

The graphic is a light orange silhouette of the state of North Carolina. The text "University Cancer Research Fund" is overlaid on this graphic in a blue serif font.

# University Cancer Research Fund

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

Submitted Nov. 1, 2011  
In accordance with G.S. 116-29.1

## A Message from the Chair

In 2007, cancer overtook heart disease as the No. 1 cause of death in North Carolina. That same year, the General Assembly created the University Cancer Research Fund (UCRF) to help fight a disease that affects one in three North Carolinians.

More than 40,000 North Carolinians are diagnosed with cancer each year. Survival rates are improving, but almost 17,500 lives are claimed by cancer each year. In addition to costing lives, the annual economic cost of cancer to North Carolina is estimated to be about \$6.1 billion, including almost \$4 billion for lost productivity due to illness and premature death.

Since its inception, the UCRF has put UNC at the forefront of innovative research to improve cancer prevention, early detection, treatment, and outcomes. Highlights include:

- Initiation of a drug discovery research program that is one of five in the country funded by the National Cancer Institute (NCI). Based on a discovery made in Chapel Hill, UNC is developing more effective drugs to treat pediatric leukemia.
- Combining physical, biologic and medical science to develop new approaches to cancer early detection and treatment. With UCRF-funded advances in mammography instrumentation and nanotechnology approaches to therapy, UNC was awarded one of seven NCI Centers of Cancer Nanotechnology Excellence.
- Adoption of new technology to bring next-generation tumor DNA sequencing into clinical research and eventually clinical care. UCRF investment allowed UNC to become part of The Cancer Genome Atlas project, the major national effort to understand cancer genomics.
- Development of large-scale data resources to understand cancer risk, patient care, and outcomes in North Carolina communities and to inform interventions to improve outcomes;
- Recruitment or retention of 100 outstanding cancer research faculty whose work helped generate \$69.2 million in outside funding this year alone;
- The launch of more than 10 new spinoff companies with private-sector jobs; and
- A growing, positive economic impact on North Carolina, reaching \$270 million for FY 2010-2011 (a 4-to-1 return on investment) and creating more than 5,000 new jobs.

Together with the NC Cancer Hospital, the new Biomedical Research Imaging Center that opens in 2013, and our outstanding translational medicine program that turns discoveries into practice, the state's landmark investment in cancer research is paving the way for better cancer care in North Carolina and beyond. This investment is also benefiting the state economy and identifying UNC and North Carolina as a premier destination in the biomedical and health care industry.

As Chairman of the Cancer Research Fund Committee, I am proud to present this report showing how North Carolina's investment in cancer research is paying dividends. Thank you for the ongoing support that helps us give real hope to countless individuals and families.

Sincerely,

A handwritten signature in black ink that reads "H. Holden Thorp".

H. Holden Thorp, PhD  
Chair, Cancer Research Fund Committee

## EXECUTIVE SUMMARY

In 2007, the General Assembly created the University Cancer Research Fund (UCRF) to provide ongoing state support for cancer research. That was the year cancer became the leading cause of death in North Carolina. Each year, more than 40,000 North Carolinians are diagnosed with cancer. Every year, cancer claims almost 17,500 lives in our state.

The legislature found that the state should provide a minimum of \$50 million annually for cancer research under UNC Hospitals, the UNC Lineberger Comprehensive Cancer Center, or both. Coupled with major investments in cancer facilities – the NC Cancer Hospital, which opened in 2009, and the Biomedical Research Imaging Center (BRIC), a research facility that becomes operational in 2013 – the University Cancer Research Fund has already had significant positive effects for North Carolina.

Investments from the Fund are guided by a Strategic Plan adopted in 2009 that focuses resources on areas where they can have maximum impact. Understanding how genetics plays a role in cancer, developing new therapies to treat patients, and optimizing North Carolinians' cancer outcomes are the Fund's primary research priorities. Also under the Strategic Plan, the UCRF funds forward-looking initiatives such as the Innovation Awards, a fiercely competitive program that promotes groundbreaking research projects with a high likelihood of success and impact. Investing in technology and other critical infrastructure, as well as promoting clinical excellence and outreach across the state, will benefit both cancer research and patient outcomes.

The Cancer Research Fund Committee, the legislatively-established oversight committee for the Fund, has published regular reports on the Fund's activities since 2008. In 2011, the General Assembly required 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 description of the cancer research impact and other performance measures.

This first financial report submitted under the requirement demonstrates that the University Cancer Research Fund has had a significant economic impact on the state of North Carolina. Based on an analysis by SRA International, an external consultant to the Cancer Research Fund Committee, from 2008 to 2011 the UCRF had the following estimated economic impacts:

- Directly supported approximately 1,140 full-time equivalent (FTE) employees.
- Created the equivalent of 5,056 new jobs, based on an outside economic evaluation.
- Had an overall economic impact that reached \$270 million in FY 2010-2011 and totaled \$674 million over the years since UCRF inception, including \$293 million in direct impact and \$381 million in indirect and induced effects.
- Increased return on investment each year, exceeding a 4-to-1 return in FY 2010-2011.

One key area of economic impact is growth in funding from sources outside the state. UCRF has performed well increasing funds brought to North Carolina for cancer research.

- In the current year, UNC was awarded \$69 million in funding linked directly to faculty recruited or retained by UCRF funds, or to technology and infrastructure resulting from UCRF investments. The economic impact of this new funding is \$152.6 million.
- UCRF has sparked a significant increase in UNC's federal funding compared to that of other universities, at a time when overall federal funding levels have fallen or remained flat.

This funding growth is due, in part, to the world-class faculty members recruited or retained using UCRF funds. Since 2007, cancer faculty recruitment efforts had an 84 percent success rate, and 88 percent of cancer researchers who had received outside job offers decided to stay at UNC. UCRF has also increased the productivity of existing faculty through technology and resource investment. In many cases, they have formed synergistic, highly successful research teams with newly recruited faculty.

Although some economic and health impacts of the University Cancer Research Fund are easy to quantify, it will take several more years to truly measure and appreciate the long-term effects this research could have on the overall health of North Carolinians. In the meantime, UCRF investments, guided by a strong research Strategic Plan, have helped propel UNC to national leadership in several areas of cancer research and care. The following report covers scientific and clinical advances in detail. Highlights include:

### **Clinical Excellence and Outreach**

Thanks to UCRF, the work being done by research teams is already making noteworthy progress in patient-oriented research and care. Participation in clinical trials has increased almost 50 percent, providing access to new medicines that could benefit the health of future cancer patients. A statewide clinical trials network has been developed with ten partner sites and more in discussion. A UCRF investment in disease-specific expertise and telemedicine is bringing top-notch multi-disciplinary oncology expertise into community practices, and is increasing patient access to cancer specialists. This program is slated for expansion in the next several years.

### **Optimizing North Carolina Cancer Outcomes**

Impacts of the University Cancer Research Fund include a 10-site pilot program in cancer prevention, focusing on worksite health promotion and disease prevention in communities or places, e.g. our community college system. We have also initiated large-scale data resources that will help researchers track and analyze differences in survivorship and quality of life. We have also initiated the nation's most ambitious study on disparities in breast cancer patients. Another example is the ***Integrated Cancer Information and Surveillance System (ICISS)***. UCRF funds are helping researchers set up an unparalleled state data resource to link cancer cases to medical claims data. Cancer cases from across the state are being linked to health care claims data from Medicare, Medicaid, state employees and BlueCross BlueShield of North Carolina. This will provide researchers with extraordinary opportunities for comparative effectiveness research, a growing area of study and rich source of federal funding. Once operational, ICISS will be used by the state as well as by UNC and collaborating researchers from other universities to put North Carolina in the lead nationally with respect to understanding how we detect, treat and follow-up cancer patients. Tracking the occurrence and treatment of cancer across North Carolina's urban and rural areas will allow planning interventions to stimulate prevention and early detection as well as enhancing the quality of patient care.

### **Understanding Cancer Genetics and Its Impact on Cancer Incidence and Treatment**

We are launching one of the country's largest projects using next-generation sequencing of a patient's cancer genetic mutations and developing methodology to link that novel information to clinical care. Institutional Research Board approval of this innovative project has been obtained and we hope to enroll up to 1,000 patients in 2012. UNC will be one of the first to link this new genetic technology to clinical care on a large scale.

In genomics – one of the most rapidly changing and exciting areas of cancer research – the Fund enabled UNC to make a major investment in genetic sequencing technologies, and to develop programs that researchers use to manipulate mouse genes and test drugs accurately and quickly. The goal is to get effective drugs to patients sooner and to improve the low rate of FDA approval. In 2009 UNC was chosen as one of only 12 centers for The Cancer Genome Atlas Grant, an unprecedented national collaboration that will provide new insight into the mechanisms responsible for the uncontrolled growth of cancer cells and their spread throughout the body. This capability is also being used to search for new inherited cancer predisposition genes in North Carolina families with breast and colon cancer.

