For more than 110 years, one of the essential foundations of the American Lung Association’s lifesaving mission has been medical research. The continuing search for better treatments and cures has helped cement our position as America’s leading organization fighting for healthy lungs. With your help, we are making strides every day to save lives by improving lung health and preventing lung disease.

Thanks to your support, this year the Lung Association is able to fund more than $6.51 million in research grants. This is a critical investment in a healthier future for millions of Americans, and can expand our understanding and advance treatments of acute, chronic and rare lung diseases.

Our research program consists of two distinct components—the Airways Clinical Research Centers (ACRC) network and the Awards and Grants program. Both programs benefit greatly from the power of collaboration. We know that we can do more, and save more lives, if we work together and combine resources.

The ACRC framework allows researchers to collaborate with each other, conducting large clinical trials across the United States that have a direct impact on care and treatment of patients with asthma and chronic obstructive pulmonary disease (COPD). This year, the ACRC network underwent a rigorous re-competition process, to produce the most qualified and robust network. The ACRC is not only the largest not-for-profit network dedicated to asthma and COPD research, but is now enhanced by the addition of new experts and partnerships with 17 centers, 25 trial sites and a data coordinating center.

Through our Awards and Grants program, we support the entire research career spectrum, from training awards to early and mid-career grants, and grants for established investigators. We are proud of the depth and diversity of this program, which funds promising research in a wide range of lung diseases like lung cancer, COPD, asthma and many others through 69 novel and innovative research projects.

The cultivation of strong strategic partnerships and collaborations have expanded our work in exciting ways and into new areas of investigation. Our research funding partners include the Alpha-1 Foundation, American Academy of Allergy, Asthma & Immunology, American Thoracic Society, Bonnie J. Addario Lung Cancer Foundation, and LUNGevity Foundation. These collaborations represent the opportunity to coordinate efforts with other non-profit partners to leverage available research funds and make the greatest impact on healthcare for patients.

We also want to thank the chartered Lung Associations that generously committed additional funds to our nationwide research program through our LUNG FORCE initiative, including the American Lung Associations of the Upper Midwest, Northeast, Southeast, Southwest, Midland States and Mid-Atlantic.

And I give our deepest thanks to all of our supporters who provided the much-needed support for our many research programs. As you read about our groundbreaking work in 2016-2017, I hope you share our pride in what we can accomplish together. With your help, we are saving lives, today and for future generations.

Harold P. Wimmer
We acknowledge and express our sincere gratitude to our research funding partners. We offer a special thanks to the American Lung Association of the Northeast and the American Lung Association of the Upper Midwest for their generous contributions for lung cancer research to the Lung Association’s nationwide initiative LUNG FORCE.

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The American Lung Association Airways Clinical Research Centers (ACRC) Network, formerly known as the Asthma Clinical Research Centers, is the nation's largest not-for-profit network of clinical research centers dedicated to asthma and chronic obstructive pulmonary disease (COPD) treatment research, attracting some of the best investigators nationwide. The ACRC Network conducts large clinical trials that will directly impact patient care for COPD and asthma.

Our Centers

The Network consists of 17 asthma clinical research centers throughout the country with 25 sites and a Data Coordinating Center managed by a team at Johns Hopkins University.

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**Effect of CPAP on Airways Reactivity in Asthma: A Randomized Sham-Controlled Clinical Trial**


**Study:** This study from the American Lung Association’s Airways Clinical Research Center Network, looked at whether continuous positive airway pressure (CPAP) reduced airways reactivity in asthma. Short-term studies of CPAP in asthma patients had previously shown reductions in airways reactivity in those using CPAP.

**Results:** Adherence to nocturnal CPAP was low and there was no evidence to support positive pressure as effective for reducing airways reactivity in people with well controlled asthma. Regardless, airways reactivity was improved in all groups, which may represent an effect of participating in a study and/or an effect of warm, humid, filtered air on airways reactivity and merits further investigation.

*The study was co-funded by the American Lung Association and the National Heart, Lung, and Blood Institute.*

**Gastro-oesophageal Reflux and Worse Asthma Control in Obese Children: A Case of Symptom Misattribution?**

Published by: *Thorax*, March 2016

**Study:** For unknown reasons, obese children report greater asthma symptoms. Asthma and obesity are both independently associated with gastroesophageal reflux symptoms (GER). Determining if obesity affects the link between GER and asthma will help us better understand the connection between obesity and asthma. The researchers conducted a cross-sectional study of lean and obese children aged 10-17 years old with persistent, early-onset asthma. Participants contributed demographics, GER and asthma questionnaires and lung function data. Researchers analyzed the results and determined associations between weight status, GER and asthma outcomes. Findings were replicated in a second well-characterized cohort of asthmatic children.

**Results:** Obese children had seven times higher odds of reporting multiple different types of GER symptoms. Asthma symptoms were closely associated with GER scores in obese patients but not in lean patients. A significant but weaker association between GER and asthma symptoms was seen in lean patients compared with obese patients in the replicate cohort. GER symptoms are more likely to associate with asthma symptoms in obese children. Better lung function among children reporting gastro-oesophageal reflux and asthma symptoms suggests that misattribution of GER symptoms to asthma may be a contributing mechanism to excess asthma symptoms in obese children.

*The study was funded by the American Lung Association.*
Predictors of Asthma Exacerbation Among Patients With Poorly Controlled Asthma Despite Inhaled Corticosteroid Treatment

Published by: American College of Allergy, Asthma & Immunology, February 2016

**Study:** The American Lung Association’s Airways Clinical Research Centers Network looked at whether an asthma exacerbation is related to decreased quality of life and more visits to doctors. All of the patients included in this study were taking inhaled corticosteroid treatment. Knowing warning signs that predict exacerbations can help doctors and patients choose the best treatments for their asthma. The researchers looked at data collected on adults and children who continued to have asthma symptoms despite being on an inhaled corticosteroid. The studies were the Study of Acid Reflux in Children with Asthma and the Study of Acid Reflux in Adults with Asthma. Both of these studies were multicenter, randomized, double-blinded, placebo-controlled trials.

**Results:** On average, younger children were more likely to have an asthma exacerbation, other patient characteristics like sex, race and obesity were not linked to exacerbations. They also showed that having to go to a healthcare provider for asthma symptoms were at higher risk as well. In adults, age, sex, race, obesity and smoking status were not associated with increased risk of exacerbations. However, scores on questionnaires that assessed current asthma symptoms or asthma related quality life were associated with future asthma exacerbations in adults. These findings could help clinicians identify patients who are at higher risk for exacerbations and thus candidates for more aggressive asthma controller therapy.

*The study was funded by the American Lung Association.*

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**What are the benefits of participating in an ACRC clinical trial?**

- Taking part in a study may help doctors understand how to better treat the condition for other patients, even if you don’t personally benefit.
- During the study, you will receive lung function testing, study treatment, physical exams, additional monitoring and health education.
- You will have opportunities to learn better ways to live with your disease.
- All study-related care and study-related treatments are provided at no cost to you or your insurance company.
- If you qualify, you will be compensated for your time and expenses.

For more information about American Lung Association Airways Clinical Research Centers studies, visit Lung.org/acrc-trials.
American Lung Association funds medical research that delivers the hope of a longer, healthier life. We are proud to be currently funding more than $6.51 million in groundbreaking lung health research. This year the Lung Association is funding a total of 69 investigator-led research projects at 50 institutions throughout 22 states.

The American Lung Association is committed to funding quality groundbreaking research to help find improved treatments and cures for lung disease. Today, the American Lung Association funds scientific research through the Awards and Grants program with one goal in mind: to save lives by improving lung health and preventing lung disease. The Lung Association is particularly interested in highly meritorious research projects consistent with our strategic imperatives:

- Reduce the burden of lung disease on patients and their families, and improve quality of life for those living with lung disease
- Improve the air we breathe so it will not cause or worsen lung disease
- Defeat lung cancer
- Eliminate tobacco use and tobacco-related diseases
We encourage original concepts that drive research including projects that focus on:

- Combination therapies
- Biomarker discovery and validation
- Novel screening for non-high risk populations
- Translational therapeutic treatments among cancer types

For more than 110 years the American Lung Association Awards and Grants program has been funding researchers at important crossroads of their careers, typically those still in training or just gaining independence as faculty at institutions. Through this 'career-ladder' funding structure, we support a community of researchers dedicated to lung health and committed to lung disease research. This ensures that there will be scientists and medical experts working to advance the pace of lung disease research progress for years to come.

**Steps on the American Lung Association Career Ladder**

[Ladder diagram with steps:

- Lung Cancer Discovery & Allergic Respiratory Awards: Mid-Career + Established Scientists
- Research Grants: Junior Level Scientists
- Senior Research Training Fellowship: Post-Doc Trainees—MD & PhD
- Lung Health Dissertation Grant: Doctoral Students]

We invite you to learn more about this year's American Lung Association Awards and Grants researchers and their important projects. Please note the research projects have been categorized by their primary research topic. Many projects have an impact on multiple topics, and to view and filter by keywords please visit Research Awards Nationwide online at [Lung.org/ran](http://www.Lung.org/ran).
LUNG CANCER

Lung cancer kills more men and women than any other form of cancer. It is estimated that more than 158,000 Americans will die of lung cancer in 2016, accounting for approximately 27 percent of all cancer deaths. Lung cancer is the second most commonly diagnosed cancer in both men and women, with an estimated 224,000 new cases being diagnosed in 2016.

**Women and Lung Cancer**

The American Lung Association continues to focus on lung cancer in women. LUNG FORCE is a nationwide initiative led by the American Lung Association to unite women to stand together against lung cancer. Lung cancer is the number one cancer killer of women and has one of the lowest five-year survival rates of all cancer types. We'd like to thank the American Lung Association of the Upper Midwest and the American Lung Association of the Northeast for their contributions to this effort.

In addition, we will invest $5 million in increasing public health promotion including awareness of early detection tools, such as CT screening; provide patients with information about clinical trials, biomarker testing and support from the first day of diagnosis; and advocate for increasing federal funding for lung cancer research from $362 million to $450 million by 2020.

