

University Cancer Research Fund

Annual Report 2013–2014

Letter from the Chair:

On behalf of the Cancer Research Fund Committee, I am pleased to present the annual report of the University Cancer Research Fund. We are grateful for your continued support of the UCRF and for the important research it funds. The state's investment in cancer research continues to reap health and economic benefits for North Carolina.

Thanks to the UCRF, every dollar invested by the state yields more than \$5 in return. Additionally, clinical trials that will improve cancer care are enrolling patients across North Carolina. We have recruited and retained more than 170 outstanding cancer researchers; many are national leaders in the fight against this disease. And we are connecting communities to better prevention efforts as well as post-treatment strategies that will improve patient outcomes.

UNC is a leader in innovative research that will improve doctors' understanding of the many different types of cancer, helping them detect tumors earlier and provide targeted treatments that work best for each individual patient. This report highlights several current studies published in the world's top journals. Many projects tie UNC to national and

international partners directly aimed at improving health and cancer outcomes in North Carolina.

Scientists are making progress in the fight against cancer, but it remains the top cause of death in North Carolina and the second-leading cause of death in the United States. The University Cancer Research Fund remains a vital investment as we continue our work toward to eliminate this disease.

Thank you for your ongoing support of the University Cancer Research Fund.

Sincerely,



Carol L. Folt, Ph.D.
Chancellor, University of North Carolina at Chapel Hill
Chair, Cancer Research Fund Committee

University Cancer Research Fund has powerful economic impact

The University Cancer Research Fund has a significant economic impact on our state in several ways — such as creating jobs, bringing and keeping great scientists here to fuel innovation, and leveraging research dollars from outside North Carolina. The UCRF yields a total return on investment of greater than 5 to 1. According to an independent economic analysis conducted last fall, the Fund's economic impacts include:

- Hiring and retaining 180 outstanding cancer researchers at UNC.
- Directly supporting nearly 1,000 employees and creating the equivalent of more than 900 new jobs.
- Maintaining a significant annual economic impact for North Carolina — \$264.8 million for fiscal year 2012–2013, leading to a total economic impact of more than \$1.2 billion over the six years UCRF has existed.

One key measure of UCRF's success is the continuing increases in research funding directly attributable to UCRF investment. Between 2007 and 2013, total extramural support to the UNC Lineberger Comprehensive Cancer Center increased from \$163.6 million to \$227.4 million.

- This year alone, UNC received \$105.8 million in new UCRF-attributable research funding from outside North Carolina.

- In FY 2012, UNC Chapel Hill ranked 7th in NIH awards and 11th in NCI awards.
- The National Institutes of Health (NIH) and the National Cancer Institute (NCI) increased awards to UNC Chapel Hill faculty between FY 2007 and FY 2012, while awards to many comparable institutions decreased during that time period.
- Between FY 2007 and FY 2012, NIH awards to UNC Chapel Hill increased by almost 17.8%, significantly ahead of public peer institutions (3.4% increase), private peer (1.4% decrease), and total agency extramural awards (4.8% increase).
- During that same period, NCI awards to UNC Chapel Hill increased 32%, significantly ahead of public peers (2.9% increase), private peers (4.9% decrease), and total agency extramural awards (1.7% increase).

The UCRF also enhances spin-off commercialization efforts and intellectual property, adding new innovations to the nation's fourth-largest cluster of life science industries. In the past six years, **18 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.

In 2007, the year cancer replaced heart disease as North Carolina's leading cause of death, the N.C. General Assembly created the University Cancer Research Fund (UCRF) to provide ongoing state support for cancer research.

The Fund, which received \$42 million from the state for FY 13–14, aims to create a nation-leading cancer research effort and to reduce North Carolina's cancer burden.

Strategic Plan

Investments from the Fund are guided by a Strategic Plan adopted in 2009 that focused UCRF resources where they can have maximum impact. The three focused primary research priorities are:

- **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 outcomes, by identifying genetic mutations that reduce the effectiveness of cancer treatments.
- **Developing Novel Therapeutics** — to create more effective therapies targeted to the specific vulnerabilities of treatment-resistant cancers, and to devise new ways of delivering drugs to reduce side effects for patients.
- **Optimizing NC Cancer Outcomes** — to build population-based datasets to track the occurrence and treatment of cancer across North Carolina in an effort to improve community prevention and early detection of cancer, and to enhance the quality of oncology and survivor care across the state.

Also under the Strategic Plan, the UCRF funds *opportunistic initiatives* such as the Innovation Awards, a competitive program that promotes groundbreaking research with a high likelihood of success and impact. Finally, UCRF supports investments in technology, training and other *critical infrastructure*, and promotes multidisciplinary clinical excellence and outreach across the state.

The Cancer Research Fund Committee is conducting a re-evaluation of the UCRF's Strategic Plan that is expected to be completed later this year.

The Committee was established in 2007 by the General Assembly to oversee the Fund. The seven-member committee is chaired by UNC-Chapel Hill Chancellor Carol Folt. The four other ex officio members are Ned Sharpless, director of the UNC Lineberger Comprehensive Cancer Center; William L. Roper, MD, MPH, dean of the School of Medicine; Robert Blouin, PharmD, dean of the Eshelman School of Pharmacy; and Barbara K. Rimer, DrPH, dean of the UNC Gillings School of Global Public Health. The ex officio members elect two additional members, representing nationally prominent cancer programs. The two elected members are Edward J. Benz, MD, president and CEO of the Dana Farber Cancer Institute; and John Mendelsohn, MD, president emeritus of M.D. Anderson Cancer Center.

Cancer Genetics

Cancer genetics — the study of the genetic changes that determine why and how tumors develop — plays a critical role in early detection, treatment, prevention and prognosis. UNC is a national leader in this rapidly growing field, which helps doctors identify which types of treatments will work best for each individual cancer patient.



UNC has sequenced more RNA samples for clinical use than any other center in the nation.

UNCseq hits enrollment milestone

Since 2013, more than 1,000 patients have enrolled in UNCseq, UNC's new genetic sequencing protocol that is helping provide customized cancer care for individual patients. The program's research is designed to make cancer treatments more effective.

