University Cancer Research Fund
2014 Legislative Report

Annual Financial Report to the Joint Legislative Education Oversight Committee and the Office of the State Budget and Management

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MESSAGE FROM THE CHAIR

The General Assembly’s continued support of the University Cancer Research Fund (UCRF) has helped make the University of North Carolina at Chapel Hill a national leader in the fight against cancer. This disease affects nearly 40 percent of North Carolinians during their lifetimes, and efforts to improve treatment and outcomes for cancer patients are critical to our state’s public health.

Doing innovative medical and public health research and caring for the people of our state are integral to our University’s mission. The UCRF has enabled us to make significant progress in both areas. We are now providing cancer care for thousands of North Carolinians all across our state through high-impact enrollment in clinical trials, the use of telemedicine, public outreach programs, and partnerships with local communities and organizations. And through outstanding faculty and infrastructure that the UCRF has supported, we are leading large-scale research efforts that aim to better pinpoint the origins of cancer, to develop more effective and personalized treatments for patients, and to help survivors lead healthier and longer lives.

As Chair of the Cancer Research Fund Committee, I am pleased to present our annual legislative report detailing the tremendous economic impacts the UCRF is having on our state, including:

- A growing economic benefit for North Carolina, with an impact of $332.8 million in this fiscal year for an economic return of over $6 dollars for every dollar invested;
- The hiring and retention of 176 outstanding cancer researchers at UNC;
- Continued increases in extramural research funding. This year, UNC received nearly $137 million in new research funding from outside North Carolina directly attributable to UCRF; and
- An increase in job creation, spinoff commercialization efforts and intellectual property.

Just as important as the economic impacts are the human ones. The UCRF has allowed us to recruit and retain outstanding faculty who are the main reason UNC has become a national leader in cancer care and research. We are recruiting the brightest and the best from around the United States and keeping world-class faculty in North Carolina. They are skilled researchers, public health specialists, caring doctors, and partners who collaborate across disciplines with the shared goal of eradicating cancer as our state’s leading cause of death.

The progress we are making in cancer research and care would simply not be possible without the University Cancer Research Fund. Thank you again for your continued support.

Sincerely,

Carol L. Folt, PhD
Chancellor, University of North Carolina at Chapel Hill
Chair, Cancer Research Fund Committee
EXECUTIVE SUMMARY

The North Carolina General Assembly created the University Cancer Research Fund (UCRF) in 2007, the year that cancer became the state’s leading cause of death. The UCRF is used exclusively to support cancer research through the University and the UNC Lineberger Comprehensive Cancer Center in an effort to defeat a disease that claims the lives of about 17,000 North Carolinians each year.

Initially supported by tobacco settlement funds, taxes on non-cigarette tobacco products such as snuff, and state appropriations, the Fund received $25 million in 2007 and $40 million in 2008 before reaching its fully authorized funding amount of $50 million in 2009. In 2013, the legislature consolidated all earmarked tobacco settlement funds into the General Fund, eliminating those monies as a source of UCRF support and thereby reducing its funding stream to $42 million annually.

To ensure that UCRF funds are invested responsibly, the legislature established the Cancer Research Fund Committee to provide continued oversight. In 2009, led by then-Chairman Erskine Bowles, former UNC President, the Committee adopted a Strategic Plan to target UCRF resources in areas where they can have the most impact. The successful plan, which is currently being updated in an ongoing effort to maintain accountability of UCRF investments, calls for funds to be invested in the following areas:

- Strategic research priorities in genetics, therapies, and outcomes;
- Selective opportunities that enable researchers to adapt to a rapidly changing field; and
- Clinical infrastructure such as technology, training, outreach and other core resources.

The Cancer Research Fund Committee has published regular reports on the Fund’s activities since 2008. In 2011, the General Assembly mandated an annual financial report including UCRF’s effects on the state’s economy, details on expenditures of UCRF monies and outside funds leveraged by UCRF support, and other performance measures.

This is the fourth financial report submitted under the legislative requirement. It demonstrates that the University Cancer Research Fund continues to have significant economic benefits for the state of North Carolina.

Meet Chad Pecot, MD

UCRF was essential in the recruitment of Assistant Professor Chad Pecot, MD, a lung cancer specialist – and a cancer survivor himself – who is studying how to use nanoparticle-based drug delivery to target the metastatic process. Metastasis is the spread of cancer from one organ to another and this process is responsible for the majority of cancer deaths. Dr. Pecot, who worked at the MD Anderson Cancer Center before coming to UNC, is working on several types of nanoparticle-based treatments that will hopefully prevent or treat metastatic cancer.
From 2008 to 2014, the UCRF had the following economic impacts:

- UCRF funding and the addition of grants from outside North Carolina supported over 2,250 jobs.
- Had an overall economic impact that reached $332.8 million in FY 2013-2014 including $179.1 million in direct impact and $153.7 million in indirect and induced effects, and totaled $1.56 billion over the years since UCRF inception.
- Has leveraged $136.9 million in extramural funding this year directly linked to faculty who were recruited or retained by UCRF funds, or to the results of innovation grants, technology and infrastructure investments by UCRF.
- Has had an increased return on investment each year, exceeding a 6 to 1 return in FY 2013-2014.

In addition to these economic benefits for North Carolina, the UCRF’s impact will continue to be felt in the years to come through the continuing advancement of cancer research, public health interventions and care. The UCRF supports the recruitment, retention and research of world-class faculty members who are leading our efforts to better understand, prevent, diagnose, and treat cancer. These faculty members, along with innovative technologies, infrastructure and other core resources, have helped UNC become a national leader in cancer research—a leadership position that would not be possible without the UCRF. Details of research highlights are featured in this report.

UNDERSTANDING CANCER GENETICS

Through critical investments in sequencing technology, other research tools and faculty support, the UCRF has helped make UNC a worldwide leader in cancer genetics. Our faculty members are leading collaborative efforts to catalog thousands of genetic identifiers that can affect the development and growth of cancer. UNC’s pivotal role in The Cancer Genome Atlas project—a role made possible largely because of UCRF investments—has put our scientists at the forefront of key discoveries that could revolutionize the way cancers are classified, diagnosed and treated.

