In 2008 an estimated 40,420 North Carolinians will be diagnosed with cancer. This disease is the number one cause of death in our state and will claim more than 17,000 lives this year. North Carolina is swimming against a demographic tide of growth and aging that will bring more than 80,000 new cancer cases in 2030. Research that leads to more effective treatment, better prevention, and improved screening is critical to answering this challenge for our children and our children's children.

In July 2007, the NC General Assembly established the University Cancer Research Fund (UCRF) to dramatically accelerate the cancer research that will take and meet cancer's challenge. In 2007 the UCRF provided $25 million to support cancer research. The fund is slated to increase to $40 million in 2008 and then to $50 million per year beginning in 2009. "We are hearing from cancer leaders in virtually every state and they are saying the same thing," remarked Dr. Shelley Earp, UNC Lineberger director. "North Carolina has taken a bold, nation-leading step and provided an extraordinary opportunity for the University of North Carolina at Chapel Hill and its Health Care System and Cancer Center to help shape North Carolina's, and in fact the nation's, future."

The UCRF's mission is to ensure that future generations are able to benefit from the Eshelman gift and the cancer community's progress and to spur large private gifts to accelerate discovery, development, and delivery. The UCRF accepted the challenge and matched the Eshelman gift: the Center for Integrative Chemical Biology and Drug Discovery; the Center for Nanotechnology in Drug Delivery; and the Center for Chemical Biology and Drug Discovery; the Chemical Biology and Drug Discovery; the Center for Chemical Biology and Drug Discovery; the Chemical Biology and Drug Discovery; the Center for Chemical Biology and Drug Discovery; the Chemical Biology and Drug Discovery; the Center for Chemical Biology and Drug Discovery; the Chemical Biology and Drug Discovery; the Center for Chemical Biology and Drug Discovery; the Chemical Biology and Drug Discovery; the Center for Chemical Biology and Drug Discovery; the Chemical Biology and Drug Discovery; the Center for Chemical Biology and Drug Discovery; the Chemical Biology and Drug Discovery; the Center for Chemical Biology and Drug Discovery; the Chemical Biology and Drug Discovery; the Center for Chemical Biology and Drug Discovery; the Chemical Biology and Drug Discovery; the Center for Chemical Biology and Drug Discovery; the Chemical Biology and Drug Delivery.

Fred Eshelman, founder and CEO of Wilmington-based PPD Inc., had a vision to improve his alma mater. He would pledge $9 million to support cancer research at the UNC School of Pharmacy if a matching gift could be found.

The Cancer Research Fund Committee of the UCRF accepted the challenge and matched the gift, generating a total investment of $18 million over five years. The funds will support the work of the UNC School of Pharmacy and UNC Lineberger Comprehensive Cancer Center researchers whose work focuses on genetics, individualized cancer therapy, drug discovery, and drug delivery.

"This gift is a wonderful example of a private gift leveraging cancer fund money through partnerships among cancer center faculty across programs. These strategies include bringing genetics and genomics to clinical care, promoting drug discovery and clinical trials, assessing cancer in our communities, applying innovations to bring world-class cancer care to the state, and developing a unique and comprehensive study of cancer survivors. The fund has also completed its governance structure, initiated a strategic planning process, conducted listening sessions around the state, and instituted a collaboration with East Carolina University. The fund is establishing an independent evaluation process and beginning to develop outreach networks to speed clinical and other innovations to communities across the state.

"We're moving quickly but prudently to get these many initiatives going," said Erskine Bowles, president of the University of North Carolina and chair of the legislatively established Cancer Research Fund Committee that oversees the UCRF. "This first year has been focused on recruiting the very best faculty and staff with the right skills and expertise, developing leading-edge programs and technologies that will speed discovery and dissemination, and funding innovative research proposals that show great promise. We are confident these start-up efforts will lead to future discoveries that will make a significant difference in the lives and health of North Carolinians."

This first in a series of annual reports highlights the UCRF's progress during its initial year. "We are mindful of the burden of cancer and, ultimately, the burden of cancer health care costs, is truly visionary."

Dr. John E. Niederhuber, Director, National Cancer Institute
Dr. Stephen Frye

Thanks to support from the University Cancer Research Fund, Dr. Stephen Frye, former worldwide head of discovery medicinal chemistry at GlaxoSmithKline, was recruited in October 2007 to lead the new Center for Integrative Chemical Biology and Drug Discovery (CICBDD) at UNC's School of Pharmacy.