### **Developing Novel Therapeutics**

One-third of the nation's cancer patients will die with advanced disease resistant to treatment; research must define vulnerabilities or weaknesses unique to the cells of advanced cancers so that cancer cells, not the body's normal cells, can be targeted. We must also develop new and better methods of drug delivery that get drugs to the tumor selectively bypassing the body's normal organs. UCRF has invested in these areas, creating outstanding programs in drug discovery and nanomedicine. Recruitment of Stephen Frye, PhD, formerly worldwide lead of medicinal chemistry at GlaxoSmithKline, has led to UNC being named one of five large Drug Development Centers funded by the National Cancer Institute. Because of this, three new grants to UNC to develop drugs for childhood leukemia, brain tumors and kidney cancer were funded by NCI in 2010-11. The retention of Joe DeSimone, PhD, one of the world's foremost innovators and chemists was made possible by UCRF allowing him to turn his attention to cancer nanomedicine. As a result, UNC was named one of National Cancer Institute's seven Centers of Cancer Nanotechnology Excellence.

### **Entrepreneurship**

To move this research into oncology practice requires commercialization. But going from lab discoveries to commercial-scale therapies that can have a widespread impact is a lengthy process. The Fund promotes entrepreneurial research with real-world applicability. Inventions, license agreements and licensing income generated by Lineberger members all have grown since UCRF was created. Faculty members have founded 10 spinoffs to help commercialize their discoveries and accelerate the speed by which discoveries benefit patients.

After a rigorous review last year, the National Cancer Institute gave the UNC Lineberger Cancer Center its very top rating for cancer centers, "exceptional." The NCI review specifically stated that UCRF was a significant reason for the center's exceptional rating. Since UCRF was created, Lineberger members brought more research funding to North Carolina, increased entrepreneurial and intellectual property activities, published more papers in scientific journals, and made discoveries that could eventually help win the fight against cancer.

By many measures, the University Cancer Research Fund has been a worthwhile investment for North Carolina. It has had positive economic impacts, increased the number of outside grants and clinical trials, and enhanced doctors' understanding of cancer and provided tools with which to improve care. The UCRF will help lead to better diagnosis, treatment and outcomes – and what a difference that will make for cancer patients and their loved ones, in North Carolina and beyond.

## 1. NORTH CAROLINA'S CANCER INVESTMENTS

The University Cancer Research Fund (UCRF) is attracting world-class cancer researchers to North Carolina and supporting research to improve cancer prevention early detection, diagnosis and treatment. UCRF research teams are initiating studies of high-powered DNA sequencing of patient cancers; inventing new mammography systems; discovering and developing new drugs to treat childhood leukemia; studying the genetics of addiction to help people quit smoking; and testing an imaging-guided radiation therapy technique at UNC for the first time in the United States. Outreach and telemedicine to doctors and hospitals are giving patients in all areas of the state greater access to oncology experts, clinical trials, and cancer care.

The General Assembly created the University Cancer Research Fund in 2007, finding that the state should invest a minimum of \$50 million per year to fight cancer (G.S. 116-29.1).

Supported by tobacco settlement funds, taxes on non-cigarette tobacco products such as snuff, and state appropriations, the Fund initially received \$25 million in 2007 and \$40 million in 2008 before reaching its full funding amount of \$50 million in 2009. The Fund dropped slightly below that level in 2010 and 2011, due to a shortfall in non-cigarette tobacco product sales.

The ongoing research support provided by the UCRF complements the state's major capital investments in cancer research and clinical care. The UNC Cancer Hospital, which sees patients from all 100 counties, was funded by the General Assembly in 2004 and opened to the public in 2009, replacing an aging cancer treatment facility originally built as a tuberculosis sanatorium in the 1950s. This has resulted in a 40 percent increase in patients seen at UNC, and the number of cancer patients at UNC Hospitals is expected to more than double in the next 25 years. The seven-story hospital provided more space and newer technology to serve more patients with enhanced care, and also serves as the clinical home for the UNC Lineberger Comprehensive Cancer Center – one of the most highly rated of the 40 such National Cancer Institute-designated centers in the country.

The legislature also funded the Biomedical Research Imaging Center (BRIC), scheduled to open in 2013, to develop drugs and devices to better diagnose and treat cancer and other diseases. The facility will house state-of-the-art research labs and radiographic equipment to expedite discovery of new drugs and treatments. Some technologies will be available in only a few other places in the world. BRIC's interdisciplinary approach – integrating the Schools of Pharmacy and Medicine and the College of Arts and Sciences – will allow UNC to accelerate discovery of new therapies and molecular imaging techniques for early detection as well as implementing nanotechnology delivery of drugs to patients with advanced disease and other breakthroughs.

When full funding for the University Cancer Research Fund was reached in 2009, the Cancer Research Fund Committee, the oversight committee established by law, adopted a Strategic Plan to guide the most effective and responsible use of the state's landmark investment. As the Strategic Plan was developed, each potential use for the Cancer Fund was evaluated according to the following questions:

- Will it address the needs of North Carolina, 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?

Guided by these questions, a clear set of ground rules was developed to determine how UCRF funds would be best spent. Planners, including then-UNC President Erskine Bowles, agreed 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.

It also was agreed 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.

The Strategic Plan comprises three primary tiers:

- 1) **Research Priorities:** A targeted number of initiatives 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 three research 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 – particularly by looking for the mutant genes in specific cancer subtypes that lead to cancer therapy failure.
  - ***Developing Novel Therapeutics*** – to devise new therapies targeted to the specific vulnerabilities of treatment-resistant cancers, and to develop new ways of delivering drugs and therapies to reduce toxic side effects for patients.
  - ***Optimizing NC Cancer Outcomes*** – to build population-based data to track the occurrence and treatment of cancer across North Carolina in order to initiate research aimed at improving community prevention and early detection of cancer, and to enhance the quality of oncology and survivor care across the state.

The first two research priorities interrelate, making key observations that will be turned into clinical applications as quickly as possible. The third aims to understand North Carolina's cancer problem at a level unprecedented in the nation and to design research interventions to rectify these problems at the community, health system, and practice levels.

- 2) **Opportunity Fund** – Allows UCRF to remain nimble, seizing 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, clinical trials methodology and fundamental research techniques ultimately provides clinician scientists with the tools to change patient outcomes. To do this also 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.

## 2. ECONOMIC IMPACT

Enhancing North Carolina's economy is a key principle guiding the investment of UCRF resources and the investment has produced a substantial economic benefit. The Fund has greatly enhanced faculty recruitment, faculty retention, interdisciplinary team science and research technology and capacity. In turn, these enhancements have led to increased extramural funding, new intellectual property and spinoff companies, and more private sector partnerships. Each year the UCRF's economic impact has grown, this year reaching a **4-to-1 return on investment**.

### Estimated Impact

To assess whether UCRF is achieving its goal of stimulating the economy, UNC hired an outside evaluator (SRA International) to estimate the UCRF's immediate and ongoing impact on state income growth and employment. The Fund's overall economic impact is estimated as the sum of its direct and indirect and induced economic impacts. Direct impact results from two major sources: expenditures from UCRF itself and expenditure of directly UCRF-attributable research funds awarded to UNC by federal, foundation, and other sources. The indirect and induced impact is calculated by applying standard multipliers to direct expenditures.

From 2008 to 2011, UCRF total expenditures were \$165 million, including \$50 million in FY 2010-2011. Assuming a mid-range multiplier for the indirect impact, SRA estimated that:

- **The overall economic impact of UCRF expenditures on North Carolina's income from 2008-2011 is \$674.1 million.** The total includes \$293.1 million in direct impact and \$381 million in indirect and induced impact.
- **The \$50 million allocation in FY 2010-2011 resulted in an economic impact of \$270 million -- approximately \$4 in additional impact for every dollar expended.**

UNC Fiscal Year	2008	2009	2010	2011	Total
<b>Direct Impact at UNC (millions)</b>					
Personnel Expenditures *	3.3	16.5	25.4	26.0	<b>71.3</b>
Capital Investment and Other Non-Personnel Expenditures *	3.2	17.8	22.3	22.2	<b>65.4</b>
Extramural Research Support **	5.0	24.8	57.4	69.2	<b>156.4</b>
<b>Total Direct Impact (millions)</b>	<b>11.5</b>	<b>59.1</b>	<b>105.1</b>	<b>117.4</b>	<b>293.1</b>
<b>Indirect &amp; Induced Impact on NC Income ***</b>	<b>15.0</b>	<b>76.8</b>	<b>136.6</b>	<b>152.6</b>	<b>381.0</b>
<b>Total Impact on NC Income</b>	<b>26.5</b>	<b>135.9</b>	<b>241.7</b>	<b>270.0</b>	<b>674.1</b>

\* Mid-range case: assumes partial out-of-state "leakage" of fringe benefits (50%) and capital purchases (50%)

\*\* UCRF-attributable Extramural Research Support indexed by grants received by faculty newly hired or retained, plus grants to those receiving Innovation Awards (principally in Round 1)

\*\*\* Assumes Direct Impact multiplier of 1.3, consistent with recent applications (see SRA report, Appendix E)

SRA also found that UCRF has generated a significant number of jobs:

- **UCRF directly supports portions of the salaries of 1,140 full-time equivalent (FTE) employees.** This number includes research staff at all levels and 205 new UCRF



researchers, including recruited and retained faculty (100) and senior research staff (105).