The UCRF has also helped create UNCSeq, a clinical trial designed to create a cancer treatment plan based on an individual patient’s tumor. More than 1,300 patients are now enrolled in UNCSeq, UNC’s genetic sequencing protocol and clinical trial designed to create customized cancer treatment plans based on an individual patient’s tumor. This protocol, funded by the UCRF, is especially important for situations where standard therapeutic options are not effective or useful.
DEVELOPING NOVEL THERAPEUTICS

Much of our research focuses on how to improve treatment delivery methods in a way that better targets tumor cells while sparing normal tissues from toxic side effects. Our researchers are developing reprogrammed stem cells, nanoparticles and other vehicles for more precise drug delivery.

UNC also received a major grant this year to support research to develop better melanoma treatments, centered on a discovery made at UNC. And enrollment in clinical trials continues to grow, allowing more North Carolinians to have access to cutting-edge treatments as part of the testing process.

OPTIMIZING N.C. CANCER OUTCOMES

This priority focuses on improving our understanding of cancer in North Carolina through the use of data; community-based research interventions; and strong partnerships with doctors, hospitals and patients. The UCRF has been instrumental in building population-based data resources and funding projects that test ways to improve prevention and early detection in communities all across North Carolina.

A powerful resource supported by the UCRF is the Integrated Cancer Information and Surveillance System (ICISS), a UCRF-funded initiative that links cancer data to support cancer research. Metrics of cancer incidence, mortality, and burden in North Carolina are linked with data sources at an individual and aggregate level that describe health care, economic, medical claims, social, behavioral, and environmental patterns. ICISS generates powerful mapping, such as the one below showing the county-by-county distribution of breast cancer death rates. These analyses enable the discovery of cancer risk factors and tell us how and where to best intervene, prevent and treat cancer.

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Federico Innocenti, MD, PhD, and his team are working to help identify patients who will benefit the most from angiogenesis inhibitors, a class of drugs commonly used in cancer therapy.

Deborah Manning, one of a record-breaking 3,000 breast cancer survivors participating in the UCRF-funded Carolina Breast Cancer Study

“The best knowledge we can provide as cancer survivors is what our lifestyles are like, what our habits are like, what our genetics are like, so maybe we can find some common thread that will link us all together and help find a cure.”
The UCRF has enabled us to recruit and retain faculty with expertise and leadership in several key clinical areas. It has also helped establish research infrastructure that is widely used not just at UNC, but by provider practices and research institutions across the state. Our telemedicine network and virtual tumor boards have connected community doctors, nurses, staff and hospitals with oncology experts in Chapel Hill.

While the UCRF plays a tremendous role for ongoing research, infrastructure and community outreach, it must be noted that the State of North Carolina also made two significant capital investments in cancer care: The N.C. Cancer Hospital, which opened in 2009 and serves patients from all 100 counties, seeing more than 135,000 patients each year; and Marsico Hall, a cutting-edge collaborative research facility that opened in spring 2014 and that houses high-capacity technology and equipment to further accelerate our research capabilities. These investments from the state will work together to advance cancer care and research for patients in North Carolina and beyond.

The University Cancer Research Fund has been a landmark initiative for North Carolina. It is an investment whose gains – not only the positive economic impacts, but also the benefits for patients and public health in North Carolina – will keep growing as UNC continues to be a national leader in the fight against cancer.

Creating Jobs for North Carolinians: The UCRF has created biotech and pharmaceutical companies that are creating jobs for North Carolinians and making impactful advances in cancer treatment and prevention. Just a few of the 20 UCRF-supported startups are profiled below.

- **Biotechnology company located in Research Triangle Park employing over 60 people**
- **UNC startup that raised $12.5 million in a Series A financing**
- **Opened a Phase I clinical trial for a drug that could reduce the toxicity of cancer treatments**
- **Tobacco tracking software company currently being used in 7 states**
- **Offering two proprietary software tools – the Store Mapper© and the Store Audit Center©**
ECONOMIC IMPACTS

To assess whether the UCRF is achieving its goal of stimulating the economy, UNC once again hired Tripp Umbach, a nationally respected consulting firm, to estimate the UCRF’s economic impact for FY 2014. Tripp Umbach examined UCRF’s immediate impact on state income growth and employment. The Fund’s overall economic impact was estimated as the sum of its direct and indirect and induced economic impacts (see separate full report in Appendix). Direct impact resulted from two major sources: expenditures from the UCRF itself and expenditure of UCRF-attributable research funds awarded to UNC by federal, foundation, and other sources. The indirect and induced impact was calculated by applying standard multipliers to direct expenditures.

For FY 2014, UCRF’s total allocation was $42.1 million. Using standard methodologies, Tripp Umbach estimated that in FY 2014 UCRF:

- Had an overall economic impact of $332.8 million. The total included $179.1 million in direct spending and $153.7 million in indirect and induced impact attributable to external grant funding;
- Generated well over $6 in economic impact for every UCRF dollar expended;
- Supported over 2,250 jobs, including the direct support of 983 jobs and an additional 1,267 jobs through the increased extramural funding and the indirect and induced impacts of those direct jobs and the spending generated within North Carolina.
- Resulted in nearly $11.4 million in tax revenues to North Carolina.

Using slightly different methodology than used by Tripp Umbach in FY 2013 and FY 2014, prior economic impact analyses by SRA International and the UNC Center for Competitive Economies (Frank Hawkins Kenan Institute of Private Enterprise) found that between FY 2008 and FY 2012, UCRF’s cumulative economic impact was $968.0 million over the Funds’ first five years. The FY14 total brings the economic impact of UCRF over its entire seven year span to more than $1.56 billion.