**Awards & Grants**

The American Lung Association Awards and Grants supports a rich array of studies in lung cancer. This year, Lung Association researchers are casting a broad net to find and develop new therapies. Much of this new work is in the area of precision medicine or "personalized treatment." These targeted therapies focus on finding the unique genetic makeup of a person’s tumor and developing and using drugs that are designed to be most effective for that patient.

We are funding research into how lung cancer tumors become resistant to drug therapy and how to stop the process. We are supporting remarkable new techniques, such as using mutant cancer genes against the tumor's own growth. One study is looking at using new formulations of treatment that may better target lung tumor cells. Another is assessing whether the effectiveness of CT screening for lung cancer seen in a national trial translates into real-world benefits in everyday medical practice. We are also funding research that could determine if radiation during heart procedures causes women to have a greater chance of developing lung cancer compared to men. Another study could lead to treatment that would stop the spread of lung adenocarcinoma. This work all addresses and attempts to reduce the burden of lung cancer.
ANKIT BHARAT, MD
Northwestern University
American Lung Association Biomedical Research Grant
Funded by the American Lung Association’s LUNG FORCE

The Role of Carbon Dioxide in Stopping Lung Healing After Lung Cancer Surgery

After lung cancer surgery, many patients have an air leak from the cut lung surface. If the leak does not heal, the person will develop abnormal connections in the airways called alveolopleural fistulae. This can lead to illness and death, as well as delaying the start of additional chemotherapy or radiation. We have observed that high carbon dioxide concentration inside the chest cavity impairs lung healing. We will study the relationship between increased carbon dioxide concentration and lung wound healing. The findings could lead to therapies that would reduce carbon dioxide or reverse carbon dioxide-induced changes in the lungs and promote lung repair.

Update: We have found that carbon dioxide impairs the ability of cells lining the air sacs called pneumocytes to move and proliferate. We have also been able to determine the way this occurs. We are continuing to study carbon dioxide and lung wound healing.

MELANIE BLEVINS, PhD
University of Colorado Denver
American Lung Association Senior Research Training Fellowship
Funded by the American Lung Association’s LUNG FORCE

Inhibiting the Formation of a Protein Complex to Treat Lung Cancer

CtBP1 is often overexpressed (meaning there are too many CtBP1 proteins produced) in certain types of cancer, including lung cancer. The CtBP1 protein interacts with many other proteins to form the CtBP1 complex, directing cellular growth and inhibiting cell death during normal organ development. When overexpressed in adult tissue, CtBP1 promotes cancer cell survival, making it an ideal drug target that could inhibit tumor growth and spread with limited side effects. We have developed molecules called peptides that can inhibit the formation of the CtBP1 complex in cell culture. We hope to further optimize our peptides to improve their effectiveness and eventually develop them into drugs for lung cancer therapy.

EMILY CHENG, MD, PhD
Sloan-Kettering Institute for Cancer Research
American Lung Association Lung Cancer Discovery Award
Funded by the American Lung Association’s LUNG FORCE

Overcoming Resistance to Newest EGFR-Inhibiting Lung Cancer Drugs

Epidermal growth factor receptor (EGFR) is a cell surface protein that promotes cell growth once controlled by epidermal growth factor. Some lung cancers have mutations in EGFR, resulting in hyperactivation of the receptor and uncontrolled proliferation of cancer cells. Most patients with EGFR mutant lung cancer initially respond to drugs that inhibit EGFR but eventually develop resistance. We will develop combination therapy to prevent and/or overcome resistance to the newest EGFR inhibitors by triggering a regulated form of cell death known as apoptosis in cancer cells. We will also investigate the mechanisms underlying resistance to the newest EGFR inhibitors.

Update: We have performed screening of a custom chemical library to identify agents that enhance apoptosis of an EGFR inhibitor called AZD9291. We have discovered molecules that work with AZD9291 to induce cell death in EGFR mutant lung cancer. We are also studying a combination strategy that may be able to overcome acquired resistance to AZD9291 and another EGFR inhibitor.

ERIC COLLISSON, MD
University of California, San Francisco
American Lung Association Lung Cancer Discovery Award
Funded in partnership with the American Lung Association of the Upper Midwest

Using Genomics to Attack Lung Cancer

While we are gaining insight into the workings of the lung cancer cell by the use of genome sequencing, our efforts at personalizing treatments currently only help about one in five patients. We will use new
therapies being developed to attack lung cancer, using mutant cancer genes against the tumor’s own growth. We will examine how a gene complex responsible for managing the way other genes are packaged affects the transformation of normal lung cells to cancer cells. We will also look at how mutations in a specific gene affect the formation and the progression of lung cancer.

**Update:** We have been studying a class of genes called the SWI/SNF genes in lung cancer. Our experiments have shown that mutations in these genes are likely early events in the establishment and evolution of cancer. We now think the genes may be involved in both early initiation of the cancer and its later growth and are trying to learn more about the liabilities cancer cells harboring these mutations have, and how we might capitalize on them.

**TUSHAR DESAI, MD, MPH**  
Stanford University  
*American Lung Association Lung Cancer Discovery Award*  
Funded by the American Lung Association’s LUNG FORCE

**Genetic Tools Help Shed Light on Lung Cancer Progression**

New methods are desperately needed for earlier detection of lung cancer as well as improved therapies that can eradicate the disease when it has spread. Fundamental to developing such approaches is understanding how lung tumors develop, grow and spread. We will use genetic tools to study these events using a mouse model of lung cancer that will allow us to observe changes at incredibly high resolution. This includes marking and tracing the behavior of individual tumor cells within the 3-D context of a growing lung tumor. These studies will pave the way for devising novel approaches to treat patients.

**Update:** We have made progress in year one measuring the contribution of specific lung cell types to adenocarcinoma, a type of lung cancer. We are having success in our strategy for tracking the activity of rare cells in established tumors. We will conduct experiments that will directly measure the contribution of individual cells to tumor expansion and provide insight into how this occurs.

**ANTHONY FABER, PhD**  
Virginia Commonwealth University  
*American Lung Association Lung Cancer Discovery Award*  
Funded by the American Lung Association’s LUNG FORCE

**Re-sensitizing Cells to Lung Cancer Targeted Therapy**

Genetic variations and cell mutations contribute to the growth and development of cancer. Drugs called targeted therapies are designed for specific gene mutations in particular cancers. One effective targeted therapy are EGFR inhibitors, which target lung cancers that have mutations in the EGFR gene. These mutations are often found in nonsmoking young patients. EGFR inhibitors are often effective for many of these patients but most eventually become resistant to the drugs. This can occur through a process in the cancer called epithelial-mesenchymal transition (EMT). We will screen for drug compounds that can reverse this effect in EMT cells and re-sensitize them to EGFR inhibitors.

**Update:** Cell studies have identified a mechanism of EMT-mediated resistance that is active in both EGFR-mutant lung cancers as well as KRAS-mutant lung cancers. Drug strategies to reverse this resistance have been identified, have shown to be effective and are being further tested.

**DAVID M. FELDWER, PhD**  
University of Pennsylvania  
*American Lung Association Lung Cancer Discovery Award*  
Funded by the American Lung Association’s LUNG FORCE

**Targeting Molecular Pathway Could Lead to Lung Adenocarcinoma Treatment**

Lung adenocarcinoma is a common malignancy of the lung. Although effective treatment options do exist for a small subset of these cancers, therapies that are widely applicable for these patients are lacking. We will study one molecular pathway, known as the Rb Pathway, which commonly malfunctions in lung adenocarcinoma. Our preliminary work has identified a critical mechanism that could be targeted therapeutically to restore function to the Rb Pathway. Our objective is
to better understand this therapeutic strategy, in order to develop treatments that will be effective in the vast majority of lung adenocarcinoma patients.

MARK M. FUSTER, MD
Veterans Medical Research Foundation & University of California, San Diego
American Lung Association Lung Cancer Discovery Award
Funded by the American Lung Association’s LUNG FORCE

Disrupting Complex Sugars on Immune Cells Could Inhibit Growth of Lung Cancer

We will identify how disrupting a unique complex sugar molecule known as heparan sulfate (HS) on immune cells called dendritic immune cells (DCs) may inhibit cancer growth. DCs in lung cancer often become poorly functional and immature, ultimately promoting suppression of the immune system by inhibiting the actions of anti-tumor immune cells called T cells. We will study the mechanisms that govern the movement and maturation of dendritic immune cells that are dependent on HS, examining how the targeted molecular changes affect their movement and ability to interact with T cells. Using mouse models of lung cancer, we will also begin to examine how novel HS inhibitors might boost the ability of dendritic cells to fight cancer. This research could lead to new strategies to cure cancer through the immune system.

SHARAD GOYAL, MD
Rutgers, The State University of New Jersey
American Lung Association LUNG FORCE Lung Cancer in Women Award
Funded by the American Lung Association’s LUNG FORCE

Does Radiation From Heart Procedures Increase Risk of Lung Cancer?

Heart disease is the leading cause of death in the United States and patients often need procedures to see the extent and location of the disease. These procedures all expose patients to radiation, which is thought to cause cancer. Our goal is to determine if radiation during heart procedures causes women to have a greater chance of developing lung cancer compared to men. We believe our findings may reduce the incidence and mortality of lung cancer in patients. By being able to discuss the risks, benefits and alternatives to medical imaging, patients will be better informed of their risk of developing cancer.

LIDA HARIRI, MD
Massachusetts General Hospital
American Lung Association Senior Research Training Fellowship
Funded by the American Lung Association of the Northeast

Does Tumor Environment Promote Drug Resistance in Lung Cancer Cells?

Despite advances in personalized lung cancer therapy, nearly all patients develop resistance to therapy within 6-12 months and their prognosis remains poor. We will study how non-tumor cells in the environment can help tumor cells survive during drug therapy. We will use a combination of cell culture studies and cutting-edge optical imaging to carefully track tumor cells, their environment, and their response to therapy in lung cancer mouse models. Our results will help us determine if the tumor environment promotes drug resistance in lung cancer cells and how this occurs. Our findings could uncover methods to detect and inhibit drug resistance, which would improve response to therapy and increase survival in patients with lung cancer.

