TAINSKY, PhD**

Wayne State University, Karmanos Cancer Institute, Detroit, MI

*Lung Cancer Discovery Award* • Funded in partnership between the American Lung Association and the LUNGevity Foundation

#### ***Developing Noninvasive Blood Test To Detect Early Lung Cancer***

##### **Autoantibody Biomarkers For The Detection Of Lung Cancer.**

If lung cancer is detected at an early stage, there is a much greater chance that it can be treated. An inexpensive, noninvasive early detection test that could detect early stage lung cancer would reduce deaths from lung cancer. The researchers have developed a strategy for early detection of cancer that takes advantage of the responses of the human immune system to identify cancer-associated proteins that bind to antibodies present in the blood of cancer patients but not in the blood of healthy subjects or those with noncancerous diseases. They hope to develop a noninvasive screening blood test for early detection of lung cancer using these cancer-associated proteins. Along with blood from lung cancer patients, the blood from other cancer patients will be tested so that the researchers can identify markers for lung cancer that do not falsely identify other cancers or benign lung conditions as lung cancer.

### **CARLOS SEREZANI, PhD**

University of Michigan, Ann Arbor, MI

*Senior Research Training Fellowship* • Funded by the American Lung Association

#### ***Gathering Facts About Inner Workings of Lung's Immune System***

##### **Modulation Of Alveolar Macrophage Antimicrobial Functions By Eicosanoids: Role Of Lipid Rafts And Signaling Molecules.**

More than four million people die from pneumonia each year worldwide, and in the United States, pneumonia is the number one cause of death from infection. This problem is further compounded by the increasing number of people with compromised immune systems and the growing number of infections caused by multi-drug resistant organisms. A type of immune cell called the alveolar macrophage (AM) is the resident defender of lung sterility, patrolling and clearing invading organisms by releasing compounds that affect ingestion and kill bacteria in the lung. In the absence of intact AM clearance, otherwise innocuous bacterial infections become lethal. The researchers will study an important cell-signaling mechanism that affects AM function, focusing on lipid mediators called eicosanoids. Understanding how these mediators affect the AMS defense against microbes may lead to development of treatments that could be of significant use in preventing pneumonia in people with damaged immune systems or enhancing the effectiveness of antimicrobial therapies.

## OHIO

### **ANNE-KARINA PERL, PhD**

Childrens Hospital Medical Center-Cincinnati, Cincinnati, OH

*Biomedical Research Grant* • Funded in partnership between the American Lung Association and the Alpha-1 Foundation

#### *Stopping Airway Wall Thickening to Improve COPD Survival*

#### **Role of EGF Receptor in Regenerating Airway Epithelium and Airway Wall Thickening.**

Injury of the cells lining the airways can lead to airway wall thickening. Airway wall thickening has been identified as a major predictor of the severity of airway obstruction in COPD patients. It is also implicated in bronchiolitis obliterans syndrome (BOS), which is the main chronic complication after lung transplantation. Using a mouse model, the researchers will study airway regeneration after acute injury and airway wall thickening after chronic injury. They will focus on the role of epithelial growth factor receptor (EGFR), a substance that is present in the membrane of the lung cells. Previous research has shown that EGFR is increased after cell injury, and that inhibiting EGFR signaling reduces lung scarring. The long-term goal of this study is to get a better understanding of the molecular events that control the steps that lead to airway wall thickening and to use these findings to develop effective therapeutic strategies to improve long-term survival in COPD and after lung transplantation.

### **AMAL AMER, MD**

Ohio State University, Columbus, OH

*Biomedical Research Grant* • Funded by the American Lung Association

#### *The role of caspases in Legionella pneumophila pulmonary infection*

Legionella pneumophila is a bacterium that can cause severe pneumonia especially in the elderly and in individuals with low immunity leading to death. Recently, Legionella has been detected in AIDS and in cancer patients. It is not know how Legionella persists in the host cell and multiplies to cause disease. We have been studying specific molecules called caspases and trying to understand their role in host response against microbes. Caspases have been always implicated in host cell death and have well characterized pathways for activation during the demise of the cell. Recently we found that caspases can restrict bacterial infection without affecting the survival of the host cell. We also propose that there are other yet non identified routes to activate caspases during infection. In the case of Legionella, mice cells do not allow Legionella infection. Notably, in these cells the activation of certain caspases restricted the infection. Interestingly, human cells are permissive to Legionella and do not activate specific caspases when infected with Legionella. Therefore, we will study how caspases prevent Legionella from establishing infection and causing disease in the mouse cell. Our long term aim is to use this information to design molecules that can manipulate caspases in the human cell and use them to combat Legionella and other lung microbes

## **OHIO cont.**

### **ANASUYA SARKAR, PhD**

Ohio State University, Columbus, OH

*Biomedical Research Grant* • Funded by the American Lung Association

#### ***ARDS: Injury from Microvesicular Caspase-1***

Acute respiratory distress syndrome (ARDS) is a dangerous disease condition that develops in 20-50% of patients suffering from severe conditions such as major trauma, sepsis or shock and over 40% of these patients die. It is the most common cause of lung injury in patients suffering from severe conditions and is characterized by damage to lung epithelium. Despite the physician's best efforts to treat this disease state, there has been little progress in treating this devastating disease. Recent scientific work suggests the role of cell death of the epithelium leading to severe injury of the lung to be the major cause for death from this disease. Our recent work have shown that a protein caspase-1 normally involved in activating different other proteins involved in infection, is also uniquely capable of killing cells. The process of caspase-1 regulation is very complex. In order to develop more effective therapeutic strategies, it is necessary to understand the precise mechanism of this caspase-1 mediated lung injury. The present proposal seeks to expand upon the clues provided our work on caspase-1 biology and extend these processes to dissect the details of lung injury in ARDS. This research proposal provides a new opportunity to understand how caspase-1 signaling events may regulate the complex biology of caspase-1 and lung epithelial cell interactions and thereby create new therapeutic opportunities to prevent and treat ARDS and other inflammatory diseases. Successful completion of this study will provide novel insights into ARDS mediated lung injury and create new therapeutic opportunities to prevent and treat ARDS and other inflammatory diseases.

## TENNESSEE

### WILLIAM LAWSON, MD

Vanderbilt University Medical Center, Nashville, TN

*Dalsemer Research Grant* • Funded by the American Lung Association

#### *Genetic Mutations May Yield Information On Idiopathic Pulmonary Fibrosis*

#### **Dysfunction In The Alveolar Epithelium In Pulmonary Fibrosis.**

Idiopathic pulmonary fibrosis (IPF) is a severe lung disease in which patients develop shortness of breath, decreased exercise capacity, lung scarring (fibrosis) and difficulty with oxygen exchange. Once diagnosed, most IPF patients gradually develop respiratory failure and die within 2-4 years. There is no cure for IPF. While most cases of IPF occur in people who do not have family members with the disease, some cases of IPF are found in families, called familial IPF. The researchers found genetic mutations in telomerase in several families with IPF. Telomerase is the enzyme that maintains stability of the end of a chromosome, the region referred to as a telomere, throughout the life of the cell and during cell division. Lack of telomerase can lead to telomere shortening, resulting in cell death. The researchers suspect that telomerase dysfunction in cells lining the alveoli, or air sacs at the end of the airways, is responsible for the development of lung fibrosis in people with IPF with telomerase mutations. They also think that similar processes may be at play in non-familial IPF. They will determine how telomerase dysfunction and telomere shortening affect alveolar cells and impact IPF. These studies will identify key components that may serve as future therapeutic targets in IPF.