

**American Lung Association of the Midland States  
Research Funded – 2008-09 Fiscal Year**

**OHIO**

**MATTHEW EXLINE, MD**

The Ohio State University, Columbus, OH

*Biomedical Research Grant* • Co-funded by the American Lung Association and the American Lung Association of the Midland States

***Protein May Help Protect Against Death From Sepsis***

**Apoptosis In Sepsis: The Role Of Humanin, A Novel Anti-Apoptotic Peptide.** While sepsis is a potentially deadly condition triggered by our immune system's response to severe infection, it appears that patients with sepsis do not die directly from their infection. Recent studies suggest that septic patients die due to a weakening of the body's immune system through a process of cell suicide, called apoptosis. Animal studies have shown that if apoptosis is halted then death from sepsis is reduced. A protein called humanin has been shown to block apoptosis. The researchers plan to verify that humanin is present in immune cells, and to study whether humanin is reduced in the blood of septic patients. They will evaluate whether the concentration of humanin in the blood helps predict the outcome of a septic patient, and whether a synthetic humanin can protect against death. This work will significantly improve the understanding of apoptosis in the immune system during sepsis and may lead to new therapies for septic patients.

**ROXANA ROJAS, MD, PhD**

Case Western Reserve University, Cleveland, OH

*Biomedical Research Grant* • Co-funded by the American Lung Association and the American Lung Association of the Midland States

***Gaining Insight Into How TB Germ Hides From Immune System***

**Regulation Of CD4+ T Cell Adhesion And Migration Induced By Mycobacterial Phosphatidy-linositol Mannosides.** Tuberculosis (TB) is a bacterial disease that primarily affects the lungs and is caused by Mycobacterium tuberculosis (Mtb). Many studies have shown that control of infection requires an intact, healthy immune system. However, control of infection does not eliminate all organisms from the lung (a state called latent TB.) Persons infected with Mtb are at risk of having the latent bacteria become reactivated. This is particular concern for those who may have suppressed immune systems, such as persons with HIV infection. There is a need to improve therapy against TB as well as develop preventive measures such as vaccines. Knowing how Mtb escapes recognition by the immune system and remains latent is important to design new approaches for TB control. Mtb's immune evasion mechanisms can affect two types of cells: macrophages and T lymphocytes. The researchers will study how Mtb affects T lymphocytes and regulates their functions. Ultimately this research will contribute to efforts to develop more effective therapies and vaccines against TB, which remains a major public health threat worldwide.

**HUAJING WAN, PhD**

Children's Hospital Medical Center, Cincinnati, OH

*Senior Research Training Fellowship* • Co-funded by the American Lung Association and the American Lung Association of the Midland States

***'Master' Regulatory Gene In The Lung Influences Disease And Repair Of Injury Roles Of KLF5 In Lung Morphogenesis And Injury.*** KLF5 is a master regulatory gene that influences many genes in the cells lining the embryo's airways during formation of the lung. This gene is also found in respiratory cells that play a role in repair after injury. The researchers found that mice without the gene died from respiratory failure at the time of

birth. Their initial studies demonstrated that the loss of the gene resulted in abnormalities in the growth of airway smooth muscle, a lung tissue that plays a key role in airway inflammation and bronchial hyper-responsiveness (airway “twitchiness”). Overgrowth of airway smooth muscle can lead to respiratory disorders, including asthma, chronic obstructive lung disease, and bronchopulmonary dysplasia in preterm infants recovering from respiratory distress. Preliminary data also showed that KLF5 is rapidly induced following extensive injury of the adult lung. The researchers will study mice to identify genes and processes that KLF5 regulates in the surface of the airway walls that signal to the underlying smooth muscle. Understanding the roles of KLF5 in the lung will provide knowledge to better understand lung diseases and find novel ways to treat them.

**SCOTT WESSELKAMPER, PhD**

University of Cincinnati, Cincinnati, OH

*Biomedical Research Grant* • Co-funded by the American Lung Association and the American Lung Association of the Midland States

***Seeking Genes That Control Susceptibility To Dangerous Respiratory Infection***  
**Host Susceptibility To Pseudomonas Aeruginosa Respiratory Infection.**

*Pseudomonas aeruginosa* (PA) is a common bacteria that is a major cause of respiratory infections in patients who have recently received treatment in a hospital or a health care service unit. Patients whose immune systems are in a weakened state are at increased risk for PA infection. It is also the leading cause of illness and death in patients with cystic fibrosis. The bacteria can develop resistance to antibiotics, and is able to flourish in harsh environments. This also makes PA lung infections difficult for doctors to treat. The researchers hope to identify genetic factors that control susceptibility to PA respiratory infection. They will use several strains of mice and examine the clearance of the bacteria from their lungs, as well as the ability of immune-system cells known as macrophages to engulf the bacteria. They will analyze the results to determine unique genes that link to PA respiratory infection, which can be further studied to develop new therapeutics for the treatment and prevention of infection.

**MICHIGAN**

**CARLOS SEREZANI, PhD**

University of Michigan, Ann Arbor, MI

*Senior Research Training Fellowship* • Co-funded by the American Lung Association and the American Lung Association of the Midland States

***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 world-wide, 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 AM's 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.

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

Wayne State University, Karmanos Cancer Institute, Detroit, MI  
*Lung Cancer Discovery Award* • Funded in partnership among the American Lung Association, the LUNGevery Foundation, and the American Lung Association of the Midland States

### ***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.

## **TENNESSEE**

## **WILLIAM LAWSON, MD**

Vanderbilt University Medical Center, Nashville, TN  
*Dalsemer Research Grant* • Co-funded by the American Lung Association and the American Lung Association of the Midland States

### ***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.