Update: Some lung cancers have mutations in a gene called EGFR, resulting in uncontrolled proliferation of cancer cells. We have shown that secreted factors from cells called fibroblasts enable EGFR mutant lung cancer cells to survive during targeted therapy with a treatment called gefitinib. We have also found other factors that protect EGFR mutant lung cancer cells from gefitinib therapy. We will continue to investigate the role of fibroblasts in drug resistance using both in vitro techniques and mouse models of EGFR mutant lung cancer.
LUNG CANCER

KHALED HASSAN, MD
University of Michigan, Ann Arbor, MI
American Lung Association Lung Cancer Discovery Award
Funded by the American Lung Association’s LUNG FORCE

Overcoming Resistance to Lung Cancer Drugs

Recently, multiple genetic mutations have been identified in patients with lung cancer. These mutations are responsible for tumor growth and are valuable targets for treatments. Epidermal growth factor receptor (EGFR) is a protein on the surface of cells that is mutated in lung cancer. Drugs that target EGFR activity, called EGFR inhibitors, are very successful in shrinking tumors and extending life. Unfortunately, almost all patients treated with these drugs develop resistance, and their cancers progress. Understanding how this resistance occurs is vital in prolonging response and survival. We aim to reveal the mechanism of resistance to EGFR inhibitors, which will provide new targets for treatment. Combining EGFR inhibitors with drugs that prevent resistance development could be introduced to early phase clinical trials within a few years.

JUNG-WHAN KIM, PhD
The University of Texas at Dallas
American Lung Association Lung Cancer Discovery Award
Funded by the American Lung Association’s LUNG FORCE

Protein May Hold Key to New Treatments for Squamous Cell Lung Cancer

Squamous cell carcinoma is a type of lung cancer accounting for 25-30 percent of all lung cancers. Most currently available targeted therapies are not effective for this type of cancer, and the prognosis of treating squamous cell carcinoma with conventional chemotherapies is poor. Therefore, it is imperative to identify molecular abnormalities that are uniquely associated with squamous cell carcinoma in order to develop new treatments. We have found that glucose transporter 1 (GLUT1), a protein that uptakes cancer cell’s major nutrient, glucose, is remarkably elevated in squamous cell carcinoma as compared to other types of lung cancer. We will test if elevated GLUT1 is an essential contributor to the growth of squamous cell carcinoma and if targeting GLUT1 or glucose consumption can stop the growth of this disease.

MICHELLE CHRISTINE MENDOZA, PhD
University of Utah
American Lung Association Biomedical Research Grant
Funded by the American Lung Association’s LUNG FORCE

Stopping Lung Cancer Cell Invasion

The growth of lung cancer involves cancer cell invasion, which can lead to loss of lung function and accelerated cancer progression. Understanding how invasion is controlled is essential to improving therapeutic strategies for early-stage locally advanced tumors. Common lung cancer mutations increase their signaling, or communication, through a cell pathway called ERK. Our preliminary data show lung cancer movement is blocked when ERK signaling is blocked. We will determine the mechanism by which lung cancers gain high levels of ERK activation and how ERK promotes lung cancer invasion. We hope to identify targets for lung cancer treatment by inhibiting the ERK pathway.

SWETA MISHRA, PhD
Massachusetts General Hospital
American Lung Association Senior Research Training Fellowship
Funded by the American Lung Association of the Northeast

Discovering Protein’s Role in Resistance to Lung Cancer Chemotherapy

Resistance to chemotherapy is a major challenge in the treatment of patients with lung cancer. Cancer cells possess the ability to amplify parts of their genome, which in turn, protects the cells from chemotherapy. We have recently discovered a protein responsible for amplifying specific regions of the genome involved in resistance. We will investigate the role of this protein, KDM4A, and how the environment present inside lung tumors, such as low oxygen, can regulate KDM4A levels. We will also determine how tumor cells respond to drugs that inhibit KDM4A regulators. Our research could identify novel therapeutic targets for treating drug-resistant non-small cell lung cancer.

Update: We have identified a network of chromatin...
regulators—chemicals that play fundamental roles in the regulation of gene expression and chromosome maintenance—that impact a cancer gene called KRAS. This mutation, currently untreatable, is amplified and mutated in non-small cell lung cancer. The discovery of chromatin regulators for KRAS will result in the identification of novel therapeutic targets, with clinical implications for lung cancer diagnosis and therapy.

JOHN POIRIER, PhD
Memorial Sloan Kettering Cancer Center
American Lung Association/LUNGevity Foundation Career Development Award
Funded in partnership with LUNGevity Foundation
Molecular Mechanisms of Acquired Drug Resistance in Small Cell Lung Cancer

Small cell lung cancer (SCLC) is an aggressive, and exceptionally lethal type of lung cancer that is remarkably sensitive to therapy with a combination of two drugs, cisplatin and etoposide, even in patients with extensive-stage disease. However, many patients find their SCLC tumors return, now resistant to chemotherapy. We will study how SCLC tumors acquire resistance using two parallel approaches: studying resistance in patient samples and in patient tumors grown in mice. Targeting the key determinants of acquired chemo-resistance could be integrated into first-line treatment, and may drive rational targeted therapeutic studies for recurrent disease.

Update: We are studying the mechanisms of resistance to chemotherapy in SCLC. We have identified two mechanisms of resistance—an increase in expression of a protein called TWIST1 and loss of a protein called SLFN11, which is required for tumors to respond to cisplatin and etoposide chemotherapy. SLFN11 appears to be silenced through mechanisms involving a third gene called EZH2. Small molecule inhibitors of EZH2 are capable of restoring SLFN11 protein expression, and sensitivity to chemotherapy. We are now investigating the possibilities of translating this finding into treatment.

LINDA RESAR, MD
Johns Hopkins University
American Lung Association Lung Cancer Discovery Award
Funded in partnership with the American Lung Association of the Upper Midwest
Therapy Blocks Protein Involved in Lung Cancer Growth

To address the urgent need for more effective lung cancer treatments, we are developing an innovative therapy called Spiegelmers. Spiegel means “mirror” and Spiegelmers are small molecules that bind as “mirror images” to critical regions of a protein to disrupt its function. Our Spiegelmers target a key regulator protein, called HMGA1, which is required by lung cancer cells to grow, invade and spread to distant sites. Spiegelmers that block other proteins have already been shown to be safe and effective in patients with other types of cancer. We expect to rapidly translate our results to the clinic to improve therapy for lung cancer patients.

Update: In our preliminary results, we found that blocking expression of HMGA1 halts cancer cell growth in most cancer cells tested. The anti-HMGA1 Spiegelmer, however, was not effectively delivered to the majority of the cancer cells. We are therefore testing different delivery approaches for HMGA1 inhibitors. In addition, we are testing a new Spiegelmer (NOX-A12) to block a related pathway in lung cancer. This Spiegelmer also enhances immune cell infiltration into tumors, which we expect to improve outcomes for lung cancer patients. We will continue to test our new Spiegelmer and other delivery approaches to target HMGA1 in lung cancer cells for lung cancer.
SAMEEK ROYCHOWDHURY, PhD, MD  
The Ohio State University  
**American Lung Association Lung Cancer Discovery Award**  
Funded in partnership with the American Lung Association of the Midland States

**Identifying Gene Mutations in Lung Cancer That Can Be Attacked With Smart Drugs**

We now understand that lung cancer is not a single disease, but instead classified by different gene alterations or mutations that are either inherited or arise spontaneously. Despite dramatic advances, up to 50 percent of patients do not have gene alterations that can treated with targeted therapies, also known as “smart drugs.” We will implement a precision cancer medicine study for patients with advanced lung cancer who do not have effective standard treatment options, and offer them an innovative testing strategy using customized targeted DNA and RNA sequencing to identify genetic mutations that can be attacked with existing targeted therapies.

**Update:** We have developed two testing strategies utilizing DNA and RNA sequencing to identify novel gene mutations in patients seen in our precision cancer medicine clinic. In year one of the project, we have evaluated 38 patients and identified patients with mutations that led to treatment with novel therapies.

BRITTANY SEXTON, PhD  
Massachusetts General Hospital  
**American Lung Association Senior Research Training Fellowship**  
Funded by the American Lung Association’s LUNG FORCE

**Discovering Inner Workings of Enzyme Could Lead to Lung Cancer Treatment**

Abnormal duplication of genes contributes to lung cancer risk and associated drug resistance. We will study the enzyme KDM4A, which is overexpressed (makes too many copies) in lung cancer, and leads to a higher frequency of copies of genetic regions linked to drug resistance and increased potential for the spread of lung cancer. KDM4A overexpression in cancer cells also results in reduced response to chemotherapy. We will determine the relationship between KDM4A expression levels, extra copies of drug resistant regions and their impact on drug resistance in lung cancer. These studies could lead to development of new treatments for lung cancer.

DAVID SHACKELFORD, PhD  
University of California, Los Angeles, Los Angeles, CA  
**Momentum Research Award**  
Funded in partnership with the Addario Lung Cancer Foundation

**Selectively Targeting Metabolic Needs Unique to Lung Cancer**

Many women with lung cancer bear mutations in the epidermal growth factor receptor (EGFR) gene that drives cancer. For the majority of women with EGFR mutant lung tumors, the initial response to treatment that targets the mutation is temporary, eventually developing a resistance to the treatment. We are testing drugs that inhibit the tumor’s ability to metabolize nutrients such as glucose and amino acids. The restriction of metabolism causes an "energetic crisis" in the tumor cells and kills the cancer cells while preserving the health of the normal surrounding tissue. We will tailor precise therapies to inhibit tumor cell metabolism and growth. This approach represents a new strategy for the treatment of this disease as we move toward developing personalized therapeutic strategies that selectively target the metabolic needs unique to the patient’s lung tumor(s) as a novel way of overcoming therapy resistance.

SAMIR SONEJI, PhD  
Dartmouth College  
**American Lung Association Lung Cancer Discovery Award**  
Funded by the American Lung Association of the Northeast

**Does the Effectiveness of CT Screening Translate into Real-World Benefits?**

For the first time, a tool used in screening for lung cancer has been shown to reduce lung cancer deaths. The National Lung Screening Trial (NLST) concluded that computed tomography (CT) screening, compared to chest
X-ray, reduced lung cancer mortality by 20 percent. Yet the effectiveness of CT screening demonstrated in NLST may not translate to similar reductions in lung cancer deaths as screening is implemented in everyday practice. Barriers, including lack of knowledge and high rates of treatment-related complications may reduce the benefit of CT screening. We will assess the challenges facing patients and healthcare providers to fully realize the benefits observed in NLST. The study will improve clinical practice and narrow racial disparities in lung cancer mortality.

