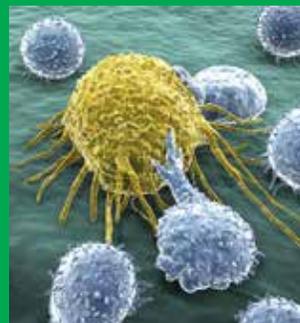


Lung Cancer Research Program



Congressionally Directed Medical Research Programs

HISTORY

The Office of the Congressionally Directed Medical Research Programs (CDMRP) was created in 1992 from a powerful grassroots effort led by the breast cancer advocacy community that resulted in a congressional appropriation of funds for breast cancer research.

This initiated a unique partnership among the public, Congress, and the military. Since then, the CDMRP has grown to encompass multiple targeted programs and has received over \$11 billion in appropriations from its inception through fiscal year 2016 (FY16). Funds for the CDMRP are added to the Department of Defense budget, in which support for individual programs, such as the Lung Cancer Research Program (LCRP), is allocated via specific guidance from Congress.

APPLICATION REVIEW PROCESS

The CDMRP uses a two-tier review process for application evaluation, with both tiers involving dynamic interaction among scientists and disease survivors and their families (consumers). The first tier of evaluation is a scientific peer review of applications measured against established criteria for determining scientific merit. The second tier is a programmatic review conducted by the Programmatic Panel, which is composed of leading scientists, clinicians, and consumers. The Programmatic Panel compares applications to each other and makes recommendations for funding based on scientific merit, potential impact, adherence to the intent of the award mechanism, relevance to program goals, and portfolio composition.

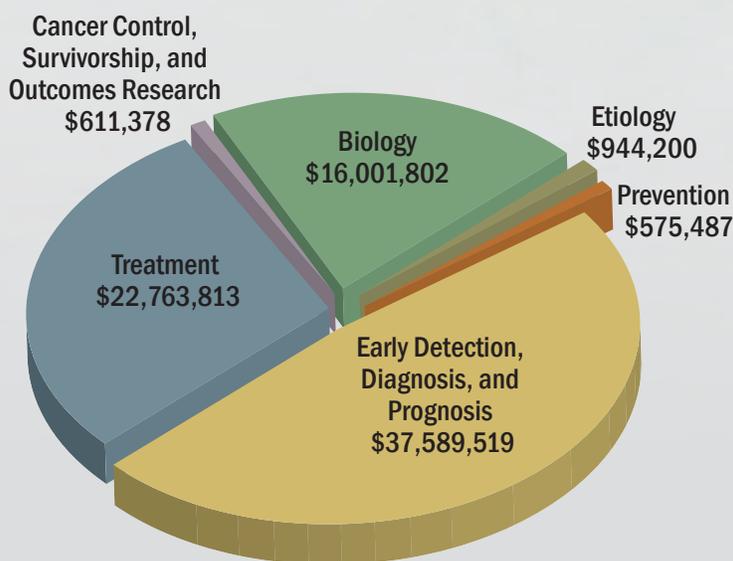
Lung Cancer Research Program

Vision: Eradicate deaths from lung cancer to better the health and welfare of the military and the American public

Mission: Support and integrate research from multiple disciplines for risk assessment, prevention, early detection, diagnosis, and treatment for the control and cure of lung cancer

About The Program

Lung cancer is the leading cause of cancer deaths in the United States. It is estimated there will be more than 221,000 new cases of lung cancer this year and over 158,000 associated deaths. The LCRP was established in FY09 with a congressional appropriation of \$20 million (M) and, over the past 7 years, it has played a critical role in supporting high-impact, innovative research within the military and general public for risk assessment, prevention, early detection, diagnosis, and treatment for the control and cure of lung cancer. The dedicated efforts by lung cancer advocates to increase public awareness of this disease, as well as federal funding for its research, have led to a total appropriation of \$101.5M to the LCRP, including \$12M for FY16. To address the critical needs of the lung cancer research and patient community, the LCRP adapts its investment strategy annually, focusing its support on underfunded and underrepresented areas. In addition, it is important to note that military personnel are at a higher risk of developing lung cancer than the general population due to increased rates of smoking, as well as an increased likelihood of exposure to environmental carcinogens during their service. To address our military's higher risk, all applicants to the LCRP's funding opportunities are required to describe how their research is relevant to the healthcare needs of military Service members, Veterans, and their families.