FACULTY JOB CREATION AND RETENTION

Faculty drive the UCRF. They lead the teams that conduct the groundbreaking research to push the boundaries of our knowledge and advance cancer treatment, prevention and early detection. Faculty also hire staff, evaluate technology, earn research funding from outside North Carolina, and train students and fellows. UCRF has had a tremendous positive impact on cancer research faculty at UNC during the six years from 2007 - 2014:

- **Recruitment:** UCRF has supported the recruitment of 144 faculty in the College of Arts and Sciences, the Schools of Nursing, Public Health, Medicine, Pharmacy and Journalism and Mass Communication. These faculty members are developing a wide range of research programs in nanomedicine, quantitative biology, cancer genomics, health outcomes, health communications, multiple cancer types, and other areas critical to improving cancer prevention, diagnosis and treatment in our state.
- **Retention:** UCRF support has led to the retention of 32 faculty.
EXTRAMURAL FUNDING GROWTH

Virtually all extramural funds come to UNC from outside North Carolina and add to the state’s economy. The UCRF Strategic Plan establishes extramural research funding – particularly competitive federal funding – as a key metric for UCRF success. According to this metric, UCRF funds are being invested very effectively. UCRF support is leveraging extramural research funds for North Carolina at a time when national funding levels are decreasing, keeping the state at the forefront of research nationally. Key trends include the following:

- FY 2014 funding from outside sources that is directly attributable to the UCRF totaled $136.9 million in annual total cost dollars.
  - This amount is based on a snapshot of active attributable extramural funding held by faculty in the first quarter of FY 2014-2015. The dollars represent one year of funding. A complete list of the awards is included in the Appendix.
  - The positive effects of faculty recruitment and retention, technology enhancement, and developmental projects have accumulated. The UCRF attributable extramural funding has risen from $5 million in FY08. By FY11, it was $69 million and in FY13 was $106 million. This year, UNC has seen a $30 million increase to over $136 million. Many of the currently active awards will continue for several more years, and we fully expect new awards to add to the total.
- Between 2007 and 2014, the overall extramural support for cancer-related research to UNC Lineberger increased from $163.6 million to $243 million; support from the National Cancer Institute grew from $48.5 million to $68.1 million.

INTELLECTUAL PROPERTY, INNOVATION, AND ENTREPRENEURSHIP

The UCRF focus on innovation has promoted entrepreneurship that has created jobs and spinoff companies. The UCRF, in collaboration with UNC’s North Carolina Translational and Clinical Sciences Institute, is fostering an entrepreneurial mindset at UNC. UCRF supports specialized staff to maximize the development and licensing of university intellectual property. In the past seven years, 20 startup companies have been launched or expanded their scope with direct UCRF help. These new companies are attracting external grant support and venture capital investment, as well as creating private-sector jobs.

Featured UCRF Startup: EpiCypher

Many UCRF-supported faculty members have helped lead or support research endeavors that have translated into commercial opportunities. For example, Dr. Brian Strahl, PhD, was a scientific founder of EpiCypher, a bioscience company that develops new tools and technologies to support epigenetic and chromatin biology research worldwide. In June 2014, the company moved from Texas to the Research Triangle Park. Dr. Strahl’s research continues to explore ways that histones, which are a class of proteins that regulate DNA, affect other enzymes and processes that influence cell growth and the development of disease.
RESEARCH IMPACTS

The UNC Lineberger Comprehensive Cancer Center holds an “exceptional” rating from the National Cancer Institute – a rating given to only a handful of the nation’s 41 NCI-designated cancer centers. NCI specifically cited the University Cancer Research Fund as a significant reason UNC earned the institute’s top rank.

To direct the most effective and responsible use of the state’s investment, the Cancer Research Fund Committee adopted a Strategic Plan in 2009 when the UCRF reached its full funding amount of $50 million. The plan includes three primary tiers: Research Priorities, the Opportunity Fund, and Critical Infrastructure. This section of our report highlights noteworthy successes in each tier.

1) **Research Priorities:** Three targeted research priority areas where with focused investment in major scientific programs, disease-based initiatives, or cutting-edge research platforms, UNC could have substantial impact and become a world leader. The priority areas are as follows.

   • **Understanding the Role of Genetics in Cancer Causation and Treatment** – to discover the genes that predispose families to cancer and that predispose cancer patients to poor treatment outcomes – especially by looking for the various genetic mutations in specific cancer subtypes that lead to cancer therapy failure.

   • **Developing Novel Therapeutics** – to devise new therapies that are targeted to the specific vulnerabilities of treatment-resistant cancers, and to develop new ways of delivering treatments that reduce toxic side effects for patients. This research priority relates closely to the genetics initiative, and makes key observations that will be utilized in clinical applications as quickly as possible.

   • **Optimizing NC Cancer Outcomes** – to enhance the quality of oncology and survivor care, and to build population-based datasets that track the occurrence and treatment of cancer across North Carolina to support research designed to improve community prevention and early detection. The ultimate goal is to understand North Carolina’s cancer problem at a level unprecedented in the nation and to design research interventions aimed at rectifying these problems at the practice, health system and community levels.

2) **Opportunity Fund:** Allows UCRF to remain nimble, seizing basic, population or clinical research or clinical opportunities as they arise and providing the top minds in the field with the resources they need. Examples include competitive, innovative pilot projects; seed funds to recruit top researchers; support of leading-edge technology and equipment for use by multiple faculty members; and the development of shared research resources.

3) **Critical Infrastructure Fund:** Provides critical resources for cancer research that are not readily obtainable by outside funding but upon which future progress relies. Investing in imaging, informatics and fundamental research technologies ultimately provides UNC scientists with the tools to change population and patient outcomes. This requires enhancement of multidisciplinary excellence in cancer care and the development of a statewide infrastructure to help bring leading-edge clinical research and applications into community practices.
Changing the Face of Clinical Trials

UNC Lineberger secured three major grants from the National Cancer Institute (NCI) this year as part of a new NCI clinical trials research network designed to improve treatment for the more than 1.6 million Americans diagnosed with cancer annually. UNC is one of only five cancer centers in the nation to be awarded all three grants.