**Update:** We have identified high rates of major complications and post-surgical mortality in everyday practice for lung cancer patients. This could represent a significant barrier to effective lung cancer screening in the U.S. population. In year two of the award, we will assess contemporary rates of screening in the U.S. population. We will also quantify the potential long-term benefit of lung cancer screening given prevailing rates of complications.

**SRINIVAS SRIDHAR, PhD**
Northeastern University
*American Lung Association Lung Cancer Discovery Award*
Funded by the American Lung Association’s LUNG FORCE

**Injectable Lung Cancer Therapy with PARP Inhibitors Could Better Target Tumor Cells**

Lung cancer is relatively insensitive to chemotherapy with platinum drugs and radiation therapy. An enzyme called Poly-ADP-ribose-polymerase (PARP) repairs damaged DNA. Treating tumors with PARP inhibitors like olaparib results in selective tumor cell death. Current oral delivery of olaparib is highly inefficient due to low bio-availability, meaning only a small proportion of the drug enters the circulation and accumulates in the tumor. Using nanotechnology, we will develop and test two injectable nanoparticle formulations of olaparib. These novel targeted nanoparticle formulations will ensure the delivery of clinically relevant doses of olaparib and cisplatin specifically to the lung tumor, increasing the ability to kill cancer cells while minimizing toxic effects for both localized and metastatic tumors.

**ERIC SWEET-CORDERO, MD**
Stanford University
*American Lung Association Lung Cancer Discovery Award*
Funded in partnership with the American Lung Association of the Upper Midwest

**Examining Cell-to-Cell Communication for Clues about Lung Cancer**

Normal cells and tumor cells communicate with each other in similar ways. Often, the genes involved in communication in normal cells are “hijacked” by tumor cells to promote unregulated growth and survival. One mechanism of communication between cells that seems to be important in lung cancer is called the Notch signaling pathway. We will study how Notch is activated in lung cancer and what changes occur in cells as a consequence of this activation. Understanding how Notch proteins are activated in tumor cells may identify novel therapy approaches for non-small cell lung cancer.

**Update:** Our preliminary studies have begun to provide insight into Notch proteins. We have been able to perform RNA sequencing of Notch-positive and Notch-negative cells. We anticipate that the analysis of this sequencing will provide insight into the gene pathways that are altered by Notch activation in non-small cell lung cancer.

**PHUOC TRAN, MD, PhD**
Johns Hopkins University
*American Lung Association Lung Cancer Discovery Award*
Funded by the American Lung Association’s LUNG FORCE

**Targeting a Gene Involved in Lung Cancer Drug Resistance**

Many lung cancers are caused by cell mutations that make them highly responsive to targeted treatments, such as the EGFR inhibitor erlotinib. Lung cancers with EGFR mutations initially respond very well to erlotinib but all patients eventually develop resistance. One way resistance develops is through a change called epithelial/mesenchymal transition (EMT). A gene called Twist1 is one of the key regulators of EMT. Our previous work suggests Twist1 is overly active in many lung tumors and plays a role in development
of the cancer. We will study the role of Twist1 in erlotinib resistance in EGFR mutant lung cancers. The findings could lead to therapy that reverses Twist1-induced erlotinib resistance.

**Update:** Part of our research has involved determining whether Twist1 may regulate the NOX4 gene and whether inhibiting NOX4 could reverse Twist1-induced drug resistant lung tumors. We have preliminary data that showed a significant difference in treatment response when a NOX4 inhibitor is used in combination with the lung cancer drug erlotinib as compared to erlotinib alone, in a genetically engineered lung cancer model specifically designed to be resistant to erlotinib.

**LINDA VAN AELST, PhD**  
Cold Spring Harbor Laboratory  
**American Lung Association Lung Cancer Discovery Award**  
Funded in partnership by the American Lung Association of the Northeast

**Seeking Treatment to Stop Spread of Lung Adenocarcinoma**

Detection of lung adenocarcinoma (ADC) is difficult and most patients are diagnosed at an advanced stage of the disease. Cancerous cells frequently metastasize, so that even when the tumor is removed from the lung, patients quickly relapse as the cancer spreads. These facts suggest that tumor cells seed distant organs prior to diagnosis or initial treatment. Therefore, effective treatments must target metastases. Little is known about how this process occurs. We have established an animal model for metastatic lung ADC that will allow us to identify and characterize the genes that drive growth of metastatic lung ADC tumors. Screening these potential drug targets against patient data will confirm which of these genes are clinically important.

**GUANGHU WANG, PhD**  
Georgia Regents University  
**American Lung Association Biomedical Research Grant**  
Funded by the American Lung Association of the Southeast

**Fighting Drug Resistance in Lung Cancer**

Lung cancer treatment is hampered by a lack of understanding of how the cancer becomes resistant to treatment, and how the disease spreads. We will study the function of a gene called Spns2 and investigate whether a decrease in activity of this gene causes drug resistance. Additionally, we will examine whether a combination of two FDA-approved drugs reduces lung cancer drug resistance for patients who have reduced Spns2 activity. Our hope is that these results will provide vital insights into the molecular mechanisms of lung cancer drug resistance, which will lead to more comprehensive treatments for patients with advanced lung cancer.

**Update:** We have found that a decrease in activity of Spns2 increased drug resistance in non-small cell lung cancer cell lines. We are in the process of testing drug resistance in lung cells from mice that are deficient in this gene. We have also determined which enzymes are altered when Spns2 activity is decreased and are in the process of determining the molecular pathways through which this decreased activity occurs.
HENNING WILLERS, MD
Massachusetts General Hospital
American Lung Association Lung Cancer Discovery Award
Funded in partnership with the American Lung Association of the Northeast and the American Thoracic Society

Attacking Lung Cancer Before It Develops Drug Resistance

Targeted drugs like erlotinib commonly shrink lung cancers that depend on mutated EGFR (EGFRmut). However, invariably cancer cells survive, become drug resistant and cause tumor regrowth. In this study, we propose attacking the tumor before drug resistance and recurrence occur. We will take advantage of a unique clinical trial that allows us to biopsy EGFRmut tumors before drug resistance develops. Coupled with laboratory studies we will find out how tumor cells manage to survive the targeted therapy and how we can disrupt this ability. Our research may lead to a dramatic change in how we treat EGFRmut cancers, thereby prolonging lives and perhaps even achieving cures in some patients.

LUNG FORCE is a nationwide initiative led by the American Lung Association to unite women to stand together against lung cancer.

- We work to improve awareness of lung cancer and be a force that changes the startling facts.
- We aim to change people’s minds about what it means to have lung cancer—so that everyone understands that anyone can get lung cancer.
- We raise our voices for research innovation that will lead to early detection for all and better treatments that give everyone a fighting chance.

Learn more—get involved: LUNGFORCE.org
Tuberculosis (TB) is a worldwide epidemic that kills approximately 1.5 million people each year. Given that TB is transmittable and that global travel and migration has increased, this international problem remains of great concern to Americans.

Tuberculosis is of special importance to the American Lung Association. Our organization was the first voluntary health agency in America, founded as the National Association for the Study and Prevention of Tuberculosis by a group of doctors and concerned citizens. Over a difficult 50-year fight, the Lung Association played a critical role in developing and funding increasingly effective weapons to prevent, detect and treat the disease, and TB is now largely eradicated in the US. Today we continue to fund research with these same goals.

Many people who are infected with the bacterium that causes TB, called Mycobacterium tuberculosis (Mtbc), do not go on to develop active TB - their immune system protects them. But those with immune systems damaged by AIDS or other illnesses may develop active TB.

**Awards & Grants**

The American Lung Association is supporting research seeking to identify genes that contribute to TB susceptibility, which will improve understanding of the body’s response to this deadly disease.

It was recently discovered that Mtbc secretes nanometer-sized particles called membrane vesicles that likely contribute to Mtbc survival and lung disease. One study is looking at factors that regulate the production of Mtbc membrane vesicles during infection, which could lead to a new potential target for new TB drugs.

Another major problem in the treatment of TB is the development of resistance to standard drugs. We are funding a project that is investigating whether a novel protein essential for the growth of TB bacteria and might be an ideal drug target.

In addition, TB is difficult to diagnose in children and treatment delays can lead to severe and fatal forms of TB. One of our researchers is seeking to understand missed diagnosis and treatment delays in pediatric tuberculosis, in order to prevent this problem from occurring in the future.

Lastly, people who are infected with Mtbc are prescribed antibiotics to reduce the risk. Since they feel well and have to take the medication for many months, as few as one-third complete treatment. A research project we are funding will investigate whether daily text message reminders improve compliance with TB treatment.
GILLIAN BEAMER, VMD, DACVP, PhD
Tufts University
American Lung Association Biomedical Research Grant
Funded in partnership with the American Lung Association of the Northeast

Seeking to Identify Genes That Contribute to TB

Our project focuses on discovering new genetic mechanisms that contribute to pulmonary tuberculosis (TB), which causes disease and death in millions of people each year. We will use three novel strategies. The first is a new experimental mouse population that closely models the human population. The second is the use of computer algorithms to study traits of granulomas (aggregations of cells that are a hallmark of TB) and sites of lung damage. Third, we will integrate the complex data into testable models of TB. This research will allow us to identify genes that contribute to TB susceptibility and to improve understanding of the body’s response to this deadly disease.

Update: We are the first to show that the experimental mouse population we are using contains a remarkable spectrum of responses to TB, with mice that are highly susceptible and those that are relatively resistant to infection. We published the first report of M. tuberculosis infection in this experimental mouse population and showed we could predict the disease susceptibility category with 77 percent accuracy using three molecular indicators. Now we are focusing on increasing the amount of data that we have acquired to study gene expression profiles in the lungs of super susceptible, susceptible, resistant and non-infected mice.