FY09-FY15 LCRP Portfolio by Research Area

Portfolio analysis is by research dollars

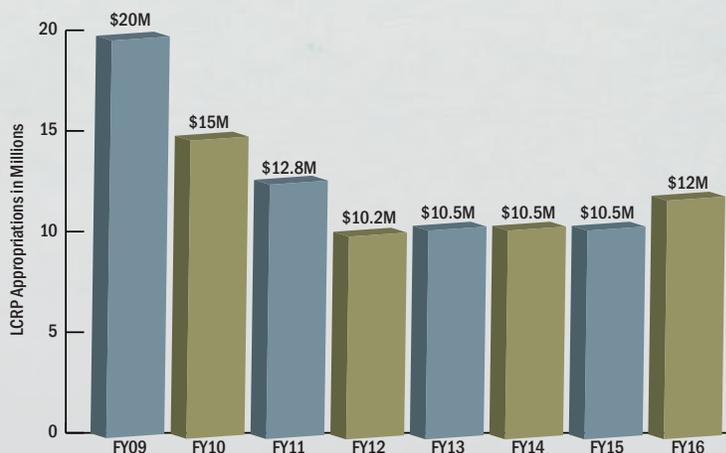
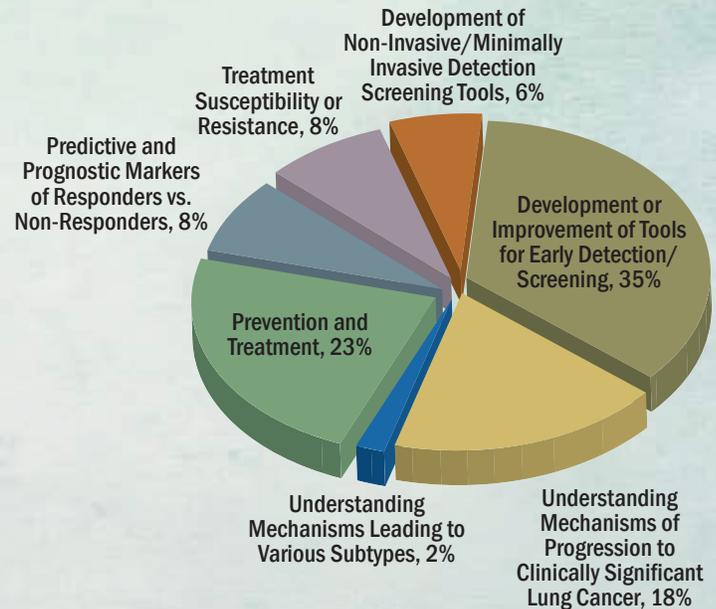
LCRP Areas of Emphasis

When the LCRP was established in FY09, the Programmatic Panel developed seven areas of emphasis to assist researchers in concentrating their projects around program priorities. The LCRP requires applications to address at least one of the areas of emphasis. In FY16, the LCRP Programmatic Panel decided the program's funding should be focused on the following seven areas of emphasis:

- Identify or develop noninvasive or minimally invasive tools to improve the detection of the initial stages of lung cancer.
- Identify, develop, and/or build upon already existing tools for screening or early detection of lung cancer. Screening may include, but is not limited to, imaging modalities, biomarkers, genetics/genomics/proteomics/metabolomics/transcriptomics, and assessment of risk factors.
- Understand the molecular mechanisms of initiation and progression to clinically significant lung cancer.
- Identify innovative strategies for prevention and treatment of early and/or localized lung cancer.
- Understand predictive and prognostic markers to identify responders and non-responders.
- Understand susceptibility or resistance to treatment.
- Understand contributors to lung cancer development other than tobacco.

FY09-FY15 LCRP Portfolio by Areas of Emphasis

Portfolio analysis is by research dollars



FY09-FY16 Appropriations

This is the first year that the Programmatic Panel introduced a focus on contributors to lung cancer other than tobacco. Nearly 18% of lung cancer deaths in patients over the age of 35 are attributed to causes other than tobacco use.¹ Most never-smokers diagnosed with lung cancer are diagnosed with an adenocarcinoma, and more never-smokers are diagnosed with stage III or IV cancer than smokers.² Never-smokers are also more likely to be symptomatic at the time of diagnosis than smokers. This may be due to the use of smoking history as a primary screening criteria—never-smokers without symptoms are less likely to be screened than patients with a long smoking history.

¹ Source: 2014 Surgeon General's Report: The Health Consequences of Smoking—50 Years of Progress, Chapter 12, Table 12.4.

² Ayesha Bryant, Robert James Cerfolio, "Differences in Epidemiology, Histology, and Survival Between Cigarette Smokers and Never-Smokers Who Develop Non-small Cell Lung Cancer," *Chest*, Volume 132, Issue 1, July 2007, pages 185-192, ISSN 0012-3692, <http://dx.doi.org/10.1378/chest.07-0442>.

Fostering Collaboration Leads to Early

Since its inception, the LCRP has issued funding mechanisms that focus on collaboration and the development of new researchers' careers in the field of lung cancer. In the following research highlights, the LCRP's commitment to funding research partnerships that establish new and productive collaborations, as well as the rewards of fostering up-and-coming Principal Investigators' careers, are showcased. All of these awardees have been successful in contributing to the LCRP's goals of advancing lung cancer research toward clinical applications.