- UNC Lineberger will serve as one of 30 NCI Lead Academic Partnership Sites from across the country. As a LAPS, UNC Lineberger will provide NCI with scientific leadership in the development and implementation of clinical trials.
- UNC Lineberger also secured entry into an elite network focused on experimental clinical trials — the NCI’s Experimental Therapeutics Clinical Trials Network. UNC Lineberger, along with two partner institutions, will conduct early phase NCI-sponsored cancer clinical trials to expedite the drug development process.
- We are one of only five institutions across the country funded to develop genomic tests for the clinical trials within the National Clinical Trials Network. Our group will be providing high-throughput RNA and DNA sequencing and regulatory assistance to partner institutions in the new network. As a Network Group Integrated Translational Science Center, UNC Lineberger will become one of the world’s foremost centers for high volume, regulatory compliant clinical genetic sequencing.
RESEARCH PRIORITY 1: UNDERSTANDING THE ROLE OF GENETICS

One of the most rapidly changing fields of cancer research, cancer genetics involves the study of how a person’s individual genetic makeup can affect the risk and development of disease. This is done by sequencing a patient or family member’s normal DNA obtained from their blood. The other important aspect is examining the genetic changes that occur in a patient’s tumor. This information can tell us how various types of enzymes, proteins and genetic mutations influence tumor growth. UCRF investments in new faculty as well as high-powered sequencing technologies, massive data resources, and other important analytical tools have helped make UNC a world leader in cancer genomics.

Reclassification of cancer could revolutionize diagnoses, treatments

As part of the Cancer Genome Atlas (TCGA) – a $40 million national research project in which UNC is a lead research institution – UNC researchers headed the largest, most diverse tumor sequencing project ever done. Taking National Institutes of Health cancer data representing 100 billion base pairs of DNA, UNC researchers worked with 10 other centers to analyze more than 3,500 tumors from 12 different tissue types, including breast, bladder and lung cancers. As the main TCGA site for RNA analysis, UNC sequenced over 50 trillion bases of RNA and was the principal site for analysis of all the data.

The bulk of traditional cancer research has identified cancer as not a single disease, but as many types and subtypes, with a tumor defined by the tissue – breast, lung, colon, and so on – in which it originated. Under this approach, treatments were tailored to which tissue was affected; however, questions have always existed about the effectiveness of this approach because some treatments work, and fail for others, even when a single tissue type is involved.

Instead, UNC’s analysis of TCGA data found that cancers are more likely to be genetically similar based on the type of cell in which the cancer originated, compared to the type of tissue in which it originated. For instance, researchers found that in several cancer sites, multiple distinct cancer types exist. Additionally, some tumor types appear in more than one tissue type.

“In some cases, the cells in the tissue from which the tumor originates are the same. But in other cases, the tissue in which the cancer originates is made up of multiple types of cells that can each give rise to tumors,” said Katherine Hoadley, Ph.D., a UCRF recruit and UNC assistant professor in genetics and lead author of the massive TCGA analysis recently published. “Understanding the cell in which the cancer originates appears to be very important in determining the subtype of a tumor and, in turn, how that tumor behaves and how it should be treated.”

For example, UNC research had shown that breast cancer actually consists of four previously known subtypes; luminal A, luminal B, HER2-enriched and basal-like. The TCGA’s analysis found that the basal-like breast cancers actually looks more like ovarian cancer and cancers of a squamous-cell type origin, rather than other cancers that arise in the breast. Bladder cancers were also found to be very diverse, possibly representing at least three different disease types that also showed differences in patient survival.
The study, published online in the scientific journal *Cell* in August 2014, found that one in 10 cancers would be re-classified under this new approach, said Chuck Perou, PhD, professor in genetics and pathology, a UNC Lineberger member and senior author of the paper. The TCGA project will help doctors more accurately diagnose cancer and help biotech and pharmaceutical companies develop more targeted drug therapies. This type of analysis will allow researchers to focus more on the creation of treatments targeting larger groups of cancers with genomic similarities instead of to a single tissue-based tumor type, the current way that drugs are developed.

**UNC researchers steer project to sequence rare kidney cancer**

UNC scientists led another critical TCGA project that has revealed new insights into the unique genetic changes that contribute to a rare form of kidney cancer. The study – a comprehensive integrated analysis of the molecular and genetic features of chromophobe renal cell carcinoma, a rare form of kidney cancer that affects roughly 2,000 new patients each year – was published in the journal *Cancer Cell*.

So far, all the treatments for this type of cancer have been based on the biology of the more common kidney cancer type, but this new analysis of 66 tumor samples revealed significant genetic mutations that show chromophobe cancer to be genetically different from more common kidney cancers.

UNC Lineberger member and associate professor Kimryn Rathmell, MD, PhD, co-chaired the project, and in all there were 27 UNC authors who contributed to this manuscript. UNC played several roles in the study: In addition to working on the data analysis itself, UNC served as the RNA analysis site as well as a tissue source site contributing samples for the study.

The analysis found frequent mutations in the TP53 and PTEN genes as well as a whole or partial loss of chromosomes necessary for DNA packaging and replication. These are two major discoveries that could change the ways that physicians treat this type of cancer, pointing to future therapies that target the unique biology of the tumor.

“We found virtually no similarities between these cancers. They appear to originate from different segments of the kidney nephron, have completely distinct genetic patterns, and differ in methylation profiles,” said Dr. Rathmell.

**UNCSeq reaches patients statewide through clinical trials**

UNC has turned the UCRF-developed genomics capabilities towards North Carolina patients. More than 1,300 patients are now enrolled in UNCseq, UNC’s genetic sequencing protocol and clinical trial designed to create customized cancer treatment plans based on an individual patient’s tumor. This protocol, funded by the UCRF, is especially important for situations where standard therapeutic options are not effective or useful.