- **UCRF expenditures have created an estimated 5,056 new jobs.** The estimate is based on the effects of UCRF expenditures on North Carolina employment from 2008-2011. It assumes an employment multiplier of 17.25 jobs/\$1M in direct impact spending, an approach that is consistent with U.S. Department of Commerce methodology and base-case multiplier assumptions in National Institutes of Health economic impact analyses.

### **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, buy equipment, 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:

- **Recruitment:** From 2007 through July 2011, UCRF has supported the recruitment of 84 faculty in the College of Arts and Sciences, the Schools of Nursing, Public Health, Medicine, Pharmacy and Journalism and Mass Communication. These faculty 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:** During the past four years, 17 cancer researchers at UNC received outside offers to leave the university. UCRF support led to the retention of 15 faculty – an 88 percent retention rate. During the last two years, the University’s faculty retention rate has been lower than 50 percent.
- **Diversity:** UCRF has provided the impetus and partial support for the recruitment of seven African-American faculty.
- **Program Development:** In some cases, UCRF faculty support has made possible cancer research programs that otherwise would not exist. For example, although budget cuts have reduced the size of the School of Nursing’s general faculty, UCRF has helped to create a cancer research program in quality of life and cancer care involving five faculty.

### **Extramural Funding Growth**

Virtually all extramural funds come to UNC from outside North Carolina and add to the state’s economy. These funds mean jobs for hundreds of research staff, as well as support for the fellows and graduate assistants, who will be the next generation of bioscientists, research scientists, and industry experts for North Carolina’s life sciences economy.

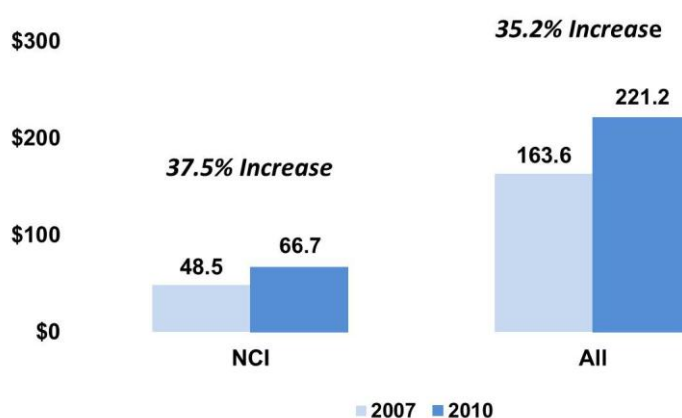
The UCRF’s Strategic Plan establishes extramural research funding – particularly competitive federal funding – as a key metric for UCRF success:

*“If UCRF funds are being spent wisely, UNC researchers will be able to compete more successfully for additional research support. An increase in federal grants will serve as an important validation of the quality and value of UCRF investments. It will also satisfy a critical goal for the UCRF articulated during the planning process – to be catalytic, and provide leverage for additional funding from extramural sources.”*

Using this metric, UCRF funds are being invested effectively. They are leveraging extramural research funds for North Carolina at a time when national funding levels are decreasing and keeping the state at the forefront of research nationally. Key trends include:

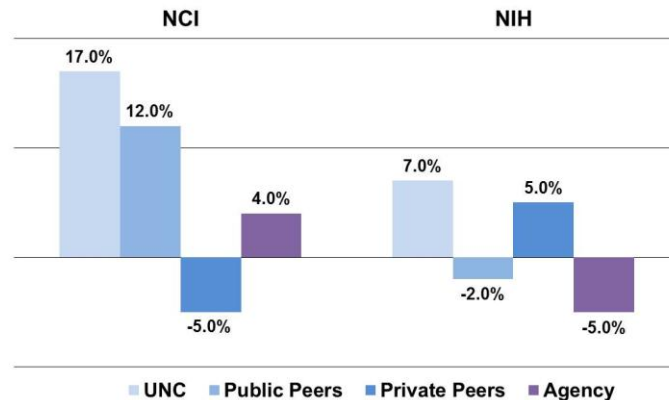
- **FY 2010-2011 the funding from outside sources that is directly attributable to the UCRF totaled \$69.2 million in annual total cost dollars.**
  - This amount is based on a snapshot of active attributable extramural funding held by faculty in the first quarter of FY 2011-2012. The dollars represent one year of funding. A complete list of the awards is included in the Appendix.
  - The attributable extramural funding has risen from \$5 million in 2007-2008 as the positive effects of faculty recruitment and retention, technology enhancement, and developmental projects has accumulated. 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 2010, extramural support to the UNC Lineberger Comprehensive Cancer Center increased from \$163.6 million to \$221 million; support from the National Cancer Institute grew from \$48.5 million to \$66.7 million.**

**Growth in UNC Lineberger Extramural Funds**  
(\$ millions)



- **Despite declining federal funding, the National Institutes of Health (NIH) increased awards to UNC Chapel Hill faculty between 2007 and 2010, while awards to many comparable institutions decreased during that time period.**
  - Overall, NIH awards across UNC Chapel Hill increased by 7 percent, slightly ahead of private peers who gained nearly 5 percent and significantly ahead of public peers who lost more than 2 percent. During this same period, NIH grants overall declined at a rate of 5 percent.
  - R01 awards for investigator-initiated research are the mainstay of NIH funding. From 2007-2010, NIH R01 awards to UNC Lineberger members rose by 29 percent.

## NCI and NIH Funding Trends 2007-2010 UNC vs. Peers and Agencies



- **Extramural funding from the National Cancer Institute (NCI) to UNC Chapel Hill has greatly increased since 2007, a trend not shared by many comparable public or private peer institutions.**
  - UNC showed one of the highest NCI funding increases from 2007 to 2010 (17 percent) while public peers increased 12 percent and private peers decreased nearly 5 percent. During this period, NCI grant funding increased only 4 percent overall.
  - From 2007-2010, NCI individual project awards (R01 grants) to UNC-Chapel Hill grew 28 percent.
  - During the same time period, NCI team science funding increased 8 percent.

### Leveraging Additional Support

In addition to stimulating extramural funding, UCRF support has attracted and enabled UNC donors to make cancer-focused contributions. For example, alumnus Fred Eshelman pledged \$9 million to support cancer research at the Eshelman School of Pharmacy, if a matching gift could be found. UCRF matched his gift to generate an \$18 million investment over five years in research on genetics, individualized cancer therapy, and drug discovery and delivery.

### Intellectual Property, Innovation, and Entrepreneurship

The UCRF's focus on innovation has helped researchers create inventions, licenses, and patents.

- **Reports of Invention and Licensing Agreements have increased.** In the five years before UCRF was established, UNC Lineberger members reported 46 inventions and made 18 licensing agreements. Since UCRF was established in 2007, members have reported 150 inventions and made 38 licensing agreements.
- **Licensing income has increased.** Licensing income attributable to UNC Lineberger members has nearly tripled since 2007.
- **Patents.** The number of patents issued to UNC Lineberger members has remained relatively constant over the past several years. However, obtaining a patent takes an average of almost two years, and for many of the reports of invention filed, there has not yet been sufficient time to mature into patents.

UCRF support also has promoted entrepreneurship that has created jobs and spinoff companies:

- **NC Kickstart:** The University Cancer Research Fund, in collaboration with UNC's TraCS Institute is developing an entrepreneurial mindset at UNC. UCRF supports specialized staff who help faculty develop these start-up companies and maximize the use of intellectual property. In the past four years, 10 startup companies directly attributable to UCRF-funded research have been launched, creating private-sector jobs.

#### Spinoff Companies Attributable to UCRF

Coordination Therapeutics	Enci Therapeutics, Inc.
Exigent Pharmaceuticals	Qualiber
G-Zero	XinRay
GeneCentric Diagnostics	XinNano Material, Inc.
Liquidia Technologies	Xintek

These intellectual property and entrepreneurial activities are in early stages and are not yet fully evaluable. However, the success stories below are examples of how these efforts are having significant positive economic impact that adds to the overall impact estimated by SRA.

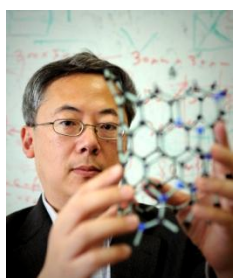
#### **SUCCESS STORY: How one cancer research spinoff is creating jobs, gaining outside funding, and working to make cancer treatments less toxic.**



In 2008, Ned Sharpless, MD, founded a North Carolina startup company to help commercialize technology he developed based on his UCRF-funded research at UNC. His goal was to create a way to protect patients from cellular damage caused by radiation or chemotherapy. Radiation and chemotherapy are common cancer treatments, but their side effects can be devastating to patients. His patents also extend to the use of the companies' products to prevent organ damage even when taken after exposure to accidental radiation exposure.