The new Center is a joint initiative supported by the UCRF, the UNC School of Pharmacy, the Lineberger Comprehensive Cancer Center, the UNC School of Medicine, and the Department of Chemistry in the College of Arts and Sciences. Frye is a research professor in the School of Pharmacy.

To increase the impact of translational research, the Center for Integrative Chemical Biology and Drug Discovery is bringing medicinal chemistry expertise to bear on biological targets of therapeutic potential for cancer and other diseases. CICBDD scientists are creating dedicated, multidisciplinary project teams with other groups on campus to move these targets through the drug discovery and pre-clinical development process.

One of the first projects involves a collaboration to discover a new potential therapy for acute lymphoblastic leukemia in children. The Center is also building a collaborative plan with the Structural Genomics Consortium and the National Institutes of Health National Chemical Genomics Center to discover chemical probes.

Dr. Joseph DeSimone

While bringing the best and brightest researchers to UNC is fundamental to achieving our goals, keeping our best is equally important. During this past year, the University Cancer Research Fund has been invaluable in our retaining key faculty, none more so than Dr. Joseph DeSimone, William R. Kenan, Jr. Distinguished Professor of Chemistry and Chemical Engineering, and director of the UNC Institute for Advanced Materials, Nanoscience, and Technology.

DeSimone is a nationally recognized and highly acclaimed chemistry and materials science researcher, whose discoveries have led to more than 100 patents and the founding of several companies. His ground-breaking research in developing novel ways to create nanoparticles has resulted in the founding of a UNC spin-off company located in the Research Triangle. Potential use of this nanotechnology process in delivering targeted cancer therapy and imaging helped UNC become one of eight Centers of Cancer Nanotechnology Excellence in the country, joining the likes of Cal Tech, Harvard/MIT, and Stanford.

Application of nanotechnology to the delivery of cancer drugs, including both standard chemotherapy and new biologic therapies, holds outstanding promise for the next generation of cancer treatment that not only works more effectively but also with fewer side effects. This field of nanomedicine, which melds the physical and biomedical sciences to improve patient outcomes, will be a major focus of the UCRF.

DeSimone's outstanding research and entrepreneurship has made him a recruiting target for the nation's top institutions, especially those backed by large private endowments. Losing DeSimone would have been a severe setback for UNC's plans to become a premier institution and leader in cancer nanomedicine. UCRF funding, in partnership with the College of Arts and Sciences and other University units, will provide the resources to Dr. DeSimone and his colleagues to help build a cancer nanomedicine research enterprise that will lead the nation.

Dr. William Zamboni

Dr. William Zamboni was one of the first scientists recruited with help from the University Cancer Research Fund. Zamboni, who came to UNC from the University of Pittsburgh, is an associate professor in the School of Pharmacy’s Division of Pharmacotherapy and Experimental Therapeutics and a member of UNC Lineberger. He is also a member of the School of Pharmacy’s Institute for Pharmacogenomics and the Carolina Center of Cancer Nanotechnology Excellence.

Zamboni will direct a drug development and clinical pharmacology lab focusing on the translational development of drugs, anticancer agents, and nanoparticles. The lab will have the capacity to support all pharmacologic studies required in translational drug development.

He will also establish a Good Laboratory Practice (GLP) Analytical Facility at UNC, one of a few such labs in an academic center in the entire country. This facility will provide a unique and globally impacting resource that will foster and accelerate internal and external drug development and provide training in translational drug development and clinical pharmacology.

The ability to perform initial preclinical pharmacologic studies of investigational agents discovered at UNC in a GLP analytical laboratory can significantly accelerate the development of these agents and will be used as a tool to recruit investigational agents developed by the National Institutes of Health, the National Cancer Institute, and pharmaceutical companies to UNC. This facility will make UNC more competitive when applying for grants from federal agencies and providing the best environment in which to develop new therapies for UNC Lineberger's Early Phase Clinical Trials Program.

Dr. Donald Rosenstein

This fall, Dr. Donald Rosenstein will join the UNC School of Medicine to develop and lead a psychosocial oncology program that will provide exceptional clinical services to patients and families facing cancer. Rosenstein comes to UNC from the National Institute of Mental Health, one of the member institutes of the National Institutes of Health, where he served as Clinical Director and led clinical care, training, and research programs.