Under UNCseq, researchers analyze tumor samples obtained from a biopsy or surgery, using next-generation sequencing to identify the molecular or genetic changes that may influence outcomes or choice of therapy. Once sequencing is complete, the study calls for a molecular tumor board, which is run similarly to a cancer multidisciplinary conference. Clinical information about the study patients and sample reports from the genomic data are presented and discussed, and variants that need to be confirmed in the clinical lab are identified. If researchers find and validate a molecular alteration that can be treated with a drug targeted to that change, UNC oncologists will provide this information to the
patient and his or her doctor so that they can discuss this treatment option. Normal DNA from a patient’s blood is also sequenced so that we can accurately determine if the changes in the tumor are truly mutations. This information can also help determine if the patient and their family have a gene that would predispose them to specific cancers.

The UNCseq clinical trial is open to patients with all cancer types, and its ultimate aim is to provide every patient with tumor analyses that will allow their doctors to prescribe targeted and efficient therapies on an individualized basis.

**RESEARCH PRIORITY 2: DEVELOPING NOVEL THERAPIES**

As we improve our understanding of how cancer develops and grows, we can work toward new ways of treating this disease more effectively. Roughly one third of U.S. cancer patients will die with advanced disease that is resistant to treatment, and it can take more than 10 years for a new drug to go through the comprehensive testing required for widespread patient use. The UCRF has been critical in helping UNC researchers further their work to develop and test new therapies and drug delivery methods, protecting normal cells and doing less harm to patients.

**Major grant award to support research on melanoma target discovered at UNC**

A team of scientists from UNC Lineberger, the University of Colorado and the Hebrew University of Jerusalem received a $1 million grant this year for research aimed at improving the treatment of melanoma, the most aggressive type of skin cancer. At the center of the research is a type of regulatory protein called MerTK, a new target for melanoma cancer which was originally discovered in the lab of UNC Cancer Care Director Shelley Earp, MD.

Earp and Stephen Frye, PhD, director of the Center for Integrative Chemical Biology and Drug Discovery at the UNC Eshelman School of Pharmacy who has synthesized a series of molecules that inhibit MerTK activity, are leading the UNC research team. Additional collaborators are Rotem Karni, PhD, and Tal Burstyn-Cohen, PhD, both of the Hebrew University of Jerusalem; and S. Gail Eckhardt, MD, and Douglas Graham, MD, PhD, of the University of Colorado Anschutz Medical Campus. Dr. Graham was a UNC medical student working with Dr. Earp when MerTK was first discovered and they have continued to collaborate on this project for over a decade. The team which included melanoma surgeon Dr. David Ollila, medical oncologist Dr. Stergios Moschos, and pathologist Ryan Miller found that MerTK is elevated in metastatic melanoma. They have also shown that the team’s prototype drug could slow the growth of melanoma cells – both alone and even more effectively in combination with some of the newly approved melanoma drugs.

**Developing targeted stem cell therapeutics for brain cancer**

Safe and effective drug delivery to treat brain disorders is a major medical challenge due to the brain’s structure and complexity. UNC Lineberger member and UCRF recruit Shawn Hingtgen, PhD, assistant professor at the Eshelman School of Pharmacy, is working to develop innovative and precisely targeted drug delivery methods to treat glioblastoma (GBM), a very aggressive brain cancer.

Previous research has found that using neural stem cells (NSCs) to treat brain disorders is more effective than traditional delivery methods because NSCs can better target tumor sites and be used for continuous long-term drug delivery to those sites. Hingtgen’s current work aims to further advance NSC-
based therapy for glioblastoma by using cellular reprogramming technology. He hopes to develop and evaluate a novel type of NSC by deriving stem cells starting with a patient’s own fibroblasts. He could then use these induced NSCs as vehicles for GBM treatment of the same patient without fear of rejection. Eventually, his team including neurosurgeon Dr. Matt Ewend hopes to be able to biopsy a patient’s skin, convert those cells to stem cells, add therapies to those cells, and then reimplant them for treatment. The goal is to create a model for the use of personalized patient-specific NSCs to treat aggressive GBMs.

**RESEARCH PRIORITY 3: OUTCOMES**

The UCRF is an integral part of our work to improve the outcomes for cancer patients in North Carolina. It has enabled us to build unprecedented data sources that can give researchers a comprehensive look at cancer incidences in our state, including how patient outcomes can vary by geographic, economic and other differences. UNC has also taken a leadership role in designing national standards that integrate the voice of patients into the evaluation of care. These patient-reported outcomes will provide a new standard for both care and approval of new cancer therapies. Additionally, support from the UCRF is also helping to test different intervention strategies that reduce cancer risk factors and enhance a patient’s ability to access screenings, treatments, and other information that could affect their decisions about cancer care.

**Patient-reported outcomes critical to improving cancer care**

Interdisciplinary collaborators in the UNC School of Medicine and the UNC Gillings School of Global Public Health are helping to create national guidelines for patient-reported outcomes in cancer care.

UNC’s Pediatric PRO Research Network is working to design and validate a questionnaire for children and adolescents to self-report symptomatic adverse events they are experiencing while undergoing cancer treatment. The ultimate goal is to enhance the validity and precision of adverse event reporting in oncology trials and to improve the healthcare for children with cancer by directly including their voice.

Several key UNC researchers are playing a role in this effort. Dr. Ethan Basch, MD, MSc, was recruited here last year from Memorial-Sloan Kettering with support from the UCRF. He now serves as Director of Cancer Outcomes Research at UNC. His research expertise includes patient-reported outcomes and developing ways to better evaluate patient symptoms and adverse events. Dr. Basch, who leads the National Cancer Institute’s Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) initiative to develop a standardized patient reporting system, has spearheaded efforts to create standardized patient reporting tools for clinical use. By gathering and using patient feedback during cancer treatment, doctors can better understand what their patients are feeling both physically and emotionally, leading to improved quality of care.