This genetic sequencing analysis will help doctors create a cancer treatment plan for an individual patient based on the genetic details of that patient's specific tumor. By using next-generation sequencing to analyze tumor samples obtained from biopsies and surgeries and then comparing the genetic changes in the patient's tumor samples to normal DNA from blood, doctors can pinpoint the genetic differences that may influence patient outcomes and choice of cancer treatments.

Thanks to the UCRF, UNCseq will be especially important in cases where standard therapeutic options may not be effective or applicable. For example, if researchers find and validate a mutation that can be treated with a drug targeted to that change, UNC oncologists will provide that information to the patient and his or her doctor so they can discuss that treatment option. Findings may also provide patients with information leading to their enrollment in a clinical trial of a targeted therapy for that specific molecular mutation.

In addition to providing more individualized cancer care, UNCseq will fuel research on new treatments and test the effects of clinical therapies already being studied. It also enables researchers to analyze RNA, blood and other types of samples, not just DNA.



William Kim, MD, led the discovery of a bladder cancer subtype that reflects breast cancer

UNC scientists play key roles in bladder cancer research

UNC Lineberger Comprehensive Cancer Center members William Kim, MD, and Katherine Hoadley, PhD, were members of a multi-university team of researchers who completed a comprehensive genomic sequencing of 131 urothelial bladder carcinoma tumors to provide scientists and drug developers with a roadmap of the genetics of the cancer. Bladder cancer is an understudied cancer that is diagnosed in 70,000 Americans each year.

Current treatment for bladder cancer includes surgery, cisplatin-based multi-agent chemotherapy and radiation, but there are no FDA-approved targeted therapies at this time. The sequencing study identified potential therapeutic targets for urothelial carcinoma, a form of bladder cancer that invades the muscle tissue of the bladder. Along with revealing new genes and pathways that are disrupted by the disease, the project also found that, at the molecular level, some subtypes of the cancer resemble subtypes of breast, head and neck, and lung cancers.

The sequencing project was published in the journal *Nature* as part

of The Cancer Genome Atlas (TCGA) project, a large-scale cancer research collaboration managed by the National Cancer Institute (NCI) and the National Human Genome Research Institute (NHGRI), both parts of the National Institutes of Health (NIH), to categorize the genomic changes that occur in cancer. Investments from the UCRF helped provide the infrastructure needed to enable UNC to take a leadership role in TCGA. In 2009 UNC was chosen as one of just 12 TCGA centers and was slated to receive \$20 million in outside funding over five years.

In addition to contributing to TCGA, Kim, along with Jeffrey Damrauer, a graduate student in the Curriculum of Genetics and Molecular Biology, spearheaded a UNC-based genetic analysis of bladder cancer tumors that found the disease shares genetic similarities with two forms of breast cancer.

Their analysis of 262 bladder cancer tumors, published online by the Proceedings of the National Academy of Sciences, reveals that the invasive form of the disease can be classified into two distinct genetic subtypes – basal-like and luminal. These subtypes are very similar to the basal and luminal subtypes of breast cancer first described by Charles Perou, PhD, May Goldman Shaw Distinguished Professor of Molecular Oncology at UNC Lineberger.

The mapping of the genetic signaling pathways of the breast cancer subtypes has led to development of drugs and diagnostic aids that aid physicians in determining the best course of therapy for patients with that disease. As the identified bladder cancer subtypes share many of the same genetic signaling pathways of breast cancer, researchers hope that the identification of the genetic subtypes can lead to similar advances.

Kim's lab has developed a gene map, BASE47, that was successfully used as a prognostic aid when applied to the tumor samples in the study. The PAM50 genetic test, a similar genetic map developed in the Perou lab, was recently approved as a clinical diagnostic tool by the FDA.

The study also revealed a possible answer for why women diagnosed with bladder cancer have overall poorer outcomes compared to males. Analysis from female patients showed a significantly higher incidence of the deadlier, basal-like tumors, but researchers said that more research is needed before a definite link between the subtype and survival can be confirmed.

UNC researchers take leadership role in whole-genome sequencing studies

As scientists continue exploring DNA and molecular genetics to better tailor cancer care for individual patients, UNC researchers are leading the way by developing key resources for doctors to use as genetic information becomes more commonly used at the clinical level.

Thousands of variations within specific genes can play a role in whether, and how, tumors develop — but information about these variations is scattered throughout many different studies.

In an ambitious project to develop a more readily available resource, UNC geneticists Jonathan Berg, MD, PhD, assistant professor in the Department of Genetics, and Jim Evans, MD, PhD, Bryson Distinguished Professor of Genetics and Medicine, are creating a detailed database of all the genetic variants that are thought to be related to human disease. Ultimately, Berg and Evans hope to have the database serve as a free, publicly available resource.

Evans and Berg have received a four-year, \$4.8 million grant from the National Institutes of Health to develop this database, as part of an NIH effort to recruit dozens of researchers, clinicians and gene-sequencing labs around the nation to collect variant data and review it for clinical significance, and find new ways to determine whether — and to what extent — the variants are able to influence the development of diseases.

Berg said: “We need to be able to say for each variant: what do we know about it? How many times has it been seen in medical cases and in controls? What do our prediction algorithms say about it? What is its predicted effect on the structure of a protein? Is it in an important functional domain?” Answering these and many other questions will help Berg's team score each variant's potential to cause disease.

Evans also spearheads a project called NCGENES, which uses whole-genome sequencing to assist in diagnosing genetically caused diseases. NCGENES helps to pinpoint people who are at high risk for diseases before they show symptoms, as well as guide new disease treatments.

Traditional genetic testing usually involves gene-by-gene analysis — a process that is too costly and time-consuming to be practical for analysis of a whole genome. NCGENES streamlines the process by focusing the analysis on genes known to be involved in specific diseases.