MOLLY FRANKE, SCD
Harvard Medical School
American Lung Association Social Behavioral Research Grant
Funded by the American Lung Association of the Northeast

Understanding Missed Diagnoses and Treatment Delays in Pediatric Tuberculosis

Tuberculosis (TB) is difficult to diagnose in children and treatment delays can lead to severe and fatal forms of TB. Because children often cannot cough up sputum for testing and often have TB that is undetectable with usual tests, clinicians must diagnose TB based on signs and symptoms. We will study children who meet the standardized definitions for unconfirmed TB but in whom TB was not diagnosed by a physician. We will look for missed TB diagnoses and uncover the reason for discrepancies. We will also conduct interviews with parents, providers and field healthcare workers to better understand the factors that impede or facilitate rapid TB treatment initiation following a TB diagnosis.

YASU S. MORITA, PhD
University of Massachusetts Amherst
American Lung Association Biomedical Research Grant
Funded by the American Lung Association of the Northeast

Developing New TB Drugs That are Not Resistant to Antibiotics

Developing new tuberculosis (TB) drugs is particularly challenging because the bacteria that cause the disease have impermeable cell walls that block antibiotics. These cell walls contain a unique set of compounds categorized as glycolipids. Having shown that changing the structure of these glycolipids increases the antibiotic sensitivity of TB bacteria, our goal is to identify a protein involved in the production of glycolipids that can be targeted by new drugs. We have identified a novel protein that is involved in this process. We will investigate whether this protein is essential for the growth of TB bacteria and if it is located within the surface of the cell wall, making it an ideal drug target.
Using Texting to Encourage People to Take Their TB Medicine

While one-third of the world’s population is currently infected with the tuberculosis (TB) germ, only about 10 percent of those infected will develop TB disease. The remaining 90 percent have latent TB, meaning their immune system can successfully fight the infection. Treatment of latent TB with an antibiotic reduces the risk it will progress to active disease. However, since these individuals feel well and have to take the medication for many months, as few as one-third complete treatment. We will investigate whether daily text message reminders help people to take their medication, preferences for receiving the messages, and whether this approach is affordable for TB clinics.

Update: We have completed our form and database development, created a web-based texting application and have begun participant enrollment in our study. We plan to continue exploring the acceptability and feasibility of a texting intervention for increasing latent TB treatment adherence.

Particles in TB Membrane Could be Target for Treatment

Current tuberculosis (TB) treatment regimens involve taking several antibiotics for six to nine months, and compliance is a major issue. The incidence of drug-resistant TB is projected to cause a global health crisis in the coming decades and new TB drugs must be developed. It was recently discovered that the bacteria that causes TB, Mycobacterium tuberculosis (Mtb), secretes nanometer-sized particles called membrane vesicles that likely contribute to Mtb survival and lung disease. We will study the factors that regulate the production of Mtb membrane vesicles during infection. With this knowledge, we will develop experimental systems to study the role of membrane vesicles in TB and will explore vesicle secretion as a potential target for new TB drugs.

Who Will Develop Nontuberculous Mycobacterium Lung Disease?

Chronic lung disease due to nontuberculous mycobacterium (NTM) is increasingly common in the United States, usually affecting women and people over age 50. Mycobacterium avium complex (MAC) causes most NTM lung disease and is regularly found in municipal water supplies and soil. Most people inhale NTM during their lives but suffer no chronic infection, while others develop chronic, debilitating NTM disease that can require more than two years of antibiotic therapy. We will follow patients newly identified as being infected with NTM and evaluate whether their immune cell function predicts who will develop progressive disease. These results will help us better prevent and treat NTM.

Update: In year one we have enrolled over 200 NTM patients in our clinical trial, representing the broad spectrum of NTM disease. At the start of the study and again 12-18 months later, we collect blood, conduct health-related quality of life surveys, and do a complete medical history. In pilot evaluations we identified differences in response by immune cells called lymphocytes between various groups of patients. We will continue to follow up with further evaluations.
Asthma, allergy and chronic obstructive pulmonary disease (COPD) are all obstructive lung diseases, characterized by inflamed and easily collapsible airways, obstruction to airflow in and out of the lungs, and frequent doctor visits and hospitalizations. It is estimated that 32 million Americans have obstructive lung disease, with asthma and COPD being most common.

Asthma is a chronic but reversible disease that affects 24 million Americans, including 6.3 million children under the age of 18. Asthma can be a life-threatening disease if not properly managed.

COPD is not reversible and gets progressively worse over time. COPD, consisting of chronic bronchitis and emphysema, is now the third leading cause of death in the United States, killing 143,000 per year. In 2014, an estimated 10.9 million adults had COPD, but lung function tests suggest millions more may be undiagnosed. Although the major risk factor for COPD is cigarette smoking, there are other important risk factors such as air pollution and genetics.

**Awards & Grants**

This year the American Lung Association has a diverse portfolio of grants related to asthma, COPD and bronchopulmonary dysplasia.

Researchers are studying ways to reduce mucus production in both asthma and COPD. They are investigating how genes influence the development of cigarette smoke-induced COPD and how cigarette smoke leads to lung damage in emphysema. One study is looking at the role of excessively multiplying cells in pulmonary hypertension, a common complication of COPD. Another is examining lung stem cells that repair air sacs, which could lead to new treatment for emphysema. We are also funding a study looking at ways to increase adherence to supplemental oxygen therapy in people with COPD.

We are supporting several studies focused on the relationship between influenza and asthma. While asthma was the most common chronic condition among adults hospitalized during the 2009 influenza pandemic, asthmatic patients hospitalized with flu were half as likely to die or require intensive care compared to people without asthma. Findings from this research may lead to new influenza treatments.

Another researcher is exploring ways to block the development of cells involved in steroid-resistant asthma. Other areas of research include the regulation of lung inflammation in asthma; the immune system's role in asthma; genes important in controlling the immune system's response in allergic asthma; and the effect of mold in the lungs on severe asthma. All of these studies could lead to improved therapy for people with asthma.
ASTHMA

SUZANNE CASSEL, MD
Cedars-Sinai Medical Center
American Lung Association/AAAAI Foundation Allergic Respiratory Award
Funded in partnership with the AAAAI Foundation

Blocking Development of Cells Involved in Steroid-Resistant Asthma

It is becoming increasingly clear that asthma is not a single disease with one underlying cause. Treatments including inhaled or oral steroids are effective for many patients but not for all. Some people, most commonly those with severe or steroid-resistant disease, have a different type of inflammation in their airways that involves immune-system cells called Th17 cells. Better understanding of the way Th17 cells develop is important to devising new treatments to block them. We will identify the pathways by which different subsets of Th17 cells develop, which will provide insight to new ways to successfully treat these patients.

Update: In year one we have published our preliminary findings showing the central role of molecules called IL-1alpha and IL-1beta in driving asthma involving Th17 cells. We are continuing to research the impact of these molecules on Th17 cells in asthma.

NORA BARRETT, MD
Brigham and Women's Hospital, Inc.
American Lung Association/AAAAI Allergic Respiratory Diseases Research Award
Funded in partnership with the AAAAI

Understanding Role Receptor Involved in Lung Inflammation Plays in Asthma

People with asthma have high levels of molecules that play a role in inflammation called cysteinyl leukotrienes (cysLTs). Recent data from our group and other laboratories suggest that cysLTs promote asthma in unexpected ways. We plan to study the recently discovered cysLT receptor GPR99 and determine the way in which it controls lung inflammation. This research should advance our understanding of asthma development and uncover novel therapeutic targets for intervention.

SANGWOON CHUNG, PhD
The Ohio State University
American Lung Association Biomedical Research Grant
Funded by the American Lung Association of the Midland States

Deepening Our Understanding of Immune System’s Role in Asthma

The immune system normally protects against foreign bacteria and viruses. In asthma and other allergic diseases, the immune system can cause worsening symptoms. Asthma is widely considered to be a type of immune system response called “type 2,” which is linked strongly to allergic inflammation. Growing evidence indicates that inflammatory immune cells called monocyte and tissue macrophages influence the initiation, progression and resolution of type 2 immune responses. We will study a protein called FoxO1, which has a crucial role in a worsening type 2 immune responses. Understanding the role of FoxO1 and its effect on macrophages could lead to treatment approaches that will alleviate suffering and improve the health of patients with severe asthma.

YOICHI FURUYA, PhD
Albany Medical College
American Lung Association Biomedical Research Grant
Supported by the Mary Fuller Russell Fund

Does Asthma Protect Against Getting Sick With Flu and Pneumonia at the Same Time?

Asthma was the most common chronic condition among adults hospitalized during the 2009 influenza pandemic. However, asthmatic patients who were hospitalized with pandemic influenza were half as likely to die or require intensive care compared with people without asthma. There may be a connection between asthma and a less severe disease outcome. We have found that mice with asthma are resistant to being infected with both the influenza virus and bacteria that causes pneumonia. Understanding the mechanism of increased resistance to co-infection
may lead to development of new treatments for patients infected with both the influenza virus and pneumonia bacteria.

**Update:** We have found that asthma provided protection against a type of pneumonia infection in mice infected with a strain of influenza that is different from the one seen in the 2009 pandemic. This suggests our preliminary result is not due to the unique 2009 pandemic strain, and may apply more broadly to influenza A virus infection. We also found influenza-infected asthmatic mice were also resistant to methicillin-resistant Staphylococcus aureus (MRSA) infection. MRSA is an emerging bacterial pathogen associated with recent seasonal and pandemic influenza. These additional data strongly increased the clinical significance of our research.

**SUNIT JARIWALA, MD**
Albert Einstein College of Medicine, Inc.
American Lung Association/AAAAI Foundation Allergic Respiratory Award
Funded in partnership with the AAAAI Foundation

**Developing and Testing Software Tools to Help Manage Children's Asthma**

The ASTHMA-Educator is an innovative project that strives to improve asthma control in Bronx, New York. We developed and pilot tested an adult version of the ASTHMA-Educator, which is a software program (available for tablets and smartphones) that uses interactive touch-screen technology to deliver comprehensive asthma education to patients. Through videos and personalized algorithms, the tool covers asthma education topics such as the role of rescue versus controller medications, demonstration of inhaler technique, asthma action plan, environmental control and self-management strategies. This study will expand the existing ASTHMA-Educator software program to include pediatric patients. Our hope is that the program will lead to improved asthma outcomes, patient satisfaction and patient knowledge.