The new UNC program will incorporate all inpatient and outpatient psychiatric and psychosocial services including individual consultations and counseling, group therapy for patients, and family support services through the existing Patient and Family Resource Center. Additionally, the program will provide training for medical students, oncology care providers, and community outreach efforts.

The University Cancer Research Fund supports Dr. Rosenstein’s recruitment and the development of the new program. Rosenstein said, “The mission of this new program will be to provide exceptional clinical service to patients at the NC Cancer Hospital and superb training to UNC health care professionals who work with cancer patients.”
Jeanne Lucas Study Focuses on Breast Cancer Risk Factors

"It's clear that breast cancer is not just one disease, but a group of related though biologically distinct diseases," says Dr. Lisa Carey, associate professor of medicine and medical director of the UNC Breast Center. "So it doesn't make sense to ask 'what causes breast cancer'? We should rather ask 'what causes the different types of breast cancer'?"

That's the purpose of The Carolina Breast Cancer Study III (CBCSIII), part of an ongoing population-based case-control study of incident breast cancer in North Carolina. "One of the more aggressive forms of breast cancer is called the basal-like subtype, which is insensitive to our targeted therapies," Carey explains. "Fortunately it is sensitive to chemotherapy." The basal-like subtype makes up more than 35 percent of breast cancers in younger African-American women, compared with only about 15 percent in other women. The CBCSIII aims to understand why.

"If we can identify underlying causes of breast cancer, we can determine ways to prevent it from occurring in the first place," says Bob Millikan, professor of epidemiology and principal investigator of the study. "And if women do get breast cancer, we can offer more effective treatments that target their particular type of cancer. Both of these efforts together will lower the death rate.

Funds from the UCRF will enable CBCSIII researchers to more than double the number of African-American women in the study. This will help investigators understand how specific factors such as breastfeeding and physical activity could be modified to lower a woman's risk of breast cancer.

The CBCSII is also known as the Jeanne Lucas study in honor of the first African-American woman senator in North Carolina, who was a leading force for public education in our state, and died last year from breast cancer. Lucas was a strong voice for cancer programs at UNC and throughout North Carolina as well as a determined breast cancer advocate. CBCSIII is a continuation of the Carolina Breast Cancer Study I and II, which began in 1993 and culminated in 2001 and investigated the causes of breast cancer in black and white women in North Carolina. Today it is one of the largest African-American breast cancer databases in the United States.

"The Jeanne Lucas study will depend upon the cooperation and efforts of dozens of hospitals, physicians, nurses and women throughout the state," Millikan notes. "It will truly be a statewide effort, with benefits for all women in North Carolina." The study will open in June 2008.
Imagine a Mammogram That Doesn't Hurt!

Otto Z. Zhou, Ph.D., Lyles Jones Distinguished Professor of Physics and Materials Sciences in the Department of Physics and Astronomy, is helping to adapt nanotechnology for the development of novel methods of cancer detection. Zhou has used carbon nanotubes to invent a new way to generate x-rays. This technology has the potential to significantly enhance the performance of a range of imaging devices - from medical diagnosis to homeland security.

UCRF support has enabled Zhou and his colleague, Jinping Lu, to apply new technology to develop a new mammography system for breast cancer early detection. This new system will enable radiologists to detect tumors earlier and without painful compression of the breast. The UCRF purchased the equipment they are now using to build a prototype. They have licensed this new technology to Xintek, a UNC start-up company, and their research has attracted one of the world's largest medical instrumentation companies which intends to commercialize the new system.

This research has also led to the formation of a new joint venture company called XinRay Systems, LLC formed with Siemens Medical last summer. XinRay, which is located in the Research Triangle Park, has hired recent UNC graduates and brought Siemens employees from facilities in Germany and China to the RTP area. Next year a new imaging-guided radiation therapy device based on XinRay technology will be tested in a clinical trial at the NC Cancer Hospital.

This new device allows oncologists, for the first time, to “see” the tumor in real time during treatment. Technology invented at UNC and commercialized by a UNC start-up based in North Carolina is now coming back to the NC Cancer Hospital, which will be the first U.S. test site.

There is realistic hope that within the next five years, nanotechnology-based imaging technology - developed because of the General Assembly's vision and support - will be used in hospitals across North Carolina and the world to improve our quality of life.

Statewide Cancer Data Key to Improved Care