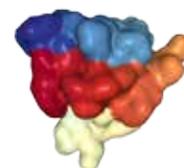
In 2009, the LCRP offered the Collaborative Translational Research Award with the intent of fostering collaboration between laboratory and physician scientists across institutions and, in so doing, promoting multidisciplinary research that would advance promising lung cancer research ideas toward clinical applications. One of the projects funded by this mechanism focused on the development of blood-based biomarkers that would improve the early detection of lung cancer and facilitate diagnosis of lesions detected by CT scans. Currently, patients diagnosed with Stage IA non-small cell lung cancer (NSCLC) have a 5-year survival rate near 50%, while patients with stage IIIA have a 5-year survival rate of less than 14%, with the number dropping further for more advanced cancers (data from the National Cancer Institute's Surveillance, Epidemiology, and End Results Program database). Effective and minimally invasive modes of early detection are expected to improve patient outcomes, increasing the number of patients diagnosed with early-stage, more-treatable forms of lung cancer.

Four research groups collaborated on this early detection project led by Drs. Samir Hanash at the University of Texas MD Anderson Cancer Center, Adi Gazdar at the University of Texas Southwestern Medical Center (UT Southwestern), Stephen Lam at the British Columbia Cancer Agency (BCCA), and David Gandara at the University of California, Davis (UC Davis). Through their work on this award, the groups were able to successfully identify a number of potential screening biomarkers and establish collaborations that have resulted in significant new projects in the lung cancer field.



University of Texas MD Anderson Cancer Center

Dr. Hanash's team at MD Anderson Cancer Center identified pro-surfactant protein B (pro-SFTPB) levels in plasma as a risk biomarker for lung cancer. Pro-SFTPB levels corresponded well with smoking status, age, and higher risks of lung cancer. While the pro-SFTPB levels did not vary sufficiently to allow discrimination between sub-types of lung cancer, its strong correlation with risk will allow physicians to identify high-risk patients in need of more in-depth early screening procedures.



As a result of the success of this LCRP award, researchers at MD Anderson were able to launch a large, prospective clinical trial (Biospecimen Banking and Biomarker Validation for Lung Cancer Early Detection in Cohort Receiving Low Dose Helical Computed Tomography Screening) aimed at validating biomarker panels for early lung cancer detection, some of which were identified by this project. This clinical trial is a feature of MD Anderson's Moon Shot Program and will involve the participation of at least 10,000 subjects at risk for lung cancer. Currently, over 10 sites are participating in this study, and many others have been invited to participate. If successful, the trial will lead to FDA approval of a blood-based test that complements CT screening for the early detection of lung cancer.

Detection Breakthroughs in Lung Cancer



University of Texas Southwestern Medical Center

Dr. Gazdar's team at UT Southwestern worked to identify genes modulated by lung cancer. They determined that eukaryotic translation elongation factor 1 alpha 2 (EEF1A2) expression is upregulated in tumors, while completely absent in non-malignant lung tissue. EEF1A2, which is responsible for expression of the alpha subunit of the elongation factor-1 complex and delivers aminoacyl tRNAs to the ribosome, was also highly expressed in exosomes from tumor cells, meaning it could possibly be used as a circulating biomarker.

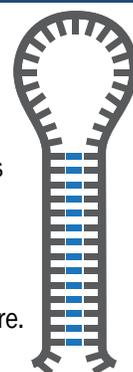


The samples collected by UT Southwestern during the course of this project have been passed on to the MD Anderson team for validation studies. In addition to this continued collaboration, Dr. Gazdar's group has determined that the four biomarkers identified during the LCRP award, including EEF1A2, serve as excellent tissue markers that can be used prognostically and to dictate therapy. One marker, in particular, ITPKA, has shown excellent capacity for predicting glioma behavior and mortality.



British Columbia Cancer Agency

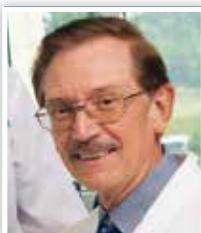
Dr. Lam's team at BCCA joined the project with the primary goal of validating pro-SFTPb and other biomarkers for early detection of lung cancer. In the Pan-Canadian screening study cohort, pro-SFTPb was found to improve the accuracy of identifying smokers at high risk of lung cancer for CT screening over and above what can be achieved with smoking history and clinical and demographic data. This work has now progressed to a new collaboration with a group in Taiwan, aiming to



use pro-SFTPb to detect lung cancer in a population of non-smokers based in Taiwan.

Successful miRNA biomarkers were also identified by this group under the LCRP award. Dr. Wan Lam's laboratory at BCCA has further refined these biomarkers and is looking to follow up on and validate these markers in the near future.