**AMIT PARULEKAR, MD**
Baylor College of Medicine
American Lung Association Clinical Patient Care Grant

**Effect of Mold in the Lungs on Severe Asthma**

Some patients with severe asthma may continue to have symptoms despite being treated with standard medicines, even at high doses. One possible reason is that some patients have fungi or mold in their airways or they are allergic to fungi or mold in the environment. However, there are limited tests to identify these patients, and we do not know whether having fungi that live in the lungs is the same as being allergic to fungi in the environment. We will try to better understand how allergy to fungi or having fungi in the lungs may lead to more severe asthma, and will test a new method of identifying fungi in the lungs.

**CATHERINE PTASCHINSKI, PhD**
University of Michigan, Ann Arbor
American Lung Association Biomedical Research Grant
Funded in partnership with the American Lung Association of the Midland States

**Studying Genes Important in Controlling Immune Response in Allergic Asthma**

While there are a number of genetic and environmental factors that drive allergic asthma, the mechanisms of the disease are still not fully understood. While many patients are able to control symptoms, some patients do not respond to treatment. We have identified a family of three genes – Hoxa5, Hoxb5 and Hoxc5 – that are important in controlling the immune response in allergic airway disease. We have shown that these genes are active in T cells, critical cells responsible for many of the symptoms of allergic asthma. This project seeks to understand how these genes function in T cells and in asthma. Understanding how these genes contribute to inflammation may help to identify new therapeutics.
AMALI SAMARASINGHE, PhD
University of Tennessee Health Science Center
American Lung Association Biomedical Research Grant
Funding in partnership with the American Lung Association of the Midland States
Molecules Found in Allergic Airways May Protect Against Influenza

Although asthma was a risk factor associated with increased hospitalization during the 2009 influenza pandemic, people with asthma were less likely to die from influenza compared with non asthmatics. Reasons for these seemingly contradictory results are unknown. Our data suggests that small proteins called resistin-like molecules, which are abundant in allergic airways, may play a role in reducing illness from influenza. The function of these proteins in respiratory viral infections has not been thoroughly investigated. We will examine the source and function of these proteins in influenza immunity. Our findings can be used to develop treatments for influenza virus infections.

Update: We found white blood cells called eosinophils have an antiviral effect during influenza infections. The availability of resistin-like molecules in the lungs correlated with the presence of eosinophils. We have determined that resistin-like molecules regulate the inflammatory response during allergic asthma and influenza. We are continuing to study how eosinophils may function as positive regulators of these molecules during influenza infection.

BRONCHOPULMONARY DYSPLASIA
KRITHIKA LINGAPPAN, MD
Baylor College of Medicine
American Lung Association Biomedical Research Grant
Protein May Play Role in Preventing Lung Problems in Premature Babies

Our research is aimed at preventing bronchopulmonary dysplasia in premature babies by identifying new therapeutic targets. We will be studying the protein GDF15 (Growth differentiation factor 15), which is believed to reduce inflammation, prevent cell death and increase blood vessel growth. We will investigate the role of GDF15 in neonatal lung injury to unravel the underlying mechanism. We will study whether mice lacking the gene for GDF15 have more lung injury. We will also investigate whether and how mice carrying the human gene for GDF15 are protected. These experiments will help us understand the role of this gene in the developing lung, thereby identifying a novel therapeutic target to improve lung health in premature babies.

COPD
HITENDRA CHAND, PhD
Florida International University
American Lung Association Biomedical Research Grant
Reducing Mucus Production in Asthma and COPD

Patients with chronic airway diseases such as asthma or COPD may suffer from abnormally high levels of mucus and chronic productive cough. This condition poses an increased risk for airway infection, decline in lung function and hospitalization. Airway plugging by excess mucus can be fatal if left uncontrolled. Exposure to cigarette smoke is strongly associated with chronic airway diseases like COPD and asthma. We will study the link between cigarette smoke exposure and excess mucus. Our studies have identified the pathways responsible for increased mucus production. We will target this pathway using a small molecule that can help reduce production of mucus.

Update: We ran a pilot experiment of cigarette smoke exposure, targeting the pathway using a small molecule to help reduce mucus production. Our studies have helped us develop a model that requires shorter exposure time to cigarette smoke to simulate disease conditions. We are currently analyzing these pathways and the effectiveness of small molecule inhibitors.
Prolonged exposure to cigarette smoke is the greatest risk factor for the development of COPD but emerging research suggests that genetic predisposition may also influence its development. We have previously shown that patients with a mutation in the gene Irp2 have increased levels of a protein called iron regulatory protein 2 and so, are more susceptible to cigarette smoke-induced COPD. Mice lacking the protein are protected from cigarette smoke-induced COPD. Using innovative experimental models of COPD, we will study how Irp2 and iron regulate responses of the lung to cigarette smoke. The findings may be useful in identifying therapeutic targets in COPD.

**Update:** In the year one, we have performed experiments to better understand the regulation of BK channels in various models of lung injury. We have examined the role of certain enzymes in immune cells called macrophages in mice bred with mutant BK channels. Through this research, we are gaining a greater understanding of the role of BK channels in emphysema development.

**MONICA GOLDKLING, MD**
Columbia University Medical Center
American Lung Association Biomedical Research Grant
Funded by the American Lung Association of the Northeast

How Does Cigarette Smoke Lead to Lung Damage in Emphysema?

Although we know that cigarette smoke is the primary cause of COPD, the way in which cigarette smoke exposure leads to lung damage is still not fully understood. Smoking has recently been identified to alter ion channel function essential for normal cellular responses to injury. We plan to study the role of the BK channel in lung destruction. Mice bred with mutant BK channels have reduced lung destruction when exposed to smoke despite developing airway inflammation. Understanding the role for BK channel function in lung injury may provide potential novel treatment approaches for patients with COPD.

**Update:** In year one of the project, 111 patients completed the instruments to measure personal and family factors likely to influence oxygen adherence. Data collection is ongoing, and will be completed in year two.
Pulmonary hypertension (PH) is a common complication of chronic obstructive pulmonary disease (COPD) that can worsen the chronic lung disease and impact patient survival. One of the main components of PH is the excessive multiplication of pulmonary smooth muscle cells, which line the lungs’ blood vessels. These cells multiply in an uncontrolled manner, causing lesions in the arteries and veins of the lung that lead to obstruction of blood flow and increased blood pressure in the lungs. This causes the right side of the heart to over-work, eventually leading to heart attacks and death. We will study why these cells multiply uncontrollably. Our findings could lead to novel therapies to treat PH in COPD that could prolong life expectancy.

Lung Stem Cells that Repair Air Sacs Could Lead to New Emphysema Treatment

In normal lungs, breathing is facilitated by tiny sacs within the lungs called alveoli, which allow oxygen and carbon dioxide to move between the lungs and bloodstream. Damage to alveoli is the hallmark of lethal lung diseases like emphysema. We have uncovered lung stem cells that, upon lung injury, are capable of proliferating and repairing damaged tissues. We showed that specific signals sent by their neighboring cells direct this stem population into forming new alveoli. We will analyze the signals between the lung stem cells and their environment to harness the mechanism of alveolar repair. This could lead to new approaches to promote lung repair and alleviate the symptoms associated with chronic pulmonary diseases.
INFLUENZA, PNEUMONIA AND OTHER LUNG HEALTH ISSUES

Pneumonia and influenza are common lung infections and together continue to be among the top ten leading causes of death in the U.S. Almost 55,000 Americans die each year from influenza and pneumonia.

Influenza is a worldwide problem and a looming threat because of the virus' uncanny ability to mutate, making previous immunizations ineffective, and because of its potential to transform into a highly contagious deadly organism capable of creating a devastating pandemic. The best way to prevent this serious lung disease is to get the flu vaccine each year. Health officials recommend that everyone six months of age and older receive an influenza vaccination each and every year.

Pneumonia is a common lung infection caused by bacteria, a virus or fungi. Pneumonia and its symptoms can vary from mild to severe. Most healthy people recover from pneumonia in one to three weeks, but the disease can be life threatening. The good news is that pneumonia can be prevented by getting an annual flu shot (as flu often leads to pneumonia), frequently washing your hands, and for the elderly and people at high risk, getting a vaccine for pneumococcal pneumonia.

Awards & Grants
The American Lung Association is funding a number of studies on influenza. One is looking at whether proteins called cytokines may help boost the immune response to influenza. Another is investigating whether probiotics can help prevent and treat infant influenza. A third is looking at how immune cells called regulatory T cells form distinct subsets in the lung during influenza infection and how these subsets may play roles in modifying parts of the immune response. We are also funding research that is examining how children's lungs are injured with infection with influenza A virus and whether certain drugs may be able to reduce the severity of this infection.

We are supporting pneumonia research that aims to better understand the immune responses generated against the bacteria Streptococcus pneumoniae, which causes serious lung infections. The findings could lead to better treatments and vaccines against pathogens that enter through the lungs.

Most major lung diseases are, to an important degree, preventable. The American Lung Association is working to save lives by reducing exposure to risk factors for lung disease.

An example of a major risk factor for lung disease is air pollution. One project we are funding is looking at the impact of climate change on lung disease, using a large dataset to study long-term exposures to both air pollution and temperature and their interactive effects on mortality. We are also supporting research on indoor air pollution and how it affects lung health in rural Africa.
INFLUENZA

ALISON CAREY, MD
Drexel University
*American Lung Association Biomedical Research Grant*

Could Probiotics Help Prevent and Treat Infant Influenza?

Death and disability from influenza (flu) infection is highest in infants younger than 6 months, an age group not currently eligible for flu vaccines. In order to study infant flu infection, we have established a model of neonatal flu infection in 3-day-old mice. We will investigate how immune-boosting microbes called probiotics help infants fight flu infection. Physicians currently have very few treatments for viral infections. Our findings will improve the knowledge of the infant immune system and lead to new therapies for respiratory viral infections. Our approach of using an immune booster instead of developing a drug for a specific virus makes the therapy more broadly applicable to infants as a whole, not just those infected with the flu.