The project, funded by a four-year, \$8 million grant from the National Human Genome Research Institute, will enroll undiagnosed patients in broad disease categories with likely genetic causes. Over the four years, about 750 patients from UNC hospitals and clinics will have their genomes sequenced and analyzed through NCGENES.

The analysis will first look for mutations in genes known to cause specific

disorders. The researchers also will look for medically relevant incidental findings by examining other genes known to influence or cause disease. By focusing on well-known and understood genetic markers, researchers hope to implement a simpler, scalable method for finding useful health related information in the huge volume of data that make up a human genome. That information can then be used to make evidence-based diagnoses and treatment decisions.

UNC researchers are also working on the ethical implications of having whole-genome sequencing available as a resource. For example, NCGENES could potentially reveal genetic information that has lifelong impacts on the study subjects — such as their likelihood of developing a fatal disease. Researchers will gather data on what people want (and don't want) to know about their genetics, which factors influence their decisions, and how information about genetic diseases changes peoples' attitudes and behaviors. Dr. Evans has called for the development of guidelines to help doctors communicate with their patients about information that could be revealed by such comprehensive tests.

A new but related study being done at UNC will consider the practical and ethical considerations of using genomic testing to screen newborns for genetic conditions. Researchers at UNC plan to sequence the entire genome of 400 infants to determine what useful clinical data can be acquired through the tests.

In conjunction with the testing, the UNC team — led by Berg and Cynthia Powell, MD, MS, a professor with the UNC departments of Genetics and Pediatrics and member of the Carolina Center for Genome Sciences — has partnered with Research Triangle Park-based RTI International to develop educational and consent tools to determine how best to educate parents and physicians about the test and its results.

The study will be funded by a 5-year, \$5 million grant from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and the National Human Genome Research Institute (NHGRI), both parts of the National Institutes of Health.

The tests will examine genomic data from a healthy group of children and a cohort of children with suspected or diagnosed genetic disorders. The ultimate goal is to determine whether genomic testing can be an effective tool for pediatricians to incorporate alongside existing tests.

A central focus of the study is the need to make sure that parents and physicians have the tools to make an informed decision. By developing best practices — from educational tools to parental consent protocols — researchers plan to build a model for making informed choices about when to test and how to use the data gathered from newborn testing.

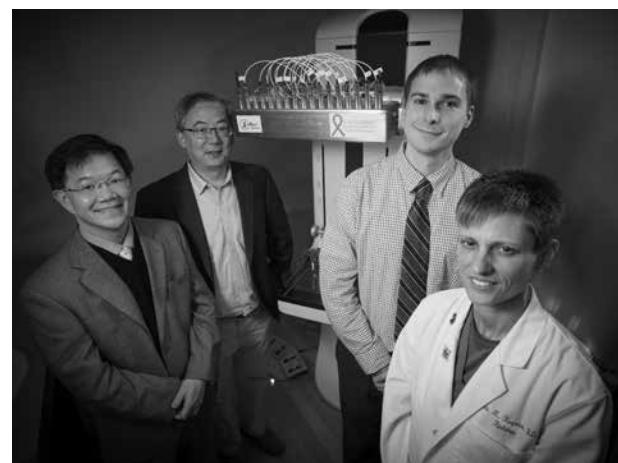
Developing New Cancer Treatments

Scientists are working to identify the unique vulnerabilities in cancer cells in order to develop new drugs and treatment delivery methods that would more effectively kill the tumor while sparing normal tissues. But it can take more than a decade to go through the process of discovery to drug development to total completion of testing, and most drugs fail to get approval from the U.S. Food and Drug Administration. The UCRF supports UNC's work to develop more effective therapies and get them commercialized so they are available to help patients as soon as possible.

Clinical trials and development under way for imaging technologies to better detect and treat cancer

Patients are now enrolled in clinical trials to test a better mammogram using a new x-ray imaging system developed by UNC Lineberger member and physics professor Otto Zhou, PhD, which could improve the early detection of breast cancer.

X-ray digital breast tomosynthesis (DBT) is an emerging technique for producing multi-slice images to provide depth resolution and improved contrast compared

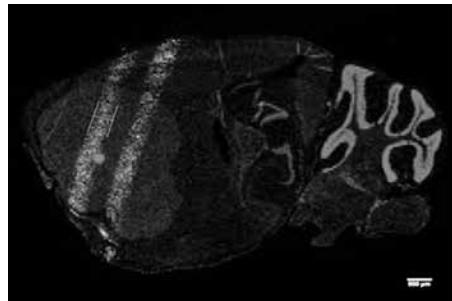


From the lab to the clinic, UNC researchers are changing the face of breast screening with new X-ray technology.

to traditional mammography, but current DBT models require long scanning time, which can lead to blurry images, prolonged compression, patient discomfort and other problems. In clinical trials, Zhou is now testing a next-generation DBT scanner that relies on a multipixel x-ray technology to increase the imaging speed,

reduce the size and cost of the equipment, and potentially reduce imaging dose while improving quality.

Zhou's DBT device is based on pioneering work he has done at UNC using carbon nanotubes (CNT) as an x-ray source. In addition to developing improved tumor detection tools like the next-generation DBT, he is working on ways to use nanotubes to develop cancer treatments that more precisely target tumor cells without harming healthy tissues.



A multidisciplinary team led by Zhou has built a device using carbon nanotube-based x-ray source array technology to generate microbeam radiation. Through tests on animals, microbeam radiation therapy (MRT) has shown tremendous promise for cancer patients because of its ability to destroy tumor cells while protecting the surrounding healthy tissue.

However, research into the clinical use of MRT — and its potential for human patients — has been limited by the enormous size of the electron accelerators, known as synchrotrons, that are needed to generate the beams. Until now, administering MRT required the use of these massive synchrotrons, but Zhou's new device has opened the doors for clinical research by scaling down the technology.

Because of researchers' limited ability to study the effects of MRT, little is known about why the radiation destroys tumors but only causes minimal damage to surrounding tissues. A more compact MRT emitter would give more researchers access to the technology and spur a greater level of research into the interplay between the radiation and biology. The UNC team has recently received a U.S. patent covering the compact MRT technology.