Today, G-Zero Therapeutics is using mice to test drugs that would stop cells from dividing, helping them resist the toxic effects of radiation and chemotherapy. The company recently received a \$3 million Phase II Small Business Innovation Research grant to further its work. The grant will be used to fund four employees and additional contractors to continue development of these drugs on a larger scale, so that G-Zero can apply to the Food and Drug Administration and to Homeland Security to begin testing on humans – the next step to manufacturing a viable drug that can help cancer patients and others who are exposed to radiation.

#### **SUCCESS STORY: Otto Zhou, PhD, and the development of better mammography**



The controversies surrounding both the age at which women should start getting mammograms and the effectiveness of routine mammography to prevent breast cancer death are actually caused by the fact that current mammography is halfway technology. Achieving the image resolution needed to improve mammography would require either a higher dose of radiation or a new approach, such as that involved in CT scans.

Fortunately, due to both pilot project and equipment funding to Dr. Otto Zhou, Professor of Physics, UCRF is potentially creating a solution that could have a

profound effect on breast cancer screening. Dr. Zhou is a pioneer in the use of carbon nanotubes as a source of electrons, a fundamental discovery that he has adapted to new ways of x-ray imaging. The source of x-rays can be miniaturized, creating an ability to take the breast image from multiple angles controlling many, small x ray sources arrayed around the breast by computer. Others have tried to create instruments to perform this process, referred to as breast tomosynthesis, using conventional CT design. The most successful company, Hologic, has created the only FDA-approved tomosynthesis device. However, the image requires a dose of radiation twice that of the normal mammogram. Dr. Zhou has created a prototype based on his UNC-patented process using UCRF funding (see picture of the third-generation prototype). The current prototype is being tested on materials and has already achieved detection at one half the dose of radiation of the current Hologic



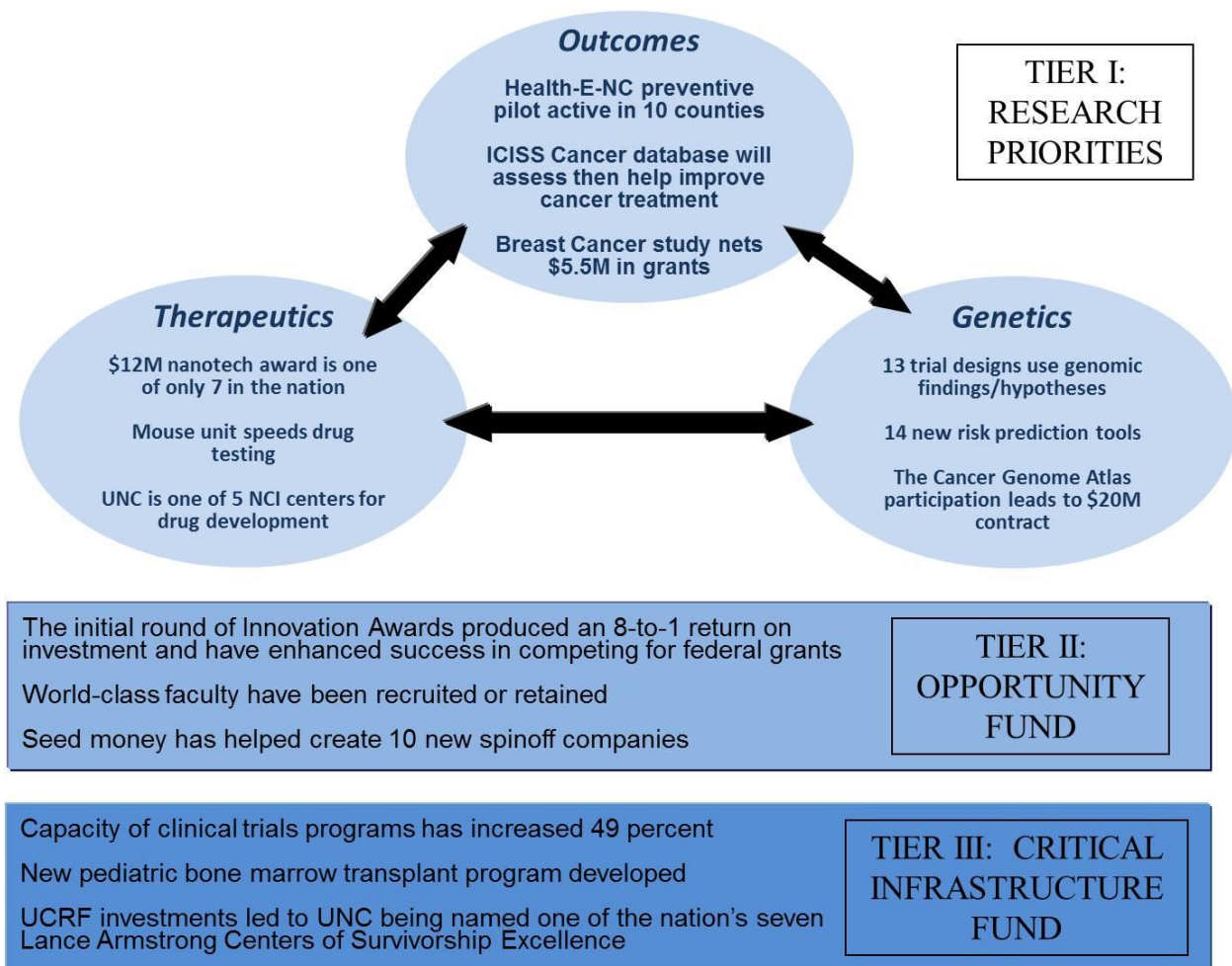
**Third Generation  
Prototype Carbon  
Nanotube Breast  
Tomosynthesis  
Device**

machine. A fourth-generation prototype will be delivered to the NC Cancer Hospital for the first human clinical trials within the next twelve months. IRB approval is being obtained by the UNC breast imaging team, in conjunction with Dr. Zhou. Dr. Zhou's UNC start-up company, XinRay, has formed a corporate partnership with Hologic, and if clinical trials demonstrate the quality of mammography that we hope for, XinRay, based in the Research Triangle, will supply the hardware necessary and will thus expand in the future, possibly dramatically.

### 3. RESEARCH IMPACTS

UCRF supports innovative and important research discoveries that are leading to improved cancer diagnosis, treatment and care for North Carolinians. While UCRF investments to expand clinical expertise and state outreach are having an immediate impact, new cancer therapies can take years to develop, test and get to market. Quantitatively demonstrating improvements in the outcomes of specific cancers in North Carolina and the United States will take time.

In the interim, however, there are measurable intermediate milestones, such as enrolling more patients in clinical trials, which can be used to assess performance. This section of the report highlights some of the UCRF's noteworthy research impacts. Following the Fund's Strategic Plan, we present highlights for the Plan's three tiers: 1) Research Priorities; 2) Opportunity Fund; and 3) Clinical Infrastructure. This report also includes other significant research-related-effects, such as publications in scientific journals and the initiation of collaborations and partnerships. The figure below shows select highlights of research achievements which, along with other effects, are further described later in this report.



#### ***Tier 1: Research Priorities***

##### **Research Priority 1: Understanding Genetics**

Genetics are a critical factor to consider in cancer patients. The presence of certain genes or gene mutations could put people at greater risk of developing cancer, could affect the way a patient responds to cancer treatments, or could have an impact on how a person copes with this

disease. A better understanding of the role genes play will help determine how to develop more effective cancer drugs and how best to enhance patients' remission rates and quality of life.

UCRF has allowed UNC researchers to make great strides in cancer genomics. In 2010 alone, researchers initiated 13 trials with genomic findings or hypotheses in their trial designs, developed 14 new risk prediction tools, and started three major projects with direct impact on future patient care.

**Becoming a Leader in Sequencing and Bioinformatics:** Technological advances are creating extraordinary opportunities that allow scientists to discover individual events causing a patient's cancer. Perhaps more important, such advances are giving us an opportunity to link these events to novel therapies and improved patient outcomes. A major UCRF investment of more than \$15 million over the first four years in sequencing technology and bioinformatics analysis and data storage has created a next-generation sequencing facility servicing basic and clinical research. Because of this investment, UNC Lineberger has moved from a non-contributor to one of the top five U.S. institutions in sequencing cancer genomes. More than \$40 million in new grants has been awarded as a result of this investment.

This technology is now ready for adoption. The interaction between UCRF-funded technology, bioinformatics, biostatistics, clinical genetics and oncologists has put UNC in a position to directly apply next-generation sequencing to clinical care at the NC Cancer Hospital. UNC is about to launch a clinical sequencing project that will introduce this next-generation sequencing into patient care at UNC Hospitals, using sequencing data to characterize tumors and, when appropriate, to help guide treatment. UNC will be one of the first places in the United States to do this. The Institutional Review Board (IRB) patient consent has already been approved and UNC's first several patients have been entered on what we believe is a nation-leading effort. It is our intention to enroll up to 1,000 patients on this protocol in 2012. The confluence of technology, tissue acquisition, informatics and patient care is tremendously exciting to our faculty. Because of UCRF, North Carolinians will be "early adopters" of using tumor sequence information in routine clinical care.