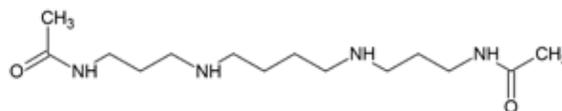
Thanks to the funding this group received from the LCRP, a number of early-career scientists and trainees have advanced significantly in their careers and are currently participating in similar collaborative projects.



University of California, Davis

The goal at UC Davis was to identify circulating metabolites that could be used as biomarkers for early detection. The group successfully identified diacetylspermine (DAS) as a pre-diagnostic serum biomarker. This compound has been found to be elevated in other cancers, but it was an unexpected biomarker for lung cancer. Not only did DAS show significant specificity for detection of NSCLC, but it was complementary to the use of pro-SFTPb as a biomarker and shows promise as a potential biomarker for early detection.

Dr. Gandara's team has been able to successfully leverage the teamwork from this award into numerous papers and funding opportunities. The most significant of these is another collaboration, an opportunity for members of Dr. Gandara's team to participate in a large, multi-institution Patient-Centered Outcomes Research Institute grant. The group has continued collaborations with the UC Davis radiology department (initiated during this award) in an effort to link CT scans with biomarkers for the purpose of early cancer screening.



Conclusion

In addition to the many research successes resulting from this award, the Principal Investigators have emphasized the award's importance in encouraging multiple face-to-face meetings and allowing these groups to collaborate and share strengths in a manner that would not have otherwise been possible. Such efforts are integral to the LCRP's mission to, "Support and integrate research from multiple disciplines for risk assessment, prevention, early detection, diagnosis, and treatment for the control and cure of lung cancer," and the program hopes to see similar successes in the coming years.

Encapsulated Solid-Liquid Phase Change Nanoparticles as Thermal Barcodes for Highly Sensitive Detections of Multiple Lung Cancer Biomarkers



Ming Su, Ph.D., Northeastern University

Through the funding provided by the LCRP Concept Award, Dr. Ming Su of Northeastern University has established a novel approach for biosensing that is applicable to lung cancer, other cancers, and infectious diseases. In this biosensing approach, the thermal properties of phase change nanoparticles can be used as reporting probes for biomarker detection.

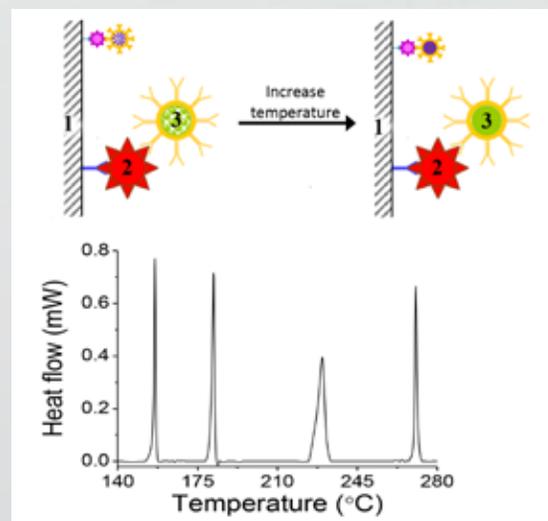
Early and accurate detection of lung cancer is crucial for effective treatment planning, maintenance of the disease, and survival. Researchers have found several potential biomarkers that could be used for early detection of lung cancers. Many of these, however, are not effective; have low concentrations; vary in presence and concentration at different stages of lung cancers; and/or require laborious sample preparation that may result in contamination, alteration, and/or loss. As a result of these challenges, there are no lung cancer screening methods using validated biomarkers that are clinically available today. A sensitive, accurate, simplified screening process remains stubbornly elusive.

Responding to the LCRP's FY09 area of emphasis addressing screening deficiency, Dr. Ming Su proposed a method that can screen multiple biomarkers while supplying critical sensitivity with minimized time, effort, and resources. Dr. Su, currently an Associate Professor in the Department of Chemical Engineering at Northeastern University, has focused his research largely on nanomaterial applications within medicine, especially thermal biosensor tools for screening of diseases. His preferred method used a novel biosensor that can incorporate nanoparticles with unique thermal properties to screen for combinations of biomarkers.

With funding from the LCRP, Dr. Su and his team investigated the use of solid-liquid phase change nanoparticles to detect multiple cancer biomarkers. The team succeeded in using a panel of nanoparticles made up of either metals or a mixture of metal and alloy to simultaneously detect four distinct proteins: rabbit IgG, human IgG, prostate-specific antigen, and biotin. Nanoparticles first bound to according antibodies, then were captured onto an antibody-modified plate after forming a sandwiched complex with antigens. The nanoparticles can be read-out using differential scanning calorimetry, wherein the melting peak position and peak area reflect the presence and concentration of biomarkers. Although this method is still a work in progress, these biosensors can potentially revolutionize early detection, not just for lung cancer, but for other cancers as well—they are capable of measuring multiple proteins at a protein concentration range of up to four orders of magnitude above baseline. This sensitivity is important because cancer biomarker protein concentration within plasma and serum can exceed 10 orders of magnitude, making it very difficult to accurately detect individual protein concentration, let alone multiple proteins.