Building on Basch’s initiative for adult patient reports, another UCRF recruit Dr. Bryce Reeve, PhD, UNC Lineberger member and associate professor of health policy and management at UNC’s Gillings School of Global Public Health, has focused on patient-centered reporting for pediatric patients. He has
received a five-year, $2.5 million grant from the NCI to design and evaluate a self-report measure of adverse events experienced by children receiving cancer treatment.

**Big data, analytics serve as powerful research tools**

Funding from the UCRF has enabled UNC to build a powerful, data-rich research tool that will give researchers an unprecedented view of the cost and quality of cancer care in North Carolina. The Integrated Cancer Information and Surveillance System (ICISS), a system funded in part by UCRF and composed of North Carolina data, links multiple population, clinical and other data sources. It contains all North Carolina’s cancer cases and links to health claims data for 5.5 million people insured by Medicare, Medicaid, State Employees’ Health Insurance, and Blue Cross/Blue Shield of North Carolina – covering about 85 percent of North Carolina’s population of cancer patients. No similar integrated population-based cancer informatics system exists at the state or national levels in the nation. ICISS could become a model for rational cancer planning in the United States and beyond.

“North Carolina is very unique in the existence of ICISS, a resource that links Medicare, Medicaid, private insurance claims and the cancer registry. North Carolina is ahead of every other state in terms of the methods that it has employed and the technology that it has developed,” said UCRF recruit and ICISS faculty director Anne-Marie Meyer, PhD.

ICISS will be used in many ways. It can evaluate the cost and geographic distribution of cancer care modalities. It is also being used to measure outcomes of cancer control activities, especially among vulnerable subgroups and communities that have been traditionally under-represented. Researchers at other academic centers in North Carolina also can access the data to inform their studies. ICISS allows scientists to consider what kinds of cancer treatments are most effective, which parts of the state need more access to cutting-edge cancer care, what kinds of environmental and economic factors may affect prognosis, and other important questions. ICISS-related research will improve scientists’ understanding of cancer in North Carolina and provide a pathway to improve cancer outcomes for patients.

**Health-e-NC reaches communities across North Carolina**

Health-e-NC, which stands for “Health for Everyone in North Carolina,” is a statewide effort funded by UCRF to improve cancer outcomes. With cancer being the state’s leading cause of death, this initiative
uses community partnerships to test intervention strategies for prevention, detection, diagnosis, treatment and survivorship – and then sharing the most effective strategies statewide. Reducing cancer risk factors like tobacco use and obesity, increasing cancer screenings and referrals, and helping people make more informed decisions about prevention and treatment options are among the objectives of Health-e-NC.

One new Health-e-NC intervention targets the health and wellness of child-care workers who older and entering the age of cancer susceptibility in North Carolina by helping them improve their physical activity and healthy eating. Lineberger members Laura Linnan and Dianne Ward, professors in the UNC Gillings School of Global Public Health, will oversee the Care2BWell initiative, which will work with personnel at 104 childcare centers across the state and is funded by a $3.4 million, five-year grant from the National Institute of Health.

Childcare workers have received very little research attention in the past, despite earning low wages and making up 1.2 million jobs in the United States. By increasing physical activity and improving healthy eating habits, workers will be put at a decreased risk for many chronic diseases related to obesity.

Healthier childcare workers are in a better position to provide excellent care for the children they work with – and serve as role models for healthy behaviors for the children in their care. “We believe they will feel great physically and mentally,” Linnan said. “And as a result, we expect they will model these healthy behaviors for the children in their care.”

**Weight loss program helps reduce cancer risks**

Obesity – a widespread problem in North Carolina – has been linked to risk of several cancers and to decreased survival rates. But many effective weight-loss programs involve intensive face-to-face treatments, meaning that they are costly and not widely accessible to the general population. Health-e-NC’s LoseNowNC initiative tested a different approach that researchers hoped would be more adaptable in communities across the state: monthly face-to-face treatment in much larger groups (approximately 200 or more), coupled with an Internet program between sessions. This more cost-effective approach was tested in Kannapolis, NC.

The project has found that a low-intensity weight loss program could be successfully delivered in a community-based setting and result in overall weight losses over time. While the Internet program is now being used in a larger physician-referred weight loss study, participants in LoseNowNC can already testify to its initial success.

**Third phase of breast cancer study focusing on access to care, other barriers to treatment**

The largest population-based study of breast cancer ever in North Carolina and one of the largest in the world, the Carolina Breast Cancer Study (CBCS) has recently enrolled 3,000 more patients and aims to improve understanding of breast cancer, especially disparities in the risk of developing cancer and the timely access to health services.

The CBCS Phases I and II were launched in 1993 and included participants from 44 of North Carolina’s 100 counties. Phase III funded in large part by UCRF has just completed accrual of 3,000 women and is now in the five-year follow-up phase. Phase III focuses specifically on how treatment decisions, access to care, and financial or geographic barriers impact breast cancer outcomes. CBCS is also a leader in
assessing whether these outcomes are affected by genetic breast cancer subtypes. The study is one of the largest ever done investigating whether subtypes of breast cancer are associated with different risk factor and prognosis profiles.

“CBCS participants are the real heroes; they will be contributing to changing our understanding of breast cancer therapy for their sisters and daughters,” said Mary Beth Bell, MPH, who manages the study.

**OPPORTUNITY FUND**

Because cancer research is an evolving field, the purpose of the Opportunity Fund is to allow us to seize research and clinical opportunities as they arise. The UCRF enables us to fund competitive and innovative pilot projects, support cutting-edge technology and shared research resources, and provide seed money to recruit and retain the top minds in the field.

