Congressionally Directed Medical Research Programs

CDMRP

Department of Defense

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Lung Cancer Research Program

Lung cancer impacts U.S. Service members and Veterans: Lung cancer is the most common cancer for both men and women in the United States and accounts for 25% of all cancer deaths. In military Veterans, the 5-year survival rate is 3 percent lower (12% vs. 15%) than the age-matched general population. According to a 2010 update on cancer incidence among patients of the U.S. Veterans Affairs Health Care System over 8200 veterans per year are diagnosed with lung cancer. Lung cancer risk for our military is significant with 24% of service members smoking compared to 19% of civilians. According to the Department of Veterans Affairs, female Veterans have a higher rate of smoking at 20.8% compared to women in the general U.S. population at 15.8%. In addition, women who smoke have a 18x greater risk of dying of lung cancer as compared to women who do not smoke.

VISION

To eradicate deaths and suffering from lung cancer to better the health and welfare of Service members, Veterans, 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

PROGRAM HISTORY

The Department of Defense Lung Cancer Research Program (LCRP) was established in fiscal year 2009 (FY09) with a Congressional appropriation of $20 million (M), and since that time it has received a total of $141.5 M in congressional appropriations through FY19. Over the past 10 years, the LCRP has played a critical role in helping to accelerate high-impact translational research, encourage innovation and stimulating creativity, bring new investigators into the lung cancer field, and facilitate the creation of unique partnerships and resources. 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.

HIGH-IMPACT ADVANCES SUPPORTED BY THE LCRP

NEW RESEARCH TOOLS

- Public biorepository of clinical data and biospecimens (Lung Cancer Biospecimen Resource Network, [LCBRN]).
- Biomarker detection and validation consortium (Detection of Early Lung Cancer Among Military Personnel, [DECAMP]).
- Animal models of lung cancer.

SCREENING, DETECTION, AND DIAGNOSIS

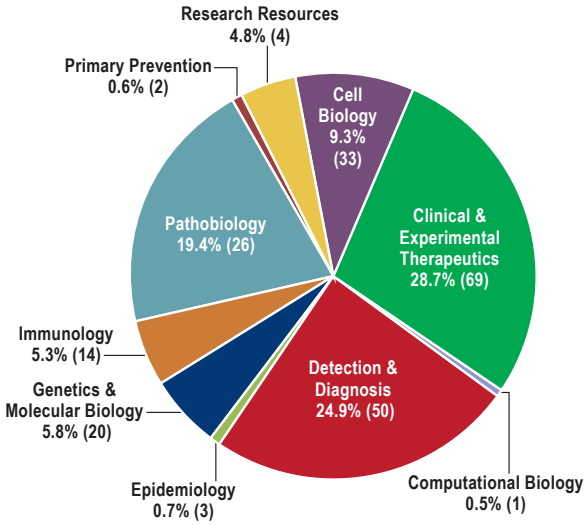
- Identification and early validation of miRNA, protein, and computed tomography (CT)-based biomarkers for detection and prognosis.
- Developed prototype endoscopic photoacoustic microscopy system to improve lung cancer stage diagnosis.

TRANSLATION TO CLINIC

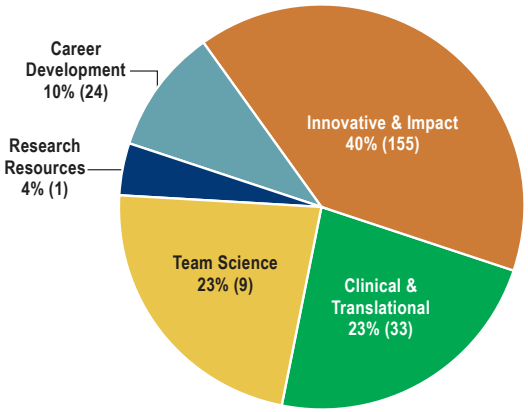
- Determination that defective apoptosis plays a large role in emergence of targeted therapy resistance in lung cancer, leading to a clinical trial testing a combination therapy of an apoptotic stimulator with targeted therapy in patients with acquired resistance (NCT02520778).
- Mesothelin-targeted chimeric antigen receptor (CAR) T-cells target and kill therapy-resistant lung cancer cells, leading to a clinical trial to determine efficacy and safety of CAR T-cell therapy in lung cancer patients (NCT02414269).

PROGRAM PORTFOLIO

Given the substantial need for further lung cancer research across the entire research spectrum (from prevention to biology/etiology, screening and detection, and treatment and cancer control/survivorship), the LCRP designed an investment strategy that emphasizes high-impact translational research, innovation, unique partnerships, resources, and development for talented new investigators who are committed to studying this disease. The following charts illustrate the LCRP investment portfolio by research area, as well as by the developmental stages of the ideas funded.



FY09-FY17 LCRP Investment Portfolio*



FY09-FY17 Portfolio by Development of Ideas*

*Percentage dollars invested and (number of awards)

RESEARCHER DEVELOPMENT

The LCRP has made funding new and promising investigators a priority since its inception, with the goal of developing successful career researchers who will remain in the field and significantly advance our understanding of lung cancer. Two promising investigators supported by the LCRP are listed below.

Dr. Sharyn Katz, funded with an FY13 Career Development Award, focused her project on the use of 18F-thymidine (FLT)-PET/CT to measure activity flares that correspond with the development of treatment resistance in non-small cell lung cancer. She successfully determined the optimal timing post-treatment to measure these flares and confirmed that the flares correspond to the development of treatment resistance to pemetrexed in preclinical studies. These results suggest that it may be possible to identify patients developing treatment resistance only hours after receiving pemetrexed. As part of her LCRP award, Dr. Katz initiated a clinical study to validate this effect in cancer patients. This study is currently open and is still enrolling patients, but early results show promise for this new CT-based biomarker.

Cloud Paweletz (left) and Geoffrey Oxnard (right)

More and more lung cancer therapies are using a personalized approach, taking advantage of targeting a patient's specific driver mutations, increasing the effectiveness of initial treatment. Unfortunately, the current methods for identifying these mutations often involve highly invasive biopsies. To solve this problem, **Dr. Geoffrey Oxnard** applied an FY13 Career Development Award to validate a droplet digital polymerase chain reaction (ddPCR) approach to genotype tumors using cell free-DNA in the patient's blood. Dr. Oxnard was able to successfully confirm that his method detects and sequences tumor DNA floating in a patient's bloodstream, as well as determine that his assay has the potential to be used as an early marker of treatment effectiveness. Since the start of his Career Development Award, Dr. Oxnard has significantly expanded assay development and is currently enrolling patients in a clinical trial to investigate the ddPCR assay in early and drug-resistant cancer. He is also working with pharmaceutical companies to test approaches that use his ddPCR assay as a predictive biomarker, as well as for therapeutic development, including the validation of next-generation sequencing of cell free-DNA to get a better picture of the cancer genotype.