BRIA M. COATES, MD
Northwestern University
*American Lung Association/ATS Foundation Research Grant*
Funded in partnership with the American Thoracic Society

How Children's Lungs are Injured From Infection with Influenza A Virus

Influenza virus (IAV) is a highly contagious virus that causes respiratory tract infections in up to 40 percent of children each year. Lung injury due to IAV infection is the result of damage from both the virus and the immune system's response to the virus. We have found that juvenile mice infected with IAV show continued activation of two inflammatory signaling pathways even after removal of the virus. This project will determine the contribution of these signaling pathways to the susceptibility of juvenile mice to IAV-induced acute lung injury. We will perform a preclinical trial to determine the effectiveness of three drugs in reducing the severity of IAV infection. Our results may support the use of medications to treat children with IAV-induced acute lung injury.

JASON GRIFFITH, MD, PhD
Massachusetts General Hospital
*American Lung Association Biomedical Research Grant*
Funded by the American Lung Association of the Northeast

Modifying the Immune System's Harmful Responses to Influenza Virus

Influenza infection continues to cause a large burden of respiratory disease despite vaccination and antiviral therapy. Respiratory failure that occurs in some patients during influenza is thought to result from excessive immune system responses. We have found that immune cells called regulatory T cells critically enhance survival after influenza infection by modulating many aspects of the immune system's inflammatory response to the influenza virus. We will study how regulatory T cells form distinct subsets in the lung during influenza infection and how these subsets may play roles in modifying different parts of the immune response. These findings could provide novel therapeutic pathways for modulating harmful immune responses to the influenza virus.

JOSEPH REYNOLDS, PhD
Rosalind Franklin University of Medicine and Science
*American Lung Association Biomedical Research Grant*
Funded by the American Lung Association of the Upper Midwest

Cytokine Proteins May Help Boost Immune Response to Influenza

Influenza virus infection is an important global health threat that is in need of improved treatment. Many people suffer severe and sometimes deadly complications following influenza infection, especially the young, the elderly and those with compromised immune systems. We will study proteins called cytokines for their role in severe influenza infection. We will focus on two cytokine proteins, IL-17 and IL-17B, which have poorly understood roles in the establishment of lung inflammation and the immune response against invading infectious organisms. We will investigate whether IL-17 cytokines promote improved immune responses to influenza. Our research may lead to new treatments for inflammation-based respiratory disorders.
**INFLUENZA, PNEUMONIA AND OTHER LUNG INFECTIONS**

**Update:** Our studies so far have demonstrated that the expression of two proteins, IL-17 and IL-17B, is critical for the development of an optimal immune response against influenza virus infection. Our studies also have indicated that one protein, IL-17B, is important for limiting early viral replication, while another, IL-17F, is important in orchestrating T cell response in the later stages of infection. This finding may have implications for the development of new treatments for inflammation-based respiratory disorders.

**PNEUMONIA**

**CATHERINE M. CROSBY, PhD**
La Jolla Institute for Allergy & Immunology
*American Lung Association Senior Research Training Fellowship*

How Immune Cell Helps Protect Body from Bacteria that Infects the Lung

Our research goals are to better understand the immune responses generated against the bacteria *Streptococcus pneumoniae*, which causes serious lung infections. We have particular interest in the role of a highly specialized immune cell type called the invariant Natural Killer T Cell, which has been shown to be critical for protection against *S. pneumoniae* in mice. We are investigating how activation of these cells affects other cell populations in the lungs, which destroy the bacteria to clear the infection. This will help us understand how this population, and perhaps other similar cell types, helps protect humans from *S. pneumoniae*. This could lead to better treatments and vaccines against pathogens that enter through the lungs.

**RISK FACTORS**

**PEGGY LAI, MD, MPH**
Massachusetts General Hospital
*American Lung Association Biomedical Research Grant*
Supported by the Mary Fuller Russell Fund

How Indoor Air Pollution from Chickens Can Affect Lung Health in Rural Africa

Indoor air pollution leads to premature deaths worldwide and is one of the most important risk factors contributing to the global burden of lung disease. We will study how microbes in the indoor environment change after the introduction of chickens to the environment in rural Uganda, and how these microbes can colonize in the airways of people in contact with the chickens and affect lung health. We will also study whether immune suppression due to HIV affects the ability of microbes in our environment to colonize the airways. The findings will allow us to develop future interventions to protect the health of susceptible populations.

**Update:** We have successfully recruited 88 women in year one of this study and have completed follow-up testing of 81 participants. The women started receiving chickens and we have completed follow-up testing of 30 participants. By year two of this study, we expect to have finished all fieldwork and will proceed with sequencing of microbial DNA to answer the question: How does introduction of new microbes in our environment affect our personal microbiome (the genetic material of all the microbes in and on our body) and our health?
How Does Temperature Affect Lung Function?

Studies have found that people with lung disease are particularly susceptible to heat-related death. High temperatures and wider temperature ranges may also trigger asthma attacks. We will examine acute effects of temperature and temperature range on lung function, and the role of temperature in modifying respiratory effects of exposure to air pollutants. Air pollution exposure is associated with lower lung function. This study will test if these effects are different if the previous day was extremely cold or hot. This project will also assess if people with asthma or COPD are more susceptible to respiratory effects of temperature. The findings could lead to more precise warnings about air pollution and temperature for people with lung disease.

Treating Claustrophobia in Sleep Apnea Patients Using Positive Airway Pressure

Sleep disordered breathing, such as sleep apnea, is commonly treated with positive airway pressure therapy (PAP), which requires patients to wear a mask worn snugly over the nose or mouth. Patients who do not adhere to the treatment have worsened health and quality of life. A common reason patients do not use PAP is claustrophobia. We will study an anxiety treatment called mindfulness-based stress reduction (MBSR) to determine its effect on claustrophobia. MBSR is a method of using meditation to cultivate awareness and reduce stress. We will determine the feasibility and patient acceptability of MBSR in PAP-treated adults with sleep apnea. We hope to reduce the burden of disease by promoting adherence to PAP through the reduction of claustrophobia.
ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) AND DISORDERS OF THE LUNG BLOOD VESSELS

Acute lung injury, also known as acute respiratory distress syndrome (ARDS), is a syndrome in which the small blood vessels in the lungs become widely impaired, causing them to leak fluid and inflammatory cells into the lungs as a response to infection, shock or the presence of noxious agents. It can develop in anyone over the age of one who is critically ill. A person with ARDS has rapid breathing, difficulty getting enough air into the lungs and low blood oxygen levels.

Approximately 190,000 Americans are affected with ARDS each year. ARDS can be life-threatening because the body’s organs need oxygen-rich blood to function well. It is a major complication of extensive infection, surgery, trauma, chemotherapy and lung transplantation.

Awards & Grants
The American Lung Association is supporting a number of research projects on ARDS this year. Much of this research is aimed at understanding the underlying mechanisms of acute lung injury, with an eventual goal of developing new treatments. This year researchers are studying the cellular mechanism of leaky blood vessels in the lung; the inflammatory properties of proteins involved in acute lung injury; and how to prevent lung damage from oxygen used to treat ARDS.

Pulmonary hypertension is an abnormal elevation of blood pressure in the vessels going from the heart to the lung. One form of pulmonary hypertension is called pulmonary arterial hypertension (PAH), which worsens over time and is life-threatening because the pressure in the arteries rises to dangerously high levels, putting a strain on the heart.

One researcher we are funding is making a "metabolic map" that will identify the pathways that are important for supporting the abnormal cell growth that is critical to drive PAH. Another is studying a group of proteins that may play a role in the development of pulmonary hypertension caused by a lack of oxygen, while a third is investigating the role of a protein in driving the development of PAH. These studies could lead to new targets for treatment.
**PATRICK BELVITCH, MD**  
University of Illinois - Chicago  
*American Lung Association Biomedical Research Grant*  
Funded by the American Lung Association of the Upper Midwest  

Preventing Leaky Blood Vessels in the Lungs in ARDS

Acute respiratory distress syndrome (ARDS) is a devastating form of acute lung injury that is common among critically ill patients. In a person with ARDS, protein-rich fluid leaks from blood vessels into the lungs. These leaky blood vessels can cause respiratory failure requiring prolonged stays in the intensive care unit. This leads to significant rates of illness and death. We will study the cellular mechanisms of leaky blood vessels in the lung, focusing on how specific proteins regulate the formation of gaps between cells that lead to the leakage of fluid into the lung airspaces. By understanding these mechanisms, we hope to be able to develop treatments for this condition.  

**Update:** We have made significant progress in characterizing a protein complex called Arp 2/3, which is required to prevent gaps from forming between endothelial cells that line the surface of lung blood vessels. We have identified Arp 2/3 as playing a key role in closing gaps between cells following lung injury and have generated novel data describing the cellular mechanisms of this process. We are now investigating the relationship between Arp 2/3 and other critical regulatory proteins involved in preventing leaky blood vessels in the lung.

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**BINOY SHIVANNA, MD, PhD, DM**  
Baylor College of Medicine  
*American Lung Association Biomedical Research Grant*  
Supported by the Mary Fuller Russell Fund  

Preventing Lung Damage from Oxygen Used to Treat ARDS

Acute respiratory distress syndrome (ARDS) is a life-threatening condition in people whose lungs are severely injured. These patients need oxygen to save their lives. But the high oxygen levels that these patients need can also escalate their underlying lung injury. We will study whether a hormone named adrenomedullin (AM) can protect and help the lungs to heal from oxygen damage. In particular, we will investigate whether AM protects the lungs by decreasing the levels of an enzyme called NOX that causes lung damage from oxygen. Our studies can lead to improved therapies such as the use of AM to prevent and treat ARDS.  

**Update:** Our results so far suggest that high AM levels protect mouse lungs from oxygen damage and low AM levels increase oxygen damage in human lung cells. We will further investigate whether AM protects the lungs by decreasing the levels of NOX. Our studies can lead to improved therapies such as the use of AM to prevent and treat ARDS.