"The innovation here, what we have done at the university, is to build equipment that is compact and can be potentially used in a hospital and achieve similar therapeutic value. The fact that the microbeam can deliver the radiation effect is known, the experiments have been done, but the use of the synchrotron-based equipment is not practical," Zhou said.

UNC discovery leads to new FDA-approved breast cancer lab test

The U.S. Food and Drug Administration has approved a laboratory testing kit — based on a gene signature called PAM 50 discovered by UNC researchers — that estimates the risk of breast cancer relapse in spite of anti-hormone treatment.

UNC Lineberger member Dr. Chuck Perou, PhD, professor of genetics and pathology, and his colleagues Dr. Joel Parker, assistant professor of genetics, and Dr. Maggie Cheang, a research associate in the Perou Lab, collaborated with scientists from three other institutions — Washington University in St. Louis, the University of Utah and the BC Cancer Agency — to design the test. The test is being distributed to pathology labs around the world and is approved for use in the European Union.

The test, called Prosigna, categorizes breast tumors into one of four main subtypes — luminal A, luminal B, HER2-enriched and basal-like — by looking at the expression of 50 genes, and develops a "risk of recurrence" score based on the subtype to predict the likelihood of a patient's disease returning within the next 10 years.

This score can help clinicians accurately identify those low-risk patients for whom standard hormone therapy is sufficient to prevent relapse. Patients with the luminal A subtype have a low risk of relapse and do well with long-term anti-hormone therapy, but the other tumor types may require more aggressive measures to prevent relapse, including chemotherapy and sometimes investigational drugs.

"This approval marks more than a decade of work with my fellow researchers and highlights the growing importance of genomic and genetic tests in the oncology clinic," Perou said. "This test is the result of data coming from modern, cutting-edge genomic technologies, and will help guide the right therapy for women with breast cancer."

Kay Yow Cancer Fund awards \$1 million research grant to UNC Lineberger

UNC researchers will lead a national study on the impact of exercise among breast cancer survivors, thanks to a \$1 million grant from the Kay Yow Cancer Fund in partnership with The V Foundation for Cancer Research.

The grant will fund a Phase II, four-year controlled trial to assess the effects of a physical activity intervention program on biomarkers of aging and body composition among breast cancer survivors, age 65 and older, who are receiving chemotherapy before or after surgery.

The study will be a national, multi-site collaboration with the Cancer and Aging Research Group, UNC Hospitals, affiliated community clinics and the Alliance for Clinical Trials and Oncology.

UNC Lineberger Geriatric Oncology Program Director Hyman Muss, M.D., will lead the study, which will build upon a well-established base of UNC research on aging



The V Foundation for Cancer Research presented UNC Lineberger with a \$1 million research grant, the largest-ever grant awarded by the organization.

and breast cancer. After the study is completed, cancer patients across the nation will have access to a proven, user-friendly, simple exercise program that will help them maintain independence and improve quality of life, which also may favorably affect genes of aging.

"Most people in the U.S. with breast cancer are now 65 and older.

As we develop treatment plans for our older patients, our goal is to pick the right treatment based on the patient's general health and preferences, not their age," Dr. Muss said. "We know that incorporating simple, routine exercise — like walking — into a patient's treatment plan helps maintain function and improve overall quality of life. We are thrilled to have the opportunity to grow this program, help more breast cancer patients and see it realized on a national scale."

Chemotherapy accelerates 'molecular aging,' UNC researchers find

Physicians have long suspected that chemotherapy can accelerate the aging process in patients treated for cancer. Using a test developed at UNC Lineberger Comprehensive Cancer Center to determine molecular aging, UNC oncologists have directly measured the impact of anti-cancer chemotherapy drugs on biological aging.

Researchers measured the level of p16, a protein that causes cellular aging, in the blood of 33 women over age 50 who had undergone chemotherapy for curable breast cancer. Samples were taken for analysis of molecular age from patients before



Hanna Sanoff, MD, MPH

and immediately after chemotherapy, as well as a year after therapy finished. The analysis showed that curative chemotherapy also caused an increase in a patient's molecular age that on average was equivalent to 15 years of normal aging. The same was true in a separate group of 176 breast cancer survivors who had received chemotherapy on average three and a half years prior.

The study, led by UNC Lineberger member Hanna Sanoff, MD, MPH, assistant professor with the UNC School of Medicine, suggests that the p16 test holds promise as a means of evaluating how chemotherapy will affect a

patient's long-term health and survival, and as a predictive biomarker for the long-term toxicity of chemotherapy.

The next step for this research involves determining whether markers of molecular age predict patients' physical function and outcome in a number of clinical settings. The p16 test seems especially well-suited as an aging marker for this purpose as it plays a causal role in biological aging, is strongly correlated with chronological aging, and increases exponentially in response to pro-aging stimuli.

The key role of p16 in human aging has been established over the last 10 years in the lab of UNC Lineberger Director Dr. Norman Sharpless. In 2004, his lab conducted research finding that the levels of p16 increase exponentially with aging, and in 2009 he developed the p16 blood test for human use.

UNC and research partners receive \$1 million grant to investigate novel melanoma target

A team of researchers from UNC, the University of Colorado and the Hebrew University of Jerusalem have been awarded a \$1 million grant for work to improve the treatment of melanoma, the most aggressive type of skin cancer.

The grant will investigate a novel target in melanoma, a type of protein enzyme called MerTK, which was discovered in Dr. Shelley Earp's lab with a then-UNC medical student and doctoral candidate Doug Graham. Dr. Graham, now a professor of pediatric oncology at the University of Colorado, and Dr. Earp have been collaborating on this project for more than a decade. They were joined five years ago by Stephen Frye, PhD, and Xiaodong Wang, PhD, UNC Lineberger members in UNC's Eshelman School of Pharmacy, who have since worked with the team to develop a drug that targets MerTK activity.