Additionally, this technology is being used to search for new genes that predispose family members to cancer. Family mutations in genes such as BRCA1 and BRCA2 have been linked to high incidence of breast cancer; likewise familial APC gene mutations predispose to colon cancer. Sequencing is now able to detect these predisposed families and create prevention and early detection opportunities. However, UNC's cancer genetics group has accumulated a number of families with either breast or colon cancer in which there are no known predisposing genes. Geneticists, Jonathan Berg and Jim Evans (see below) are using next-generation sequencing to discover the mutant genes in these families. Discoveries like this will have worldwide significance.

**A Nation-Leading Resource for Mouse Genetics (The Collaborative Cross):** Thanks to UCRF support, the Collaborative Cross – the most ambitious mouse genetics program ever devised – is now housed exclusively at UNC and holds great potential for finding the complex disease predisposition genes in these mouse populations. These mouse models mean we can map the genes underlying diseases in a genetically diverse and complex living organism. Successful mapping and experimentation on this project will allow us to apply important findings to human genes, improving understanding of how genetic variations affect the development of cancer.



## **SUCCESS STORY: UNC lands plum role in unprecedented national cancer genomics initiative, leading to major brain cancer discovery**



In 2009 UNC was chosen as one of just 12 centers created as part of an unprecedented, large-scale collaboration by the National Cancer Institute and the National Human Genome Research Institute to categorize the genomic changes that occur in cancer. The Cancer Genome Atlas grant (TCGA) is a five-year award that will bring \$20 million in extramural funding to UNC. The project will fuel rapid advances in cancer research including new ways to categorize tumors, new therapeutic targets, and methods that allow clinical trials to focus on patients who are most likely to respond to specific treatments. UCRF's technology investments were a key part of the application to join the elite project, which also includes Harvard

University, Johns Hopkins University, Memorial Sloan-Kettering, and MD Anderson.

A year later, the Atlas project yielded a major finding by UNC researcher Neil Hayes, MD. Dr. Hayes' research, which was funded in part by UCRF, suggested that the most common form of adult malignant brain cancer is not a single disease but a set of distinct diseases. Each of these distinct diseases responds differently to chemotherapy and radiation, and has its own specific molecular signature. By identifying these subtypes of what was previously thought to be a single disease, Dr. Hayes' work is leading to the development of more effective and more targeted therapies for adult brain cancer.

UNC's participation in TCGA, and Dr. Hayes' resulting discovery, would not have occurred without the support of the University Cancer Research Fund to develop genomic technology. Dr. Hayes is now assuming a national role in the analysis of TCGA lung cancer data and Dr. Chuck Perou is co-national leader of the TCGA breast cancer task force.

## **SUCCESS STORY: Leading genetics faculty use sequencing to target new family predispositions to cancer**



The recruitment of Jonathan Berg in 2009 effectively doubled UNC's capacity to deliver cancer genetics consultation for families with multiple cancer cases. Dr. Berg also brings a superb research record, helping expand UNC's capacity to find new familial cancer genes. Dr. Berg earned his PhD and MD at UNC-Chapel Hill, and spent his residency in medical genetics and a post doc researching stem cell biology at Baylor College of Medicine in Houston. His four-year residency in medical genetics is a rare program aimed at providing training broadly across all facets of clinical genetics (both pediatric and adult). In the Cancer Center, he is primarily involved in the evaluation of

individuals with a strong family history of cancer, in the hopes of identifying the primary genetic etiology for their family's cancer susceptibility and providing additional information that will help guide the management of these individuals.

Dr. Berg joined an internationally recognized senior colleague, Jim Evans, MD, PhD. In fact, this year Dr. Evans was offered the position of Deputy Director of the National Human Genome Research Institute at NIH. We used UCRF funds to support Dr. Evans' exceptional program, thus retaining him at UNC Lineberger. Together, Drs. Evans and Berg are evaluating hundreds of families who appear to have familial breast cancer or colon cancer. However, these families do not exhibit any of the known familial cancer genes. UCRF funds and the development of next-generation sequencing capability are allowing them to sequence the entire genome of key family members (as defined by family history) in an attempt to discover new familial predisposition genes in breast and colon cancers. Their goal is to discover new genes and thereby determining which people in families are predisposed to these cancers. Their work is making UNC a national center for cancer genetics analysis and, more specifically, the validation of next-generation sequencing as a clinical diagnostic test for cancer predisposition.



## **Research Priority 2: Novel Therapeutics**

The sad fact is that one-third of North Carolina's cancer patients will die of advanced disease. Cancer cells grow rapidly and can break off and go to other parts of the body (metastasis) but these attributes come at a cost to these abnormal cells creating potential targets for new drugs with which to target the cancer cell itself. UNC scientists are working to spot these unique vulnerabilities in cancer cells that would allow drugs to kill the tumor but have less toxicity for our patients. When we find new agents, it is critically important that we discover which drugs are most likely to work and design clinical trials that rapidly move them to commercialization, wide distribution, and clinical usage.

It takes more than a decade to progress from discovery and drug development to total completion of drug testing. Only one in 20 drugs entering this process receives FDA approval. With UCRF support, UNC is becoming a leader in finding a shorter path from discovery to market.

UNC has joined a highly selective consortium to work with the National Cancer Institute and develop drug compounds based on new scientific discoveries. UNC has initiated groundbreaking work to improve early testing of drugs in mouse models that mimic human cancers. UNC has also become a national leader in the exciting and rapidly evolving field of cancer nanotechnology and drug delivery. Finally, as outlined below in the section on Critical Infrastructure, UCRF's investment in UNC's clinical trials capabilities has significantly increased capacity for offering patients opportunities to receive new drugs in their testing stages.

**Cancer Drug Development:** Lineberger Cancer Center scientists are working diligently to detect the vulnerabilities in cancer cells that would allow cancer treatments to kill those cells and protect normal cells. Once identified, these cancer cell vulnerabilities can be targets for the development of new small molecule drug therapies, either intravenous or oral. UCRF support (~\$8M) recruited Stephen Frye from GlaxoSmithKline and jump started the development of a chemical biology and drug development institute that placed UNC Lineberger and the Eshelman School of Pharmacy at the forefront of academic cancer drug development. Under Dr. Frye's leadership, UNC was named one of NCI's five national drug development large-scale centers. Upon obtaining this designation, UNC was awarded three contracts to discover and develop drugs: one for pediatric leukemias, one for brain tumors, and one for kidney cancers. These contracts will exceed \$2.5 million yearly, placing UNC at the top of the nation in funding from this program.

**Innovative Pre-clinical Mouse Models of Human Cancer (the Mouse Phase I Unit):** Nobel Prize winner Oliver Smithies introduced genetic manipulation of the mouse for study of diseases to UNC and the world. Existing and UCRF-recruited faculty have used UCRF investment to establish multiple models of human cancer that can be bred in genetically identical mice. These mice can develop breast cancer, pancreatic cancer, lung cancer, ovarian cancer, melanoma, and other types of cancer with 100 percent incidence at defined times. This provides an extraordinary opportunity to test innovative therapies quickly and accurately. The UCRF investment allowed us to expand and staff a production facility for approximately 10,000 mice that develop various forms of cancer. This provides unprecedented, for a University, ability to test combination drug therapy and follow the outcome. Just like humans, these difficult-to-treat mouse tumors mimic the human condition and develop drug resistance. This allows UNC researchers to design experiments defining the genetic causes of cancer drug resistance and to devise therapies to overcome these. This capability will certainly refine our ability to create better human clinical trials. The initial investment in the MPI Unit in 2008-2009 created standard operating procedures and developed expert personnel. By 2010 and in 2011, the MPI Unit has become one of the few and certainly one of the most efficient units of its kind in the nation. In 2010 alone, the

Mouse Phase I unit tested 6 small molecule series from pharmaceutical companies Novartis, Pfizer, Abbott, Astra-Zeneca, GlaxoSmithKline and Concordia. A Phase I trial of a MEK inhibitor from GlaxoSmithKline also was conducted here. This type of pre-clinical research will inform and enhance clinical trials.

**Leading in Nanotechnology and Drug Delivery:** UCRF support has dramatically enhanced the ability of UNC Lineberger faculty in the Eshelman School of Pharmacy and Department of Chemistry to develop and test new delivery methods for cancer drugs. The retention of Joe DeSimone and other faculty and the funding of core resources for nanomedicine led to UNC being named one of the Centers of Cancer Nanotechnology Excellence by the National Cancer Institute. This \$12 million grant is one of only seven in the country. Five different groups are developing different nanomedicine platforms and testing them for both their imaging capabilities (for early detection of cancer) and direct delivery of therapy in our pre-clinical animal models. The nanomedicine groups submitted five patent applications in 2010. Two products were also commercialized.