Since completing the Concept Award, Dr. Su's team has continued to optimize thermal nanoparticle biosensing for early detection of cancer, hoping to achieve sensitive detection of biomarker concentrations within the range of 6 to 11 orders of magnitude. Dr. Su credits much of his early professional development to receiving this Concept Award, noting that this project steered him toward a focus in nanomedicine. His group has expanded their efforts to using nanoparticles as concentrators of chemotherapy and radiation therapy, thereby improving penetrating power and efficacy at low doses, and to eliminating bacteria without triggering drug resistance. Since his LCRP award, Dr. Su has received a Director's New Innovator Award from the National Institutes of Health for his team's efforts in developing nanoparticles to enhance radiation therapy.

Dr. Su's dedication to advancing cancer screening tools is not limited to his own group's research. He is a guest editor for *Nanomaterials'* special issue, "Nanomaterials for Biosensing Applications," a collection of articles sharing nanomaterials' evolving biosensors for improved detection of diseases, inclusive of cancer. This special issue has published nine papers, from September 2015 through March 2016, all of which portray unique methods. These various approaches provide optimism that improved screening tools for lung cancer and other diseases are closer to reality.



Dr. Su's methods allow for detection of protein biomarkers (2) through binding onto an antibody-tagged plate (1) and thermal readouts of phase-change nanoparticles (3). By pairing specific types of nanoparticles to different types of protein biomarkers, it is possible to determine the type and concentrations of multiple biomarkers in a single assay.

Strategic Partnerships

A key feature of the CDMRP is the integration of consumers with scientific experts in every aspect of the grant-making process. From developing investment strategies to serving on peer and programmatic review panels, consumers are encouraged to offer their perspective on key research gaps, the relevance of research, and projects meaningful to the lung cancer community. In the LCRP, consumers are patients with lung cancer who actively participate in advocacy, outreach, or support groups. This ensures that key concerns of the lung cancer community are brought to the attention of the LCRP and assists the LCRP in remaining abreast of projects currently funded by advocacy and other organizations. This insight helps the LCRP diversify its focus in the lung cancer community.

Working hand-in-hand, lung cancer researchers, physicians, and consumers ensure that the LCRP funds the most relevant, groundbreaking, and high-risk/high-reward projects—giving work that might not otherwise be funded by other organizations a chance to see the light of day. Each participant in the review process, whether consumer, physician, or scientist, has an equal voice; their thoughts are welcomed and valued by the panels on which they serve.



“The Lung Cancer Research Program plays a unique role in supporting the testing of novel ideas with promise to lead to new treatments and improved diagnostic approaches for lung cancer. Dedicated panels of scientist and consumer reviewers bring extensive knowledge and insights to the peer review process, enabling judicious election of projects that will move us closer to eradicating lung cancer. It is an inspiring program to be a part of.”

Dani Zander, MD, Programmatic Panel, Chair

“I consider it a privilege and honor to serve as a peer reviewer with the LCRP. As a stage IV lung cancer patient who was diagnosed in 2005, reviewing and rating proposals gives me a sense of purpose and makes me aware that there are many researchers working hard to find treatments/cures for this horrid disease.”

Melissa Crouse, Peer Review Panel, Consumer



“In my laboratory, we are always considering high-risk, high-reward discovery research that, in my opinion, is essential to making new discoveries to improve the treatment of lung cancer patients. While funding of this type is rare, it is critical to drive new discoveries that could improve treatment. In this regard, the Lung Cancer Research Program provides unique funding mechanisms that support the pursuit of the high-risk, high-reward medical research that is so important for making new and significant discoveries.”

David Gius, MD Programmatic Panel

“Being involved with the LCRP was one of the best things that happened to me since my diagnosis with lung cancer. Being able to advocate and help with the direction of research was an honor, and I hope to be able to help in the coming years. I thoroughly enjoyed the experience and would love to do more of this type of work.”

Susan Benson, Peer Review Panel, Consumer



“As a physician who has seen lung cancer destroy so many lives and as someone who has personally faced lung cancer twice, I had the feeling that lung cancer was forgotten. Being a member of the Programmatic Panel for the CDMRP – LCRP, I have a front row seat in seeing all of the effort being directed toward this major killer. It is more than gratifying to know that there is an army of researchers out there making serious progress in the screening, diagnosis, and treatment of lung cancer.”