In a recent study, the collaborators found that MerTK is elevated in metastatic melanoma and 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. About half of the grant funds will be used by the UNC Lineberger/Colorado team to develop their small molecule drug, while the other half will be used by team members in Israel who will concentrate on understanding how MerTK is activated from outside the melanoma cell and how its activation might be blocked in order to enhance therapy.

The grant award was made by the Melanoma Research Alliance (MRA) and the Saban Family Foundation, a charitable foundation focused on improving education and healthcare in the U.S. and Israel.

Optimizing Cancer Outcomes

The third UCRF research priority under the Strategic Plan is to work to improve cancer outcomes in the state. Through outreach initiatives and population-based studies, UNC is forming key partnerships with communities across North Carolina to determine how best to implement effective cancer prevention and control strategies. UCRF also supports results-based comparative effectiveness research that is more readily applicable to North Carolina's diverse population.

Third phase of Carolina Breast Cancer Study enrolls 3000th patient

The Carolina Breast Cancer Study (CBCS) — the largest-ever population-based study of breast cancer in North Carolina and one of the largest in the world — has enrolled its 3000th patient and is now in the five-year follow-up phase (Phase III) of a project that has already spanned two decades.

Launched in 1993 and including participants from 44 of North Carolina's 100 counties, the CBCS aims to improve understanding of breast cancer. CBCS Phase I and II made groundbreaking discoveries regarding the genomics of breast cancer in younger African-American women. Phase III will be a national model for studying why the death rate for African-American women is higher than those of whites.

The enrollment milestone was accompanied by regional meetings — in Wilmington, Greenville, Concord and Chapel Hill — so participants could learn more about the study's past findings and what researchers hope to accomplish in the next phase. Phase III of the study will focus specifically on how treatment decisions, access to care, and financial or geographic barriers impact breast cancer outcomes and whether these outcomes are predictable or altered by genetic breast cancer subtypes. The study also aims to further investigate subtypes of breast cancer that may be associated with different risk factor and prognosis profiles, continuing discoveries made in earlier phases of the study.

Participants were identified from a list of newly diagnosed breast cancer patients provided by the North Carolina Central Cancer Registry (NCCCR), which identifies and registers all new cancer diagnoses in the state. Participants were then selected through a scientifically sound, randomized process, and physicians were notified of the study's intent to contact their patient.

"We are so grateful for the tremendous interest and cooperation from the women approached for the study and our network of physicians and health care providers across the state to connect us with their patients," said Andy Olshan, PhD, the study's principal investigator, professor in Cancer Epidemiology and associate director of population sciences at UNC Lineberger.



Recruited from the National Cancer Institute, Bryce Reeve, MD, is helping to understand how pediatric cancer patients communicate their symptoms during treatment.

Lineberger member works to give young cancer patients a voice

In pediatric cancer clinical trials, doctors are required to document any major toxicities, or adverse events (AEs), that occur as their young patients undergo treatment. But UNC Lineberger member Bryce Reeve believes that the child's perspective — not just the doctor's report — also is an important AE measure.

Reeve, who was recruited to UNC with the support of UCRF resources, is working to create and validate a self-report measure of subjective AEs for children aged 7 years and older, to incorporate into the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE). He received a five-year, \$2.5 million grant to support his research.

Reeve and his colleagues surveyed almost 200 pediatric clinicians to identify which of

the 790 AEs in the current CTCAE should be included in a self-report measure for pediatric patients. According to the survey, 64 CTCAE terms were found to be subjective, relevant for use in pediatric cancer trials, and amenable to self-report by a child. Dr. Reeve is now translating these 64 AEs into child-friendly terms that will form the basis of the child-report toxicity measure. The systematic collection of these

data will ultimately improve pediatric cancer care by enhancing the accuracy and completeness of treatment toxicity reports for childhood cancer.

UNC to receive up to \$40 million over next five years for tobacco research

UNC has been awarded a total of \$40 million to establish two of the nation's 14 Tobacco Centers of Regulatory Science (TCORS) as part of a major collaboration between the U.S. Food and Drug Administration (FDA) and National Institute of Health (NIH) to inform the regulation of tobacco products to protect public health.

Despite decades of work to reduce tobacco use in the United States, it continues to be the leading cause of preventable death and disease. A new, first-of-its-kind regulatory science tobacco program, TCORS is designed to bring together investigators from across the country to aid in the development and evaluation of tobacco product regulations.

The UNC Center for Regulatory Research on Tobacco Communication (CRRTC) will receive nearly \$20 million over the next five years to research the communication and prevention strategies around the FDA constituent analysis of tobacco smoke.

"The goal is to inform and shape how the FDA regulates tobacco products by doing high impact research that will ultimately help reduce tobacco use," said CRRTC Director Kurt Ribisl, PhD, who is the program leader of Cancer Prevention and Control Program at UNC Lineberger and professor of health behavior at UNC's Gillings School of Global Public Health.

This multidisciplinary Center will work on three major studies about reinforcing communication with the public about the dangers of alternative tobacco products such as electronic cigarettes, hookahs and smokeless tobacco; the harmful effects of chemicals found naturally in tobacco and cigarette smoke; increasing the credibility of risk communications and health risks to audiences from diverse communities; and how to optimally communicate FDA authority over tobacco products.

The second TCORS grant awarded to UNC will support the UNC Center for Tobacco Regulatory Science and Lung Health, led by Robert Tarran, PhD, associate professor of medicine at UNC.

This Center will focus on better understanding which components of tobacco and which new and emerging tobacco products have an adverse effect on lung hydration and innate immune defense. This Center will work on four separate projects to comprehensively understand how new and emerging tobacco products such as little cigars and hookah used by young people can be harmful to lung health, including the development of chronic bronchitis, impaired innate immunity, tobacco-induced lung inflammation, mucus overproduction and cancer.

UNC researchers make key contributions to HPV report for US President

UNC Lineberger Comprehensive Cancer Center members played a major role in developing the recommendations in a President's Cancer Panel (PCP) report urging a widespread public campaign to increase the rate of human papillomavirus (HPV) vaccination to prevent cervical and head and neck cancer.