### **SUCCESS STORY: Integrated drug discovery leads to new research center, federal contracts**



Before being co-recruited by the UNC School of Pharmacy and UNC Lineberger in 2007, Stephen Frye, PhD, headed the worldwide medicinal chemistry unit at GlaxoSmithKline. Dr. Frye is Professor and Director of the Center for Integrative Chemical Biology and Drug Discovery (CICBDD) at UNC-Chapel Hill. Frye is the lead principal investigator for the North Carolina Comprehensive Chemical Biology Center, a UNC-based, NCI-designated center that engages in oncology drug discovery. He is one of NCI's five Comprehensive Drug Development and Chemical Biology Center contractors and has already received three contracts to co-develop drugs with the NCI. The projects are focused on three target diseases: pediatric leukemia, glioblastoma (brain cancer), and kidney cancer.

The CICBDD was created to bring medicinal chemistry expertise to bear on biological targets of therapies being developed. UCRF has invested \$8 million to develop this facility, part of the Genetic Medicine Building. The facility houses researchers undertaking chemical synthesis of materials for preclinical studies and drug discovery. Synthetic chemists, assay developers and compound profiling scientists work with Cancer Center members who have specific novel targets for cancer therapy. Faculty create dedicated, multidisciplinary project teams to discover and develop small molecule therapeutics aimed at the target. This ambitious program is timely: just as basic science and technology seem poised to create a revolution in the availability of potent, selective and safe cancer drugs, the pharmaceutical industry is struggling with organizational changes that have reduced their scientific staff and eliminated their research programs. The CICBDD will fill a key gap by translating UNC basic scientific expertise into potential human therapeutics.

### **Research Priority 3: Optimizing Cancer Outcomes**

UCRF has enabled the building and development of resources and programs that are used to conduct research directly aimed at understanding and then improving cancer outcomes in North Carolina. These efforts include: multifaceted studies that will advance our understanding of disparities in breast cancer outcomes; understanding the complex interplay among genes, tumor, and treatment that results in survival and side effects; and tracking statewide patterns of care. Researchers also have initiated studies that work with communities across the state to understand how best to implement effective prevention and control strategies. Together, these population-focused initiatives will work with and across North Carolina to conduct research that can improve lives and reduce cancer burden.

- **Carolina Breast Cancer Study (CBCS):** This is one of the country's largest population-based studies of breast cancer genetics, health services and outcomes. There is a particular emphasis on minority disparities. Approximately 2,000 cases of a planned 3,000 have been accrued. Grants that have been obtained will total \$5.5 million over the next four years. The Carolina Breast Cancer Study III (CBCS III) is exceeding its recruitment goals and proactively seeking additional funding based on preliminary data. Additional grants are being submitted to Susan G. Komen for the Cure.
- **Integrated Cancer Information Surveillance System (ICISS):** ICISS is an ambitious database including all North Carolina cancer cases linked to outcomes data from Medicare, Medicaid, state employees, and Blue Cross Blue Shield of North Carolina. This will be a nation-leading examination of a state's cancer outcome data and can be used for comparative effectiveness research. Federal grants have been obtained. In 2010, 19 researchers developed pilot data using ICISS, and eight researchers submitted new grant applications incorporating ICISS data.
- **UNC Cancer Survivorship Cohort:** We are beginning to enter 10,000 patients from the North Carolina Cancer Hospital into a cohort for long-term follow-up. This is an extraordinarily data rich project, and we will partner with SAS Institute to develop new analytics for both research and clinical care. The objective is to follow patients intensively from diagnosis through survivorship. Questionnaires, DNA from white blood cells (the DNA the patient inherited), DNA from the tumor (which contains the mutations introduced by the cancer), clinical data, exposure data, and medical treatment data will all be stored. With SAS, we will develop a database to analyze what works and what didn't for the patient's care. A heavy emphasis on following quality of life and toxicity issues will be made, integrating all data with the patient's genetic inheritance and their tumors' genetic betrayal.
- **Health-E-NC – Partnering with Communities Statewide for Cancer Prevention:** Over the past four years, UCRF has helped recruit 10 faculty members in the broad area of public health interventions. These faculty members, and UCRF support of other projects, have led to prevention and cancer control interventions in a number of North Carolina counties. In the last two years, the Health-E-NC program has been launched with a series of pilot projects. Current projects include:
  - Partnering with N.C. Community Colleges to Prevent Cancer Among Students, Employees and Community Residents
  - Healthy Stores, Healthy Communities
  - Circles of Care: Supporting African Americans with Cancer
  - Meeting the Needs of Cancer Survivors in North Carolina: Assessing and Improving the Medicaid Medical Home Model Improving Colorectal Cancer Screening in N.C. Medicaid Beneficiaries
  - Addressing Cancer Disparities by Studying Issues of Coverage, Convergence & Cost in Multiple Settings
- **Developing a Program to Assess Cancer Outcomes and Quality:** Ten faculty members who have been recruited in part with UCRF funds are developing a nation-leading program in understanding patient-reported outcomes and linking those outcomes to quality of life and clinical results for cancer patients. This group is both developing and using the Integrated Cancer Information Surveillance System (ICISS).

They've made important contributions at national meetings and obtained new grants for comparative effectiveness research from the National Cancer Institute and the Agency for Healthcare Research and Quality. Further investment and recruitment will make UNC one of the top three places in the country for research in this growing area of study.

### **SUCCESS STORY: Key faculty push nation's most ambitious breast cancer study**



In 2007, we expanded the breast cancer molecular genetic epidemiology group by recruiting **Melissa Troester, PhD**, from the University of Massachusetts. UNC's long-term commitment to studying breast cancer in North Carolina, the Carolina Breast Cancer Study, had already resulted in national recognition. With UCRF funds, we launched Phase III of this study and recruited Dr. Troester. Her combination of epidemiologic and molecular genetic expertise made her a unique faculty researcher and, with colleagues, set her up to become a leader in the study of the "normal" breast tissue adjacent to breast tumors. Her hypothesis that the response of the patient's body at a site distant from the actual tumor could predict outcome and potentially help inform therapy, is proving to be correct. Her laboratory is now staffed with five people, and she has received funding from the National Cancer Institute, the National Institutes for Environmental Health and Science, and the Avon Foundation.



In that same year, we recruited **Keith Amos, MD**, from MD Anderson to expand our breast cancer surgery group. Dr. Amos had an interest and publications in breast cancer. Drs. Troester and Amos were introduced as a potential collaborative team by Cancer Center leadership, an occurrence which has had a remarkable effect on the research programs of both. Dr. Amos is the clinical arm of the "normal breast" program. With UCRF help we were able to purchase ultrasound and biopsy module that has allowed Dr. Amos to consent and biopsy women for the research study in a timely, patient-friendly manner. He has contributed more than 200 cases to the partnership, and has become a co-author and a co-investigator on the potential grants funding this important work. In addition, Dr. Amos is also a wonderful ambassador for our UNC Breast Center efforts, tirelessly speaking to community groups regarding the need for early detection and the methods where we hope to overcome the poor outcomes in African-American women in North Carolina.

### ***Tier 2: Opportunity***

Although UCRF investment has focused on the three Tier 1 Research Priorities, research and knowledge continue to evolve and opportunities for new areas of strategically important cancer research will develop outside the initial priorities. UCRF investments have strengthened and broadened UNC's cancer research capabilities and, through highly competitive internal seed grant funding, have stimulated new research and attracted extramural grant funding.

**UCRF Innovation Awards – Developing the Next Generation of Cancer Research.** UCRF promotes innovation at UNC, with a highly competitive internal award process that has stimulated cancer research across the public health, clinical and basic science spectrum as well as providing data with which to seek new external funding.

- From 2007 to 2010, UCRF conducted six rounds of competition and received 372 applications.
- Rigorous peer reviews led to 64 awards, a funding rate of about one in six, for a total of \$10.3 million.

- Follow-up results from the initial round in 2007 found that the \$2.4 million in awards resulted in more than 20 extramural grant awards with projected total funding (all years) of \$20.4 million.
- The awards directly or indirectly contributed to one clinical trial, two patent filings, and two startup companies.

### **SUCCESS STORY: UCRF Innovation Awards support collaboration, leverage NCI funds**



Nancy Allbritton, MD, PhD, and David Lawrence, PhD, -- both recruited to UNC in 2007 with the support of UCRF funding – collaborate on research that is developing new ways to assess the proteins that drive cancer formation and provide targets for state-of-the-art cancer drugs. Being able to determine if protein activity is “turned on” or “turned off” in a particular patient is a critical yet unmet need in effective cancer treatment. A UCRF pilot project enabled their two laboratories to work together to create a technology with such exquisite detection that they can measure protein activity not just in the cancer patient but in the patient’s individual cancer cells. This pilot project advance became possible when funding allowed them to combine the Allbritton Laboratory’s strengths in inventing tools for biochemical analysis of living cells with the Lawrence Laboratory’s ability to create novel molecules that probe the cell’s biochemistry. In their first year, the collaboration made such significant progress that they used their results to obtain \$2 million in federal grants from the National Cancer Institute.