Karen Arscott, DO, Programmatic Panel, Consumer

Impact: Treatment and Resistance

Two of the LCRP Areas of Emphasis address the issue of treatment of lung cancer: “Identify innovative strategies for prevention and treatment of early and/or localized lung cancer,” and “Understand susceptibility or resistance to treatment.” Lung cancer is responsible for more deaths than any other cancer, so improved treatments and efforts to circumvent resistance to existing therapies are essential to minimize mortality and lead to more favorable outcomes for all patients. Currently, many efforts to develop lung cancer therapeutics are focused on addressing the effects of mutant proteins, such as epidermal growth factor receptor (EGFR) and KRAS, malfunctioning receptors, or on immunotherapies that encourage a patient’s immune system to target and kill cancer cells. Below are summaries of a few recently funded LCRP projects that have worked to develop improved therapeutic strategies. By funding an array of treatment paradigms, the LCRP hopes to advance its vision to eradicate deaths due to lung cancer.

The Path to Eliminating Treatment-Resistant Lung Cancer Tumors



Deric Wheeler, Ph.D., University of Wisconsin, Madison

Recently, one of the major challenges associated with lung cancer treatment is the development of resistance to the drug being used to target and kill cancer cells. One of the key players in this resistance development is a receptor protein known as EGFR. In a grant funded by the LCRP, Dr. Deric Wheeler has identified one mechanism by which EGFR subcellular localization triggers drug resistance and a treatment to restore drug sensitivity to these mutant cells.

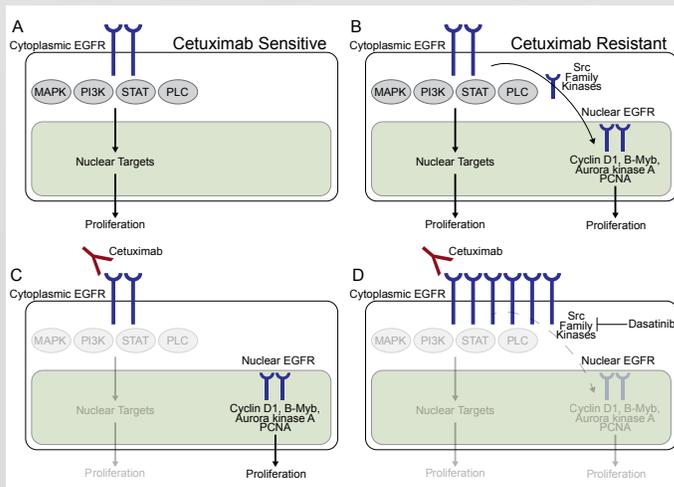
EGFR is a transmembrane protein that initiates a pathway leading to cell proliferation. Mutations inducing overexpression and overactivity of EGFR have been found to contribute to the initiation of NSCLC, as they introduce rapid and uncontrolled cell division. Since this discovery, a monoclonal antibody has been developed to target EGFR, inhibiting the cell proliferation pathway and subsequent cancer progression. However, in some forms of NSCLC, EGFR expression is increased within the nucleus (nEGFR). In these cases, cetuximab, an EGFR inhibitor chemotherapy, is unable to penetrate the cell membrane and reach nEGFR to stop cell proliferation. Dr. Wheeler and his laboratory at the University of Wisconsin, Madison, aimed to develop a therapeutic approach that would allow for targeting of both membrane-bound EGFR and nEGFR, thereby eliminating a treatment-resistant subtype of NSCLC.

With funding from a 2011 Investigator-Initiated Translational Research Award from the LCRP, Dr. Wheeler was able to identify a means to decrease EGFR translocation to the nucleus, sensitize drug-resistant tumors to cetuximab, and confirm that nEGFR expression can be used as a prognostic variable in NSCLC.

Prior to the initiation of Dr. Wheeler’s project, two protein types had been identified as possible triggers for translocation of EGFR from the cell membrane to the nucleus. Dr. Wheeler confirmed that inhibition of one of these groups, the Src family kinases (SFKs), blocks translocation of EGFR, and identified another protein, the receptor tyrosine kinase Axl, as a critical player for nuclear EGFR translocation. His research group anticipates that future efforts to target Axl may be more effective than SFK inhibition at blocking EGFR translocation, after having successfully confirmed it as a key mediator of cetuximab resistance. The group also successfully targeted nEGFR in vivo using dasatinib (an SFK inhibitor), inducing cetuximab-resistant tumors to become cetuximab-sensitive.

Currently, efforts are focusing on how nEGFR levels can be used as a predictive biomarker for treatment response.

Based on these successful findings, new therapeutic approaches can be developed to treat patients who experience cetuximab resistance, improving the outcomes of patients with otherwise difficult-to-treat NSCLC.



Potential mechanism for resistance to cetuximab: (A) Cetuximab-sensitive cells depend on classical EGFR membrane signaling. (B) Tumor cells that acquire resistance to cetuximab gain nEGFR as a second compartment of proliferation. (C) Cetuximab can abrogate signals from plasma membrane EGFR, but not nEGFR; nEGFR continues to send proliferative signals by modulation of Cyclin D1, B-myb, Aurora kinase K, and regulation of PCNA. (D) The SFK inhibitor dasatinib inhibits nuclear translocation of the EGFR from the plasma membrane, leading to increased EGFR on the plasma membrane and restoration of sensitivity to cetuximab.