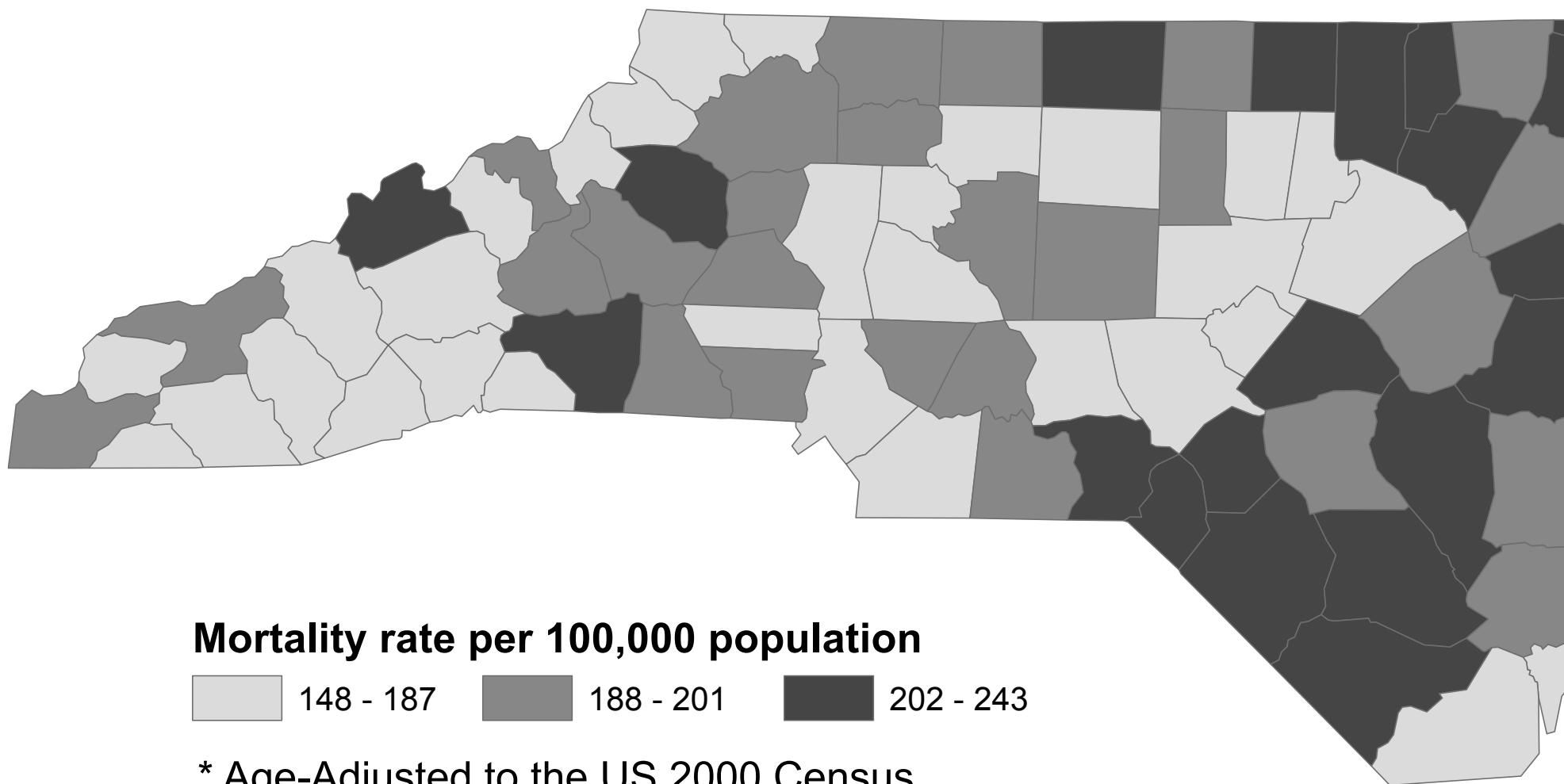
The panel, which is charged with identifying barriers to progress against cancer and reporting them to the President of the United States, has been chaired by UNC Gillings School of Global Public Health Dean and UNC Lineberger member Barbara K. Rimer, DrPH, since 2011. The panel's report found that that increasing HPV vaccination is one of the most profound opportunities for cancer prevention.

In addition to Rimer's leadership of the panel, several Lineberger members made key contributions to the report. Noel T. Brewer, PhD, director of Cervical Cancer-Free North Carolina, co-chaired one of four workshops that informed the report. Tamera Coyne-Beasley, MD, MPH, professor of pediatrics and internal medicine, also co-chaired a workshop and contributed to the report. Jennifer S. Smith, PhD, MPH, associate professor of epidemiology at the Gillings School of Public Health, also contributed to the report.

HPV has been linked to a variety of health problems. The association with cervical cancer has been known for years, but the last decade has seen a great increase in HPV-associated head and neck cancer which affects men and women similarly. The panel's report calls for a coordinated effort to increase the rates of vaccination among both boys and girls. Presently, only 33 percent of girls and 7 percent of boys in the United States have received the recommended three-doses of the vaccine. The deficit in boys is a particular problem in stopping the increase in HPV-associated head and neck cancer in men.

The report calls on health care providers to reduce missed opportunities to recommend and administer HPV vaccines. It recommends that the US Centers for Disease Control (CDC) work to increase doctors' knowledge about the benefits of HPV vaccines and encourage them to recommend vaccinations for age-eligible adolescents. The report also suggests that efforts should be made to make the vaccine more easily available, and to inform parents and adolescents about the safety and effectiveness of HPV vaccines in reducing cancer risks.

2003-2010 All Cancers Age-Adjusted Mortality



Featured UCRF Projects Impacting North Carolina

UCRF supports the prevention and treatment of cancer throughout North Carolina. The following features represent just a handful of projects touching the lives of North Carolinians. For more information on projects and UCRF updates, please visit www.unclineberger.ucrf.

