Lung Cancer Research Program

**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 $8.2 billion in appropriations from its inception through fiscal year 2014 (FY14). Funds for the CDMRP are added to the Department of Defense (DoD) 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. 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 Integration Panel, which is composed of leading scientists, clinicians, and consumer advocates. The Integration 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.

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

**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). Since then, the dedicated efforts by lung cancer advocates to increase public awareness of this disease, and federal funding for its research have led to a total appropriation of $89.5M to the LCRP, including $10.5M for FY15. To address the critical needs of the lung cancer research and patient community, the LCRP adapts its investment strategy annually, focusing its support in underfunded and underrepresented areas. Areas of specific focus include development of non- or minimally invasive detection and screening tools, understanding the mechanisms leading to various subtypes of lung cancer and the progression to clinically significant lung cancer, prevention and treatment, predictive and prognostic markers to identify responders and non-responders, and understanding susceptibility or resistance to treatment.

**FY09–FY13 LCRP Research Portfolio***
*Analysis by number of awards

**Innovative Projects in the Pipeline**

- **Mechanism for Clastogenic Activity of Naphthalene**
  Bruce Buchholz, Ph.D.
  Lawrence Livermore National Laboratory

- **Genetic and Epigenetic Determinants of Lung Cancer Subtype: Adenocarcinoma to Small Cell Conversion**
  Charles Rudin, M.D., Ph.D.
  Memorial Sloan Kettering Cancer Center

- **Exploiting Tumor-Activated Testes Proteins to Enhance Efficacy of First-Line Chemotherapeutics in NSCLC**
  Angelique Whitehurst, Ph.D.
  University of Texas Southwestern Medical Center

- **Clinical Validation of a miRNA Blood Test to Identify High Risk Individuals Eligible for Low-Dose Computed Tomography Screening for Lung Cancer Early Detection**
  Pier Paolo Di Fiore, M.D., Ph.D.
  European Institute of Oncology

- **Noninvasive Personalization of Lung Cancer Therapy Using a New, Clinical-Grade Assay for Plasma-Based Measurement and Monitoring Tumor Genotype**
  Geoffrey Oxnard, M.D.
  Dana-Farber Cancer Institute
Despite experiencing the growth and advancements in lung cancer research over the past 12 years through my advocacy work, my experience with LCRP peer review changed my outlook on the disease, and I can honestly say I am even more hopeful for the future of lung cancer research. Because of advancements in lung cancer research, patients are living longer, and the longer we live, the more time research has to make new discoveries and develop more diagnostic and treatment options.

Jill Feldman, Consumer Peer Reviewer

In the era of cutbacks and intense competition, the LCRP is a welcome source to fund very crucial lung cancer research. My involvement in LCRP peer review has convinced me that this program will impact the standards of care for this devastating disease.

Shirish Gadgeel, Peer Reviewer

**Recent Accomplishments**

**Dr. Jing Chen, Ph.D., Emory University – Novel Therapeutic Strategy**
Demonstrated that tyrosine 26 phosphorylation of the glycolytic enzyme phosphoglycerate mutase 1 (PGAM1), a common occurrence in cancer cells, provides a metabolic advantage to cancer cell proliferation and tumor growth. Translational studies using a recently developed novel PGAM1 inhibitor (PGMI-004A) exhibit promising efficacy and minimal toxicity.


**Dr. Maximillian Diehn, M.D., Ph.D., Stanford University – Residual Disease Monitoring**
Developed a non-invasive method, dubbed Cancer Personalized Profiling by deep Sequencing (CAPP-Seq), for isolating circulating DNA from blood to detect rare, cancer-associated mutations to measure disease burden. Researchers are now working toward clinical trials to see whether CAPPSeq can improve patient outcomes and decrease costs. This technology may be applicable across all cancers.


**Dr. Matthew Meyerson, M.D., Ph.D., Dana-Farber Cancer Institute – Functional Genetic Mutation Analysis**
Identified a somatic mutation, ARAF S214C, as a new oncogenic driver in lung adenocarcinoma and an indicator of sorafenib response. In lung squamous cell carcinoma, identified FGFR2 and FGFR3 mutations that can be inhibited by FGFR inhibitors, providing a rationale for future clinical studies with FGFR inhibitors in patients with squamous cell lung cancer.


**Dr. Pier Scaglioni, M.D., University of Texas Southwestern Medical Center – In the Clinical Pipeline**
Demonstrated that pharmacologic inhibition of focal adhesion kinase (FAK) in mutant K-RAS lung cancers with mutations in INK4a/ARF or p53 significantly reduces the viability and survival of these cancer cells. These findings led to a multicenter Phase 2 clinical trial of defactinib, a potent inhibitor of FAK, to treat K-RAS mutated NSCLC patients.


**Dr. Jeffrey Engelman, M.D., Ph.D and Dr. Lecia Sequist, M.D., Ph.D., Massachusetts General Hospital – Translational Research Partnership Award**
Used patient-derived resistant lung cancer cell lines to identify drug candidates and combinations effective against drug-resistant lung cancers, the results of which have led to an upcoming CTEP-sponsored clinical trial that will investigate the effectiveness of combining a Bcl-2 inhibitor with an EGFR inhibitor in treating lung cancer patients harboring T790M EGFR mutations. The clinical trial is expected to begin later this year.