### **SUCCESS STORY: Opportunity fund recruit earns one of just 15 scholar awards in US**



With UCRF support, UNC has been able to recruit a series of top-notch junior faculty. Michael Benjamin (Ben) Major is a great example. He has a fierce intellect with a skill set that puts him at the leading edge of signaling research, using the latest technology and a true systems approach. His work in multiple experimental dimensions –mass spec identification of signaling complex constituents, large scale genome wide screens, validation with small molecular probes, mutational data set analysis – is remarkable in its breadth.

Dr. Major has received a two-year \$200,000 Kimmel Foundation Scholar Award from the Sidney Kimmel Foundation for Cancer Research, one of 15 named nationally. He will use the award to support his ongoing efforts to better understand lung cancer progression. He has also been awarded one of the coveted new National Institutes of Health Director’s New Innovator Awards. The \$2.5 million grant will fund his work to identify the full complement of genes that functionally contribute to cancer cellular and disease processes.

Dr. Major’s research team comprises seven scientists, including a computer scientist who developed a new machine learning algorithm to probabilistically score, integrate and visualize the cancer signaling networks. The majority of his lab’s efforts focus on expanding the networks and defining the underlying mechanism(s) by which their discoveries control pathway activation and ultimately oncogenesis. His discoveries are providing new and therapeutically tractable nodes within the lung cancer signaling network.

### ***Tier 3: Critical Infrastructure***

Development of critical underlying infrastructure lays the foundation for success in advancing strategic research priorities and capitalizing on opportunities. The UCRF’s Strategic Plan recognized the importance of this infrastructure and established two broad categories for

investment – Clinical Excellence and Outreach, and Research & Technology Development and Training.

## **1. Clinical Excellence to Support Clinical Research and Outreach**

Though it can take years to test and develop new therapeutics for diseases like cancer, a critical step in that process is the use of clinical trials. As the Strategic Plan notes, UCRF investments designed to strengthen the level of clinical care “will have an immediate impact on the care of cancer patients, while providing the necessary conditions for cutting-edge clinical research.”

Accordingly, the number of patients engaged in clinical trials, and benefitting from important new therapies, is an important and quantifiable measurement of whether UCRF funds are being used to improve therapy. To this end:

- We have created a statewide clinical trials network with more than 10 sites across the state signing up as network partners.
- Provided patient access to the national networks for new treatments through UNC Lineberger’s ties to the National Cancer Institute.
- Initiated 20 clinical trials available through trials network partnerships.
- Increased Phase I (the earliest phase of human drug testing) testing of therapeutics. With a goal to increase Phase I and II testing by 2013, the number of patients enrolled in clinical trials has increased by 49 percent since 2007.

**Early Phase Clinical Trials:** Recruitment in the division of hematology oncology has increased our capacity to do innovative clinical research testing novel therapies in breast cancer, genitourinary cancer (kidney, prostate, and bladder), GI cancers (colon and pancreas), melanoma, head and neck cancers, lung cancer, among others. Expansion of the Clinical Protocol Office and the statewide network led to an “outstanding” rating for our clinical trials facility in the 2010 National Cancer Institute review.

**Survivorship Research:** UCRF commitments in funded research staff allowed UNC to compete for and be named one of the nation’s seven Lance Armstrong Foundation LIVESTRONG Centers of Survivorship Excellence. Our program is consistently seen as a national leader in developing mechanisms to affect the population at large. Researchers have received additional grants from this foundation to guide future directions nationally.

**Clinical Excellence and Research:** The foundation of a nation-leading clinical research program requires superb care for difficult cases and clinician scientists who are both experts in a specific disease and facile with the development of novel clinical trial protocols. The opening of the NC Cancer Hospital provided UNC Lineberger clinicians with an optimal place to practice. UCRF support has helped recruit 35 new faculty across the disease spectrum, who bring expertise from around the nation. Several clinical areas will be highlighted.

- **Pediatric Oncology:** The recruitment of four pediatric oncologists (two from St. Jude’s, one from Cincinnati Children’s, and one from Boston Children’s) has dramatically increased our capacity to care for children with cancer and create new knowledge to improve their care while lessening the toxicity. The pediatric bone marrow transplant program would not exist without UCRF support from 2007 to now.
- **Bone Marrow Transplant Program:** The opening of the Cancer Hospital and the recruitment of four new adult bone marrow transplant clinician scientists have nearly doubled the capacity to do adult bone marrow transplant.

- **Urologic Oncology:** The chief of this service was being recruited away by another prominent academic medical center. We were not only able to retain him and his partner, an expert in robotic prostatectomy, but we have doubled the size of the staff, recruiting surgeons from Johns Hopkins and Chicago. At the same time, we recruited a new head of Urologic Medical Oncology from Memorial Sloan-Kettering. Combined with our existing staff, we believe we will have one of the most scientifically oriented, clinically expert urologic oncology efforts in the country.
- **Geriatric Oncology:** The aging of the American population is resulting in an increase in the incidence of cancer. Virtually all clinical trials to date have excluded patients over the age of 65, the fastest growing cancer population. It is imperative that referral centers and academic cancer centers improve the care of older patients with cancer. We were fortunate with UCRF to recruit one of the country's foremost leaders in this area. He is developing clinical trials, a registry of older patients, and creating a training program in conjunction with the division of geriatric medicine. He has already attracted three medical oncology fellows to this emerging specialty.
- **Radiation Oncology:** The Department of Radiation Oncology has been completely revitalized with the recruitment of Larry Marks, whose startup was principally funded by UCRF. He has recruited five new faculty and has totally revamped the clinical care delivery (increasing patient volume by more than 60 percent). New faculty from Harvard, Duke, and University of Florida have been extremely successful in developing early phase clinical trials, a program in nanomedicine, new methods of therapy, and funding for comparative effectiveness research.
- **Neuro-oncology:** UCRF has funded the development of research in the surgical and medical treatment of brain tumors. The research includes support for the chair's program in brain tumor surgery, the recruitment of an MD-PhD in neuro-oncology, and the recruitment of an MD-PhD pediatric neuro-oncologist. The former is already developing a laboratory translational program with Dr. Yue Xiong dissecting how brain tumors are caused by recently discovered mutations that define a subset of glioblastomas (this work was funded by the UCRF genomics team). The pediatric neuro-oncologist has received substantial funding for his work on the causation and therapy of pediatric brain cancer.
- **Psycho-oncology and Comprehensive Cancer Support:** UCRF enabled recruitment of head psychiatrist from NIH and, more recently, a psychiatrist from Harvard to initiate a patient-directed, research oriented program in psycho-oncology. Research in the role of depression in the quality of life of cancer patients has been launched. This comprehensive program in patient support has dramatically impacted our patients and their families. For example, we have started one of the nation's first support group for single fathers who lost their wives to cancer.

**Clinical Outreach:** The full impact of UCRF will be felt when the clinical excellence and research at UNC and the NC Cancer Hospital are translated into the practice of oncology across the state. A three-pronged outreach approach to this goal is under way:

- The first is a telemedicine network that enables contact with both hospital-based practices and physician offices. This network is allowing a segment of the state's practicing oncologists to consult UNC doctors. Practicing oncologists can attend virtual tumor boards. Telemedicine has also been used in a limited way for clinical care, which we are evaluating through development of a research protocol. Areas such as psycho-



oncology and cancer genetics consults, which are unavailable across large portions of our state, are being developed.

- The second part of outreach is the development and assessment of nurse navigators, who improve access and quality of care by being an information resource for a community and for individual patients. Nurse navigator demonstration research projects are ongoing through the hospitals in Buncombe, Dare and Pitt counties. Results from these demonstrations will be used to enhance the effectiveness of nurse navigators in throughout North Carolina.
- The third aspect is the development of a clinical trials network. Agreements have been signed with ten sites across the state. The network is now in full operation with master agreements in multiple sites. The network accrued over 300 patients to clinical trials who when able are on a trial but remain at home cared for by their own doctor.

The trials network mentioned above includes practices and hospitals across the state including our sister Brody School of Medicine in Greenville. Partnerships with our two UNC School of Medicine expansion sites in Asheville and Charlotte are being initiated and some trials have already started.

A state map showing the scope of UNC's cancer outreach initiatives is included as an appendix to this report. It indicates areas that are involved in our three-pronged outreach effort, as well as communities that are part of pilot projects, research partnerships and other collaborations.

## **2. Research & Technology Development and Training**

**Technology Investments:** Investments in sequencing, genomics, bioinformatics, data storage, and microscopy has made UNC cancer researchers more competitive for grants from federal, foundation and other private sources. These UCRF technology and equipment investments are a big part of the reason UNC has attracted \$69 million in new extramural funds during FY 2010-2011. As mentioned earlier in this report, this new extramural funding had an economic impact of \$156.4 million during this fiscal year.