Optimizing MET-Targeted Therapy for Lung Cancer Personalized Treatment

Patrick C. Ma, M.D., West Virginia University Cancer Institute



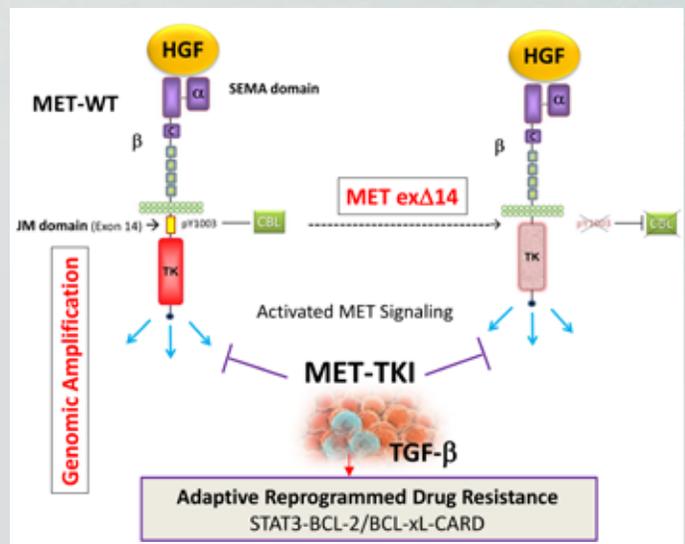
The LCRP supports the research of developing lung cancer researchers by providing awards with specific eligibility criteria. Dr. Patrick Ma was a recipient of the LCRP Promising Clinical Award in FY09. With this award, he was able to elucidate molecular causes of de novo resistance development against pivotal MET-targeted therapies and potential methods to overcome this. His contribution to this work has catapulted his influence and presence in the lung cancer clinical research community.

The protein MET is a versatile receptor tyrosine kinase. When MET is bound by its ligand, Hepatocyte Growth Factor (HGF)/Scatter Factor, the interaction induces a conformational change of MET that activates several signaling pathways involved in cell proliferation and survival, cell motility and migration, epithelial-mesenchymal transition, and cellular invasion. Research shows that human cancers can be driven by cellular processes that transform and activate the gene encoding the MET protein, such as through MET overexpression and/or more-active interaction with HGF, MET mutations, amplification, or alternative splicing, all of which perpetuate carcinogenesis progression and metastasis. This interrelationship between MET activation and cancer means MET-targeted therapies have been highly coveted. However, these precision cancer therapies have had limited success due to the development of drug resistance, especially when used to treat NSCLC.

Dr. Ma aimed to study how to overcome de novo treatment resistance by enhancing treatment to avoid adaptive resistance emergence. His group found that efficacy of MET-inhibitor XL184 in NSCLC cell lines is dose-dependent, particularly against HGF-stimulated MET activation and pro-survival signaling downstream. Dr. Ma also proposed to defeat de novo treatment resistance by defining and eradicating the emerging treatment resistance molecular profile. His group validated that the MET mutation present in juxtamembrane domains promoted tumorigenicity by increasing cellular motility, noting this potentially could be a predictive marker. In an effort to elucidate the molecular causes of emergent drug resistance to MET-targeted treatment, Dr. Ma's team explored and validated the use of EGFR tyrosine kinase inhibitors (TKI) and/or MET-TKI treatments and discovered that they can trigger early adaptive drug escape. Cells resistant to treatment emerged as early as 9 days after the initiation of MET-inhibitor treatment, regardless of initial sensitivity and response to treatment. At this time, TGFβ₂, the STAT3-BCL-2/BCL-xL complex, and other pro-survival signal molecules, such as the CARD family proteins, could be detected and were therefore noted as potential biomarkers of early adaptive drug resistance in response to MET therapy.

While advancing the lung cancer research community's understanding of MET under this LCRP award, Dr. Ma also optimized preliminary research tools, including modeling adaptive drug resistance in cells with EGFR-mutant and ALK-rearrangement and profiling single-cell gene expression via single-cell capture platforms and qPCR assays. Dr. Ma's research has helped further the understanding of MET in cancer—especially its genomic role and alterations, as well as its oncogenic function in NSCLC. His group still actively pursues research investigating personalized precision therapy, cancer genomics, epigenomics, proteomics, and metabolic profiling for biomarkers to predict and understand regulatory networks of adaptations and mechanisms of reprogramming as a result of drug resistance for lung cancer.