**Building capacity in cancer research**

While the Strategic Plan concentrates UCRF resources on three Tier 1 Research Priorities, cancer research is a continually changing field – and new opportunities for strategically important research regularly develop outside the Tier 1 priorities. Recruiting and retaining outstanding faculty is critical to our efforts to fight cancer, and the UCRF has successfully helped UNC recruit and retain researchers in order to build capacity in key areas of study. Since the UCRF was established, we have recruited 146 and retained 33 outstanding key leaders.
Breast tomosynthesis trial enrolls patients across NC

Clinical trials are under way to test a new x-ray imaging system that could improve the early detection of breast cancer. This technology, X-ray digital breast tomosynthesis (DBT), produces better imaging than traditional mammography, but current DBT models require long scanning times that can lead to blurred pictures, patient discomfort and other problems. In UNC clinical trials, UNC Lineberger member Dr. Otto Zhou, PhD, is now testing the next-generation DBT scanner he developed at UNC. The world’s first prototype relies on a multipixel X-ray technology to increase the imaging speed, reduce the size and cost of the equipment, and potentially reduce radiation doses while improving image quality. Zhou’s DBT device is based on early UCRF-funded innovative work at UNC using carbon nanotubes (CNT) as an X-ray source. The trial is being conducted by UCRF recruit and research radiologist Yueh Lee, MD, PhD.

UCRF Innovation Awards recognize collaborative projects, leverage external funds

Designed to promote the next generation of cancer research, the UCRF Innovation Awards support innovation, collaboration and cancer-focused science at UNC. Awards can range up to $100,000 a year for two years funding for individuals and up to $200,000 per year for teams, and all UNC faculty and UNC Lineberger Comprehensive Cancer Center members are eligible to apply. These awards have stimulated research across the public health, clinical and basic science spectrum and provide data with which to seek new external funding. From 2007 to 2014, the UCRF conducted 10 rounds of competition for the Innovation Awards and received 529 applications. Rigorous peer reviews led to 87 awards, a funding rate of about one in six, for a total of $14.45 million.

This spring, six UNC researchers won Innovation Awards for their groundbreaking contributions to cancer research. Award-winning projects from the Spring 2014 round include research on the impacts of electronic cigarettes, a largely unregulated product that is so new to the market that there is little medical research on its effects on consumers; a project aiming to use “suicide genes” to yield a new, less toxic cell-based therapy for acute leukemia; and a mouse-model sequencing study focusing on the therapeutic efficacy of a DNA damaging agent called temozolomide (TMZ) in therapy for low-grade brain tumors.

UNC researcher leads study of electronic cigarettes, authors policy statement

A leading UNC scientist has authored a policy statement calling for continued monitoring of the health effects of electronic cigarettes, with special attention given to youth and adolescents. Dr. Kurt Ribisl, PhD, professor of health behavior at the UNC Gillings School of Global Public Health and leader of the Cancer Prevention and Control Program at UNC Lineberger, was awarded a five-year grant of nearly $20 million from the U.S. Food and Drug Administration (FDA) and National Institute of Health (NIH) to research tobacco communication and prevention strategies. Ribisl, along with colleagues from other universities participating in the study, caution that use of e-cigarettes could be a problem at the population level. For example, e-cigarettes could fuel and promote nicotine addiction, especially in children, and acceptance of the devices has the potential to renormalize smoking behavior.
**INFRASTRUCTURE**

**Marsico Hall opens, builds collaborative research capacity**

In April 2014, the doors of Marsico Hall opened – and so did the doors to cutting-edge technologies that are available for research in only a few other places in the world. Funded by the General Assembly in 2009, the new facility is located next to the Lineberger building and near the hospital, bringing the physical and chemical sciences much closer to the cancer center and promoting multidisciplinary collaboration toward key research objectives.

Researchers now have access to three floors of imaging technology equipment that will allow us to make significant strides in cancer imaging, drug development and other areas. More than half the building is occupied by Lineberger members. The facility’s imaging component will substantially enhance translational research by bringing all small animal imaging modalities together for early pre-clinical work that helps researchers know which drugs to advance to human trials. The facility will also provide some of the country’s most modern imaging tools for human trials including MRI/PET and CT/PET scanners, a 7TMRI, a cyclotron, and radiochemistry facilities.

**Outreach and telehealth expands UNC tumor expertise**

UCRF has also been critical in the launch and success of UNC Lineberger’s telehealth program. Using the infrastructure supported by UCRF funds, healthcare providers connect across North Carolina in real time to discuss best practices for patient care and cutting-edge research.

Since 2012, UNC Lineberger has hosted over 65 lectures that have been broadcast to over 3,800 participants across the state. Topics in the last year ranged from “Parenting with Cancer” to “Which Patients to Refer for Stem Cell Transplantation and Why.” On average, each lecture reaches 62 medical professionals – nurses, doctors, and clinic managers – and cover an average of 12 sites across the state. Offering continuing education credits for RNs, MDs, NPs, radiation technologists and others also allows UNC to support the professional development of North Carolina’s health care workforce.

Affiliated physicians and hospitals have the resources to videoconference with a team of UNC experts from a wide variety of specialties, meeting to discuss treatment plans for patients during weekly Multidisciplinary Oncology Tumor Boards. Physician-to-patient consultations also are provided via telemedicine in selected specialties that are lacking in rural communities. Additionally, telemedicine allows the Comprehensive Cancer Support Program to provide mental health support for cancer patients, and enables the Clinical Genetics Program to offer genetics counseling to patients.
**UCRF Funding**
The 2007 law that established the University Cancer Research Fund stated that North Carolina should provide a minimum of $50 million annually for cancer research under UNC Hospitals, the UNC Lineberger Cancer Center, or both. The Fund initially received $25 million in 2007 and $40 million in 2008 before reaching its fully authorized funding amount of $50 million in 2009. The UCRF was initially funded by three sources of support: tobacco settlement funds, taxes on other (non-cigarette) tobacco products such as snuff, and state appropriations. In the 2013-2014 budget, the General Assembly eliminated tobacco settlement funds as a source of support, which resulted in a 16 percent reduction to the UCRF, but kept the tax proceeds and state appropriations funding streams intact. State-appropriated funding in FY2014 was anticipated to be $42 million. The actual proceeds from the tax on other tobacco products (OTP) exceeded projections by 0.3%, leading to a total funding of $42,089,447.