**Imaging:** The development of the Biomedical Research Imaging Center (BRIC) and its utilization for pre-clinical and clinical cancer research are critical for UNC's continued leadership in cancer research. Purchase of equipment has enabled the performance and analysis of pre-clinical experiments in mouse models. Large imaging instruments that can be used for human clinical trials will arrive with the opening of the Imaging building in 2013. In preparation for occupancy of the new imaging research building, UNC is recruiting faculty and developing capacity in this area.

**Training:** Developing future researchers in the basic, clinical, public health and translational sciences is a major part of both current and future research. UCRF funding has been used to expand the capacity of our training programs in basic and translational science (BBSP), public health sciences (Gillings School of Global Public Health), and the MD-PhD program (School of Medicine). These programs would be 25 percent smaller without the input from UCRF.

### **Other Significant Research Impacts**

In addition to the various initiatives outlined above, UCRF's research impact can be seen in the scholarly output and collaborations:

- **Scholarly Output – Scientific journal publication:** Another measure of progress in research is the increased presence of UCRF-supported faculty members in scientific publications. Publications in scientific journals increased since UCRF's inception and



were coupled with an increase in the average impact factor of published articles as well. UNC Lineberger members published 1,424 journal articles in 2010, up 10 percent from 2009 and 15 percent from 2007.

- **Public and Private Collaborations:** UCRF also supports collaborative relationships with both public and private partners.
  - More than 538 bioscience companies are headquartered or have operations in North Carolina, employing more than 58,000 people. UCRF has been used to support UNC researchers who work with private-sector pharmaceutical partners in clinical trials for new therapies. Examples include Novartis, Pfizer, Abbott, Astra-Zeneca, GlaxoSmithKline and Concordia.
  - UNC-Chapel Hill is working with North Carolina Central University (BBRI and BRITE) in population sciences, cancer biology case drug screening and cancer training. A National Cancer Institute grant – one of the largest grants every obtained by NCCU – has been awarded to support this UNC Lineberger-NCCU cancer partnership.
  - As noted previously, we already have nurse navigator and clinical trials research efforts at ECU and its Leo Jenkins Cancer Center. The nurse navigator evaluation is also ongoing at Mission Hospital System in Asheville. Clinical trials are being initiated in Asheville and at Carolinas Medical Center's Levine Cancer Center in Charlotte. The partnership with CMC/Levine will expand; conversations with their new Cancer Center Director are underway. Mission and Carolina Medical Center's campuses of the UNC School of Medicine are beginning to enroll their first 3<sup>rd</sup> and 4<sup>th</sup> year medical student clinical year classes. In addition to the overall statewide clinical trials network, we anticipate an active UNC Lineberger partnership in cancer education and research with ECU and CMC/Levine Cancer Center as well as with the associated cancer research faculty at UNC Charlotte.
  - The creation of ICISS required collaboration among clinicians and scientists, as well as the private insurer Blue Cross Blue Shield of North Carolina, Medicare, Medicaid, the State Employees Health Plan and the North Carolina State Cancer Registry.
  - A statewide clinical trials network is under development. It was established at six physician practices and hospitals in 2009, and expanded to 10 sites in 2010.
  - The 10,000-patient cancer survivorship cohort is unusually data rich and could help develop new analytics to assess patterns of cancer care. For this reason, we were approached by SAS Institute of Cary, NC, and have formed a three-year partnership to develop analytic approaches to these data. SAS will measurably accelerate our research progress and they will gain experience for future product development.

#### 4. BUDGET AND EXPENDITURE INFORMATION

##### Fund Balance

There is no fund balance in the UCRF. For the second year in a row, despite significant increases in the absolute amount of receipts from the tax on other tobacco products (OTP), actual receipts were less than projected. In FY 10-11 the shortfall was \$1.8 million. In FY 09-10, the shortfall was \$1.0 million.

FY 10-11 Anticipated and Actual Fund Revenue		\$ Amount *
<b>Anticipated</b>		
State Appropriation		16,020,000
Tobacco Trust Fund Transfer		8,000,000
Projected OTP Tax Receipts		25,980,000
Total		50,000,000
<b>Actual</b>		
State Appropriation (January)		16,020,000
Tobacco Trust Fund Transfer (April)		8,000,000
Actual OTP Tax Receipts		24,509,650
Total		48,169,650
<b>Shortfall Due to OTP Tax Receipts</b>		<b>(1,830,350)</b>

\* Rounded to the nearest dollar

Carryover to purchase equipment ordered but not delivered in FY 09-10 raised the anticipated FY 10-11 budget to \$54.7 million. Expenditures for FY 10-11 totaled \$54.4 million. Combined with the lower than expected OTP tax receipts, these expenditures resulted in an ending balance of (-\$1.5 million).

FY 10-11 Budget and Expenditures		Amount \$
<b>Anticipated Budget</b>		
Revenue		50,000,000.00
Carryover for committed FY 09-10 expenses		5,723,157.23
Carryover from unrealized FY 09-10 OTP tax		(1,007,069.35)
<b>Total</b>		<b>54,716,087.88</b>
<b>Actual Budget</b>		
Revenue		48,169,650.00
Carryover for committed FY 09-10 expenses		5,723,157.23
Carryover from unrealized FY 09-10 OTP tax		(1,007,069.35)
<b>Total</b>		<b>52,885,737.88</b>
<b>Expenditures</b>		<b>54,430,271.38</b>
<b>Balance</b>		<b>(-1,544,533.50)</b>

UCRF worked with UNC General Administration to address the deficit due to the OTP receipts shortfall. The budget for new FY 11-12 expenditures has been set at \$47,200,000 to absorb the year-ending balance. At mid-year, the Cancer Research Fund Committee will examine year-to-date OTP tax receipts, obtain a revenue forecast for the remainder of the year, and adjust spending as needed.

### 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, by which the Fund was created, established the Fund as a special revenue fund in the Office of the President of the University of North Carolina. This law, included in the Appendix to this report, explicitly states 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.”

To maximize the effectiveness of the state’s cancer investment and to ensure wise and responsible use of the funding, the committee adopted a Strategic Plan and developed additional restrictions on the use of these funds. It was determined 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 required by G.S. 116-29.1(g), the table below summarizes expenditures of UCRF state funds by Strategic Plan category. Additional details are included in the Appendix.

Categories	Annual Budget	YTD Actual	Cash Balance FY 2011
<b><i>Strategic Plan Categories</i></b>			
Tier 1: Research Priorities			
Understanding Genetics	10,881,133.91	10,897,437.28	(16,303.37)
Developing Novel Therapies	7,810,927.74	7,188,713.45	622,214.29
Optimizing Outcomes	7,912,653.05	7,772,889.05	139,764.00
Tier 2: Opportunity Fund	8,470,128.10	7,719,124.36	751,003.74
Tier 3: Critical Infrastructure			
Clinical Excellence - Research & Outreach	9,397,057.62	9,849,768.59	452,710.97
Research & Tech Development and Training	10,244,187.81	11,002,338.65	758,150.84
<b>Total</b>	<b>54,716,088.23</b>	<b>54,430,271.38</b>	<b>285,816.85</b>

**Administration.** UCRF's expenditures for administration are primarily included under Research & Technology Development and Training. For FY 10-11, these expenditures, which were almost entirely for personnel, totaled \$505,663.91 or approximately 1% of the initial budget of \$50 million. In addition, UCRF expended \$176,980.41 to support Planning and Evaluation activities.

#### **Expenditures of Extramural Funds Related to UCRF**

More than \$69 million in active, annual extramural grant funding is attributable to UCRF. The Appendix includes a complete list of those grant awards. The award amount represents both direct and indirect dollars awarded. The list includes all grant awards active during the first quarter of FY 11-12 for faculty recruited or retained with UCRF support. The list also includes awards directly attributable to UCRF technology and other investments, such as Next Generation Sequencing and Innovation Awards.

## 5. CONCLUSION

The fight against cancer is a lengthy and continuous effort, but every new discovery and innovation brings us closer to finding the best ways to prevent, treat, and hopefully cure this disease. The University Cancer Research Fund has proven to be an important and worthwhile investment that has resulted in job creation, economic growth, innovation, and extraordinary progress in developing new cancer technologies and treatments.

The diffusion of new information throughout the state, its agencies, communities, medical practices and hospitals is crucial to adoption of the best prevention services and early detection modalities. It is equally important to changing patient and survivorship care across North Carolina. UCRF investments in measuring these parameters are one key to targeting interventions that will change cancer outcomes in North Carolina, making the state a shining example for the nation.

The UCRF has been invested as proscribed by state law and by the Cancer Research Fund Committee's mandate to use resources responsibly and in a way that maximizes their impact. Continued funding from the state is critical in enabling researchers to continue their work to improve outcomes for cancer patients and, eventually, to eradicate the disease entirely.

### *Appendix*

Establishing Legislation  
Cancer Research Fund Committee  
Economic Impact Analysis Summary  
UCRF Outreach Map  
FY 10-11 Expenditures  
UCRF Strategic Plan  
List of Active Extramural Awards