Connecting with physicians across the state

UNC physicians connect via telemedicine with oncologists and other physicians across the state on a regular basis. UNC faculty regularly hold virtual “tumor boards” — an in-depth review of a particular patient’s case with a team of doctors — to review cancer cases across the state. Clinicians in the Comprehensive Cancer Support Program are also using the technology to connect with

patients directly, offering virtual counseling sessions or simply to answer patient questions.

Preventing lung cancer through primary care networks

Cigarette smoking remains the leading cause of preventable death in the US. Working through the UNC Practice Network, UNC researchers partnered with providers in one clinic to increase their expertise in pharmacotherapy and behavioral interventions, enabling them to better support their patients struggling to quit smoking. At the end of year one of this ongoing project, researchers found a significant increase in the documentation of counseling, cessation medications discussed or prescribed and the number of referrals to QuitlineNC.

Assessing risk factors for cancer

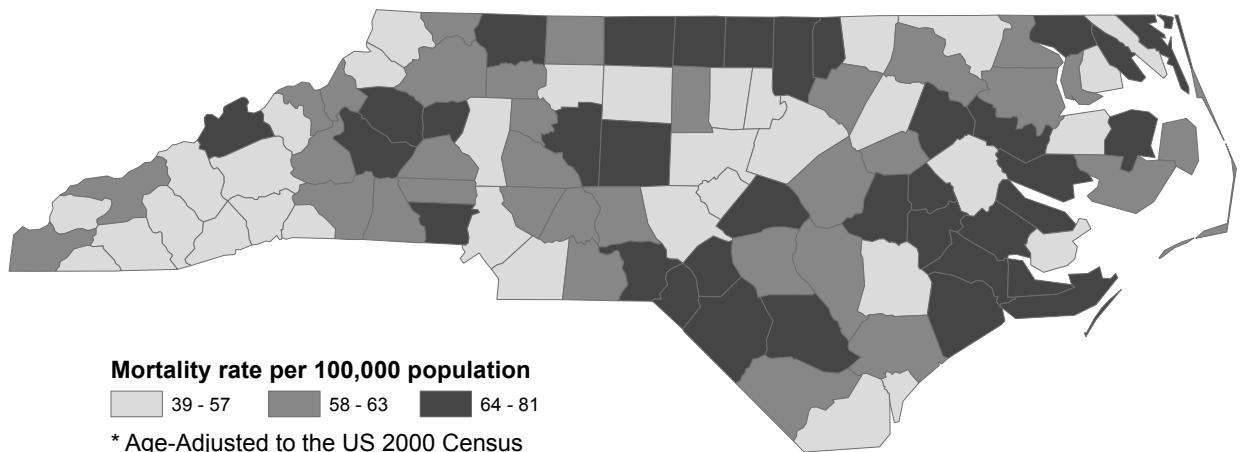
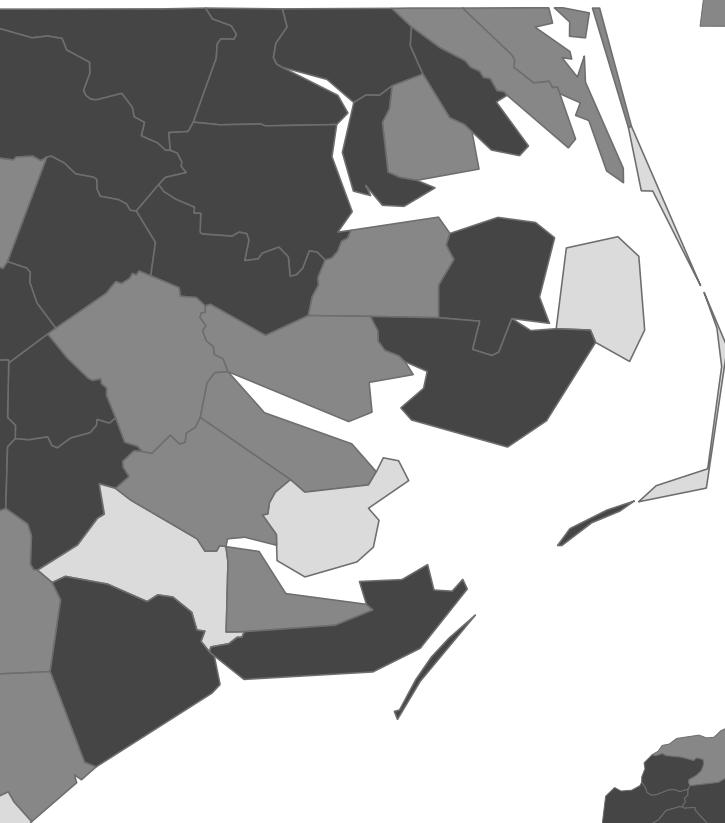
Researchers are using CHART (Carolina Health Assessment & Resource Tool), an online resource tool developed at UNC that assesses and modifies behavioral risk factors for cancer. Study participants answer module-based questions on such health behaviors as physical activity, nutrition and tobacco use, and then immediately receive personalized, evidence-based and theory-guided feedback. CHART is available online and via mobile devices and can be used in a wide variety of interventions & research to improve cancer outcomes.