<table>
<thead>
<tr>
<th>FY 13-14 Anticipated and Actual Fund Revenue</th>
<th>$ Amount *</th>
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</thead>
<tbody>
<tr>
<td><strong>Anticipated</strong></td>
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<tr>
<td>State Appropriation</td>
<td>16,020,000</td>
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<tr>
<td>Projected OTP Tax Receipts</td>
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<tr>
<td>Total</td>
<td>42,000,000</td>
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<tr>
<td><strong>Actual</strong></td>
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<tr>
<td>State Appropriation</td>
<td>16,020,000</td>
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<tr>
<td>Actual OTP Tax Receipts</td>
<td>26,069,447</td>
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<tr>
<td>Total</td>
<td>42,089,447</td>
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<tr>
<td><strong>Unanticipated OTP Tax Receipts</strong></td>
<td>89,447</td>
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* Rounded to the nearest dollar
The actual revenue and carryover from FY13 established a budget of $42,173,167. FY14 expenditures totaled $42,173,298, leaving a balance of -$131.

<table>
<thead>
<tr>
<th>FY 13-14 Budget and Expenditures</th>
<th>Amount $</th>
</tr>
</thead>
<tbody>
<tr>
<td>Budget</td>
<td></td>
</tr>
<tr>
<td>Revenue</td>
<td>42,089,447</td>
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<tr>
<td>Carryover from FY13</td>
<td>83,720</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>42,173,167</strong></td>
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<tr>
<td>Expenditures</td>
<td>42,173,298</td>
</tr>
<tr>
<td><strong>Balance</strong></td>
<td><strong>(131)</strong></td>
</tr>
</tbody>
</table>

* Rounded to the nearest dollar

**Restrictions on the Use of UCRF Monies**

The General Assembly created the University Cancer Research Fund as part of the 2007 budget. G.S. 116-29.1 established the Fund as a special revenue fund in the Office of the President of the University of North Carolina. The law also established the Cancer Research Fund Committee as an oversight measure to provide accountability, and explicitly stated that allocations from the fund “shall be made in the discretion of the Cancer Research Fund Committee and shall be used only for the purpose of cancer research under UNC Hospitals, the Lineberger Comprehensive Cancer Center, or both.”

As the Cancer Research Fund Committee, led by its Chairman, then-UNC President Erskine Bowles, developed the UCRF Strategic Plan in 2009, each potential use of UCRF resources was evaluated according to the following questions:

- Will it address North Carolina’s needs in terms of the goal of reducing the cancer burden in the state?
- Can we be world class at it? (Does it build on existing strengths, and is there an opportunity to lead?)
- Is there a strong economic model/justification for UCRF investment?

Based on these questions, the Committee developed a clear set of rules to guide how UCRF funds would be most responsibly and effectively spent. The Committee determined that UCRF funds should focus major resources on a limited set of opportunities to have the greatest impact; fund initiatives where UNC has the opportunity to establish a leadership position; be self-sustaining and provide leverage for additional extramural funding; build fundamental cancer-related research capabilities that benefit UNC research programs; and enhance North Carolina’s economy by creating jobs, intellectual property, and startup companies.
To maximize the effectiveness of the state’s cancer investment and to ensure wise and responsible use of the funding, the Strategic Plan imposed additional restrictions on the use of these funds, instructing that UCRF funds should not:

- Invest broadly in an effort to make incremental improvements everywhere;
- Provide funding that would limit future flexibility;
- Undermine faculty innovation and competitiveness by eliminating the need for extramural grant funding;
- Substitute for existing university or health system funding or new philanthropy;
- Make expenditures based upon institutional or other needs outside cancer research; or
- Negatively impact other research on campus, for example by appropriating shared research infrastructure or resources.

**Expenditures of State Funds related to UCRF**

As mandated by G.S. 116-29.1(g), the table below provides a summary accounting of expenditures of state funding related to the University Cancer Research Fund. Further details regarding these expenditures are included as appendices to this report.

More than half the funding from UCRF has been used to recruit world-class researchers to North Carolina. Only 1.2 percent of the FY14 UCRF budget is used for ongoing administrative expenses.

<table>
<thead>
<tr>
<th>Strategic Plan Categories</th>
<th>YTD Actual</th>
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<tbody>
<tr>
<td><strong>Tier 1: Research Priorities</strong></td>
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</tr>
<tr>
<td>Understanding Genetics</td>
<td>7,061,583</td>
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<tr>
<td>Developing Novel Therapies</td>
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<tr>
<td>Optimizing Outcomes</td>
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<td><strong>Tier 2: Opportunity Fund</strong></td>
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<td><strong>Tier 3: Critical Infrastructure</strong></td>
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<tr>
<td>Clinical Excellence – Research &amp; Outreach</td>
<td>7,104,732</td>
</tr>
<tr>
<td>Research &amp; Tech Development and Training</td>
<td>7,600,433</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>42,173,298</strong></td>
</tr>
</tbody>
</table>
The University Cancer Research Fund continues to spark groundbreaking, innovative research that will enhance cancer prevention, treatment, and outcomes. It promotes collaborations with other universities, with the private sector, and with communities all across North Carolina in keeping with UNC’s mission of public service. The UCRF is leveraging unprecedented amounts of outside funding, and is creating jobs and commercialization opportunities that will benefit our economy and the health of cancer patients. UCRF’s total economic impact shows a 6-to-1 return on investment.

The economic and health impacts of the UCRF have been, and will continue to be, impactful for our state in so many ways. We are thankful for the General Assembly’s ongoing support of this investment and we continue to utilize these funds responsibly, strategically and effectively. The University Cancer Research Fund has been a truly remarkable investment in cancer care that will have a lasting impact both in and beyond North Carolina – and is a critical tool in our work to defeat our state’s most fatal disease.