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**BARTOSZ SZCZESNY, PhD**  
University of Texas Medical Branch at Galveston  
*American Lung Association Biomedical Research Grant*  

Damage to Mitochondrial DNA May Trigger Inflammation in Airway Cells

Airway inflammation is the initial event in the development of several lung diseases. Although the connection between inhaled environmental pollutants and inflammatory lung disease is well established, we still do not fully understand what happens at the molecular level. We will study the role of mitochondrial DNA in inflammatory lung disease. Mitochondria are structures within cells that convert the energy from food into a form that cells can use. They have a small amount of their own DNA. We will study whether
damage to mitochondrial DNA triggers the inflammatory response in airway epithelial cells. The findings may lead to new ways to prevent or treat inflammatory lung diseases.

Update: In year one of the project, we made significant progress in the study of how damage to mitochondrial DNA triggers the inflammatory response in airway epithelial cells. We established a comprehensive picture of several critical mitochondrial and cellular functions in response to various levels of mitochondrial DNA damage.

**JING ZHAO, PhD**
University of Pittsburgh
*American Lung Association Biomedical Research Grant*

**Reducing Anti-Inflammatory Effects of Protein Involved in Acute Lung Injury**

Acute lung injury (ALI) is a syndrome in which the small blood vessels in the lungs become impaired, causing them to leak fluid and inflammatory cells into the lungs as a response to infection, shock or the presence of noxious agents. We will examine the inflammatory property of two proteins, FBXL19 and USP14, involved in ALI. FBXL19 exhibits an anti-inflammatory property, while the effect is reversed by USP14. Results from these studies could be used to develop treatments that inhibit USP14 and reduce the severity of lung injury.

**Update:** We have verified that FBXL19 exhibits an anti-inflammatory property, while the effect is reversed by USP14. A molecule called IU1 that inhibits USP14 increases FBXL19 protein levels. This suppresses infection-induced cytokine storm—a potentially fatal immune reaction—and reduces the severity of lung injury.

**PULMONARY HYPERTENSION**

**TIANJI CHEN, PhD**
University of Illinois at Chicago
*American Lung Association Biomedical Research Grant*
Funded by the American Lung Association of the Upper Midwest

**Discovering Protein’s Role in Pulmonary Arterial Hypertension**

Pulmonary arterial hypertension (PAH) is a serious disease characterized by elevated pressure in the lung circulation causing right heart failure, resulting in impaired quality of life and eventually death. We have identified a protein called PDLIM5 as a driver in the development of PAH. However, the exact mechanisms by which PDLIM5 itself is regulated and how it plays a role in the development of PAH are unknown. We will investigate the role of PDLIM5 and how it is regulated in PAH. The findings will provide novel insights into PAH, which may result in the design of novel therapeutic strategies for the treatment of the disease.

**WILLIAM OLDHAM, MD, PhD**
Brigham and Women’s Hospital, Inc.
*American Lung Association Biomedical Research Grant*
Funded by the American Lung Association of the Northeast

**“Metabolic Map” May Identify Pathways to Target in Pulmonary Arterial Hypertension**

Abnormal growth of pulmonary vascular cells causes narrowing of blood vessels in the lungs, leading to pulmonary arterial hypertension (PAH) and heart failure. Accumulating evidence indicates that PAH is associated with marked changes in cell metabolism in the pulmonary blood vessels. Having a better understanding of metabolic changes in models of PAH may enable us to develop new, targeted therapies. We will create a “metabolic map” that traces the flow of carbon atoms from food sources (like glucose) through cellular metabolic pathways in diseased lung vessels. With this metabolic map, we will be able to identify the pathways that are important for supporting the abnormal cell growth that is critical to drive PAH.
MARC SALA, MD
Northwestern University
American Lung Association Senior Research Training Fellowship
Funded by the American Lung Association of the Upper Midwest

Group of Proteins May Be Target for Treatment of Pulmonary Hypertension

Pulmonary hypertension is elevated blood pressure of the artery leading from the heart into the lungs. It is a complication of lung diseases such as chronic obstructive pulmonary disease, interstitial lung diseases and sleep apnea. The diagnosis is associated with increased risk of death and treatment options are very limited. We plan to define the role of the group of proteins known as c-Jun N-terminal kinases (JNKs), and understand the role they may play in the development of pulmonary hypertension caused by a lack of oxygen. We will use a mouse model of pulmonary hypertension to better understand the role of JNK in this disease, which may lead to a new target for treatment of pulmonary hypertension.
INTERSTITIAL LUNG DISEASE AND FIBROSIS

Interstitial lung disease is a group of disorders that cause scarring of the lung. The disease eventually affects a person’s ability to breathe and get enough oxygen into the bloodstream. It can be caused by long-term exposure to dangerous materials such as asbestos, however, in most cases the cause is not known. Once lung scarring occurs, it usually cannot be reversed. Idiopathic pulmonary fibrosis (IPF), a type of interstitial lung disease, has no known cause. Risk factors include smoking and viral or bacterial infections. Approximately 34,000 new cases of IPF are diagnosed in the U.S. each year with fewer than 50 percent of affected patients surviving five years. Unfortunately, there is no effective treatment for this disorder which is why we support research that will improve our understanding and advance treatment options for patients living with this disease.

Awards & Grants

One researcher is testing compounds to see if they will activate lung receptors that could reduce scarring in the lungs. Another is seeking to understanding which proteins activate cells that make scar tissue, called fibroblasts, in pulmonary fibrosis. A third is looking at the genetic underpinnings of IPF, using cutting-edge genomic technology. All of these studies have the potential to identify new targets for fibrosis therapy.

The American Lung Association supports an array of investigations into the basic cellular and molecular processes that underlie interstitial lung disease.

We are also funding research into a rare lung disease called autoimmune pulmonary aveolar proteinosis (aPAP), which is characterized by the build-up of grainy material in the alveoli (air sacs) of the lungs. By examining the underlying immune mechanisms that cause aPAP, the researchers hope to gain insights that could translate into treatment.
Gaining Insight into Rare Lung Disease, APAP

Autoimmune pulmonary aveolar proteinosis (aPAP) is a rare lung disease characterized by the build-up of grainy material in the alveoli (air sacs) of the lungs. This grainy material is composed mainly of phospholipid (a fat-like substance) and protein. Phospholipid and protein are the key components of lung surfactant, an important substance that coats the alveoli to prevent lung collapse and which promotes oxygen absorption by the lungs. We will use the first model for aPAP to examine the underlying immune mechanisms that cause aPAP. Insights gained through our research could translate into treatment for patients.

Update: In patients with aPAP, mechanisms that regulate the production and activation of immune cells called Csf2 cytokine-specific B cells are broken, leading to the production of disease-causing Csf2-specific antibodies. We have detected key differences in the type of Csf2-specific antibodies with aPAP. We have also identified key molecules that are required for disease development that could serve as candidate therapeutic targets for aPAP patients.

Learning How to Stop Process in Lungs That Leads to Pulmonary Fibrosis

Pulmonary fibrosis is an often fatal condition in which the lungs fill with scar tissue. The process is thought to be triggered by damage to the epithelial cells that line the lung’s air sacs. The damage activates cells called fibroblasts that then make scar tissue. To learn how to stop this process, we will first use human cells to study the interaction of epithelial cells and fibroblasts. We will also use genetically modified mice that have a label in the epithelial cells of the lung, allowing us to specifically examine these cells. Using a model of pulmonary fibrosis, we will determine what new proteins are made by epithelial cells that activate fibroblasts. This project should reveal new therapeutic strategies to combat fibrosis.

Seeking Therapeutic Targets for Idiopathic Pulmonary Fibrosis

Interstitial pulmonary fibrosis (IPF), which causes scarring of the lungs, has limited treatment options. Cells called myofibroblasts are a core contributor to lung scarring, or fibrosis. Recent studies have identified an important role for two proteins called transcription factors in activating these myofibroblasts. Stimulating a specific class of cell receptors can block these transcription factors. We will study whether activating these receptors in lung myofibroblasts will reduce these cells’ scarring effect in IPF. This class of receptors is one of the most common targets for clinically approved drugs. Many of the compounds we are testing are approved drugs with a long history of safe, effective use. We are hopeful that we can identify one or more treatments for IPF from these compounds.
Idiopathic pulmonary fibrosis (IPF) results in profound scarring of the lung. While the genetic factors that influence one's risk of developing IPF have begun to be delineated, those genetic factors that contribute to IPF progression remain largely unknown. This study aims to identify specific genes and gene variants associated with IPF disease activity. This will be done by applying cutting-edge genomic technology to previously collected blood samples from patients with IPF. We will identify gene expression patterns that change as pulmonary function declines and identify variants within genes that increase an individual's risk of dying from IPF. This research has the potential to identify new targets for IPF therapy.
The acknowledgments section of the American Lung Association® Research Awards Nationwide 2016–2017 lists the contributions of many individuals from both within and outside the organization. The text highlights the hard work of various individuals involved in the project, including the National Office staff, consultant Randy Tibbott, and Celia Vimont. The section also reminds readers of the American Lung Association assumption of sole responsibility for the content of the document.

The text is formatted in a standard academic style, with proper capitalization and punctuation. The American Lung Association assumes sole responsibility for the content of the American Lung Association® Research Awards Nationwide 2016–2017.

The document also features the usual copyright and trademark information, indicating that the content is protected and should not be reproduced without permission. The text is clear and concise, providing a comprehensive overview of the contributors and their roles in the project.
About the American Lung Association

The American Lung Association is the leading organization working to save lives by improving lung health and preventing lung disease through education, advocacy and research. For more than 100 years, we have led the fight for healthy lungs and healthy air, whether it’s searching for cures to lung diseases, keeping kids off tobacco, or fighting for laws that protect the air we all breathe.

The work of the American Lung Association is focused on four strategic imperatives: to defeat lung cancer; to improve the air we breathe; to reduce the burden of lung disease on individuals and their families; and to eliminate tobacco use and tobacco-related diseases.

Our Mission: To save lives by improving lung health and preventing lung disease.

Our Vision: A world free of lung disease.

For more information about the American Lung Association, a holder of the Better Business Bureau Wise Giving Guide Seal, or to support the work it does, call 1-800-LUNGUSA (1-800-586-4872) or visit the newly redesigned website: Lung.org.