Since receiving the LCRP Promising Clinician Award, Dr. Ma has won several awards, been recognized twice as “Best Doctor” in *Cleveland* magazine, and is now Director of the Lung Cancer Program at the West Virginia University Cancer Institute. Beyond his academic achievements, Dr. Ma has become a well-recognized figure in the lung cancer clinical and translational research field. Dr. Ma has contributed to the American Society of Clinical Oncology (ASCO) as a Scientific Program Committee member since 2015, and has been appointed to serve for the 2017-2018 term as the Scientific Program Committee Tumor Biology Track Leader. He continues to be an influential figure, building a multidisciplinary, international, collaborative research team that is currently working toward strengthening a blood and tumor tissue procurement biomarker research program. In addition, in collaboration with the West Virginia University Cancer Prevention and Control Program, Dr. Ma has worked to develop a unique West Virginia lung cancer survivorship program newly awarded through a White House Cancer Moonshot Initiative to optimize lung cancer survivors care and community engagement and to achieve the overarching goal of combating the high lung cancer disparity in Appalachian West Virginia.



Research on the Horizon:



Concept Award

Animesh Ray
Keck Graduate Institute for Applied Life Sciences

A Novel Approach to Understand and Prevent the Evolution of Drug-Resistant Lung Cancer Cells: A Feasibility Study

Dr. Ray's team aims to use genome sequencing and computational modeling to determine the mechanisms by which tumor cells develop resistance to Erlotinib, Crizotinib, and other drugs. This will serve as a stepping stone toward determining the most effective and least toxic drug treatments for a given lung cancer.



Expansion Award

Simon Spivack
Albert Einstein College of Medicine

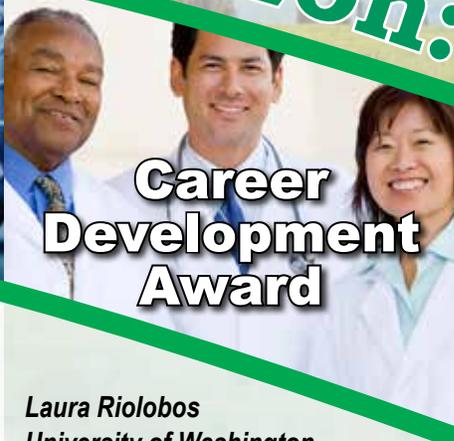
Further Development of an Exhaled microRNA Biomarker of Lung Cancer Risk

This work centers around the principle that microRNA exhaled from individuals with lung nodules can be used as a biomarker to determine whether the lung nodules are malignant or benign.

Hannah Rabinowich
University of Pittsburgh

A Novel Approach to Co-Target KRAS and YAP in KRAS-Driven NSCLC

KRAS mutant NSCLC makes up a large portion of diagnosed lung cancers, and yet there are currently no acceptable treatments. Deletion of the KRAS gene does cause tumor regression, but a second gene, YAP, is able to restore tumor development after KRAS deletion. Dr. Rabinowich's group aims to develop a successful treatment method for KRAS mutant NSCLC by targeting KRAS and YAP simultaneously.



Career Development Award

Laura Riolobos
University of Washington

Identification of Immunogenic Targets for Lung Cancer Vaccines

By identifying antigens associated with pre-malignant lung cancer, this project hopes to identify epitopes that can induce a T-cell response to tumor development, providing a protective immune response to early-stage lung cancer.

Jun-Chieh Tsay
New York University School of Medicine

Sputum Biomarkers to Detect Lung Carcinogenesis from Field Cancerization

Dr. Tsay's team aims to develop a panel of biomarkers that can be detected in sputum and lung cancer epithelial cells. This will serve as a complementary detection tool to low-dose CT screenings to improve diagnosis accuracy and minimize false positives compared to low-dose CT screening alone.



Idea Development Award – New Investigator Option

Julio Camarero
University of Southern California

Development of Novel PD1/PD-L1 Antagonists Using Circular Cys-Knotted Micro Proteins

Monoclonal antibodies (mAbs) have shown promise as options to inhibit pathways that prevent an active immune response against lung cancer cells. Unfortunately, mAbs are an extremely expensive treatment. In this project, efforts will be made to refine new drugs, known as cyclotides, to act in the same manner as mAbs and serve as a viable new treatment for lung cancer.



Idea Development Award – Established Investigator Option

Bo Lu
Thomas Jefferson University

Role of Smac in Lung Carcinogenesis and Therapy

Preliminary data have suggested that a combination of a protein mimetic and radiotherapy is capable of inducing a downstream immune response that attacks remote metastases. By investigating the mechanism of this effect and determining the optimal treatment combination, Dr. Lu's group hopes to formulate a treatment that can circumvent potential de novo drug resistance development.



Clinical Exploration Award

Taofeek Owonikoko
Emory University

Predictive Biomarkers for Novel and Established Therapies of Small Cell Lung Cancer

This project aims to identify a biomarker in patients with small cell lung cancer that indicates the appropriateness of poly ADP ribose polymerase inhibitors for treatment.



For more information, visit
<http://cdmrp.army.mil>
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(301) 619-7071