Understanding survivorship through health data

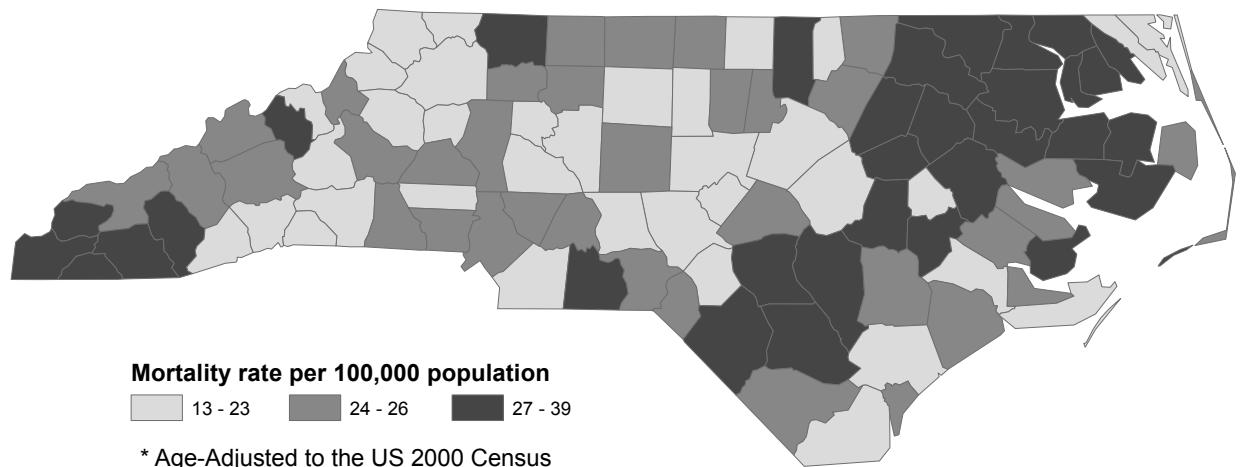
Researchers continue the enrollment of patients in the UNC Health Registry/Cancer Survivorship Cohort to support cancer survivorship research. The goal of the

2003-2010 Lung Cancer Age-Adjusted Mortality Rate* for All Races

Rate* for All Races



2003-2010 Female Breast Cancer Age-Adjusted Mortality Rate* for All Races



Registry is to better understand the causes of cancer and other diseases that affect many North Carolinians. Researchers now have access to the data of nearly 5,000 study participants and are leveraging this data to secure external research funding.

Helping North Carolinians LOSE NOW

Twenty percent of cancer is caused by overweight and obesity. Regular, face-to-face weight loss interventions, while effective, are expensive. UNC researchers have developed an effective weight loss intervention, LoseNowNC, that couples large group interventions with web-based support delivered on mobile devices. The intervention encourages and monitors ongoing progress for individuals trying to lose weight. The effort has shown promising results, with significant weight changes in two research groups over time.

Understanding barriers to colon cancer screening in underserved communities

Although colon cancer screening rates have increased in recent years, screening is underutilized in vulnerable populations. Using state cancer registry-linked insurance claims data, UNC researchers identified underserved areas in North Carolina with relatively low colon cancer screening rates and high colon cancer mortality. Seeking feedback from eligible individuals from across the state, researchers are studying the barriers to screening for this population and using this understanding to develop better screening strategies for underserved North Carolina communities.

Integrated Cancer Information and Surveillance System (ICISS)

Leveraging 'Big Data' to support discovery

The maps presented here are generated by the Integrated Cancer Information and Surveillance System, a UCRF-funded initiative that links state cancer data and health claims 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, social, behavioral, and environmental patterns. This powerful data source improves cancer outcomes in North Carolina by enabling the discovery of cancer risk factors and how to best prevent and treat cancer. For more information, please visit iciss.unc.edu.

More than 180 top experts have been recruited to or retained at UNC with the help of UCRF. During the last year, the following have joined the UNC-Chapel Hill and UNC Lineberger faculty:

CRITICAL INFRASTRUCTURE

Yueh (Ray) Lee, MD

Assistant Professor of Radiology, Neuroradiology
UNC School of Medicine
Department of Radiology

Jason Akulian, MD, MPH

Director, Interventional Pulmonology
Assistant Professor of Medicine
UNC School of Medicine
Department of Medicine – Pulmonary Diseases and Critical Care Medicine

Jason Long, MD, MPH

Assistant Professor of Surgery
UNC School of Medicine
Division of Cardiothoracic Surgery

DEVELOPING NEW TREATMENTS

Shawn Hingtgen, PhD

Assistant Professor of Molecular Pharmaceutics
UNC Eshelman School of Pharmacy
Division of Molecular Pharmaceutics (Biomedical Research Imaging Center)

Terence Wong, MD

Chief of the Division of Nuclear Medicine
Director, Molecular Imaging, Biomedical Research Imaging Center (BRIC)
Medical Director of BRIC
UNC School of Medicine
Department of Radiology/BRIC

Chad Pecot, MD

Assistant Professor
UNC School of Medicine
Department of Medicine
Division of Hematology and Oncology

OPTIMIZING NC OUTCOMES

Pascal Sheeran, PhD

Professor
Department of Psychology
Social Psychology Program at UNC Lineberger

Hazel Nichols, PhD,

Assistant Professor of Epidemiology
UNC Gillings School of Global Public Health
Department of Epidemiology

Jennifer Lund, PhD, MSPH

Assistant Professor of Epidemiology
UNC Gillings School of Global Public Health
Department of Epidemiology

Katie Reeder-Hayes, MD, MBA

Assistant Professor
Breast Cancer
UNC School of Medicine
Department of Medicine
Division of Hematology and Oncology

Angela Smith, MD

Assistant Professor of Urology
UNC School of Medicine
Department of Urology

Justin Trogden, PhD

Associate Professor of Health Policy and Management
UNC Gillings School of Global Public Health

CANCER GENETICS

Bradford Powell, MD, PhD

Assistant Professor
UNC School of Medicine
Department of Genetics

Mauro Calabrese, PhD

Assistant Professor
UNC School of Medicine
Department of Pharmacology

Nirali Patel, MD

Assistant Professor
UNC School of Medicine
Department of Pathology and Laboratory Medicine

UNC Lineberger is shaping the future of clinical trials

One of only five cancer centers to win all three awards from the NCI's national clinical trials competition

This year, the National Cancer Institute (NCI) launched a new clinical trials research network intended to improve treatment for the more than 1.6 million Americans diagnosed with cancer each year. The NCI awarded grants in the spring of 2014, and UNC Lineberger secured not only one, but three major grants as a part of this initiative.

Providing Scientific Leadership: 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.

Accelerating Drug Delivery: 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 cancer clinical trials sponsored by the NCI to help speed the drug development process.

Sharing Expertise in Genetic Sequencing: UNC Lineberger is one of only five institutions across the country measuring biomarkers 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.



THE UNIVERSITY
of NORTH CAROLINA
at CHAPEL HILL



Designated a Comprehensive Cancer Center by the National Cancer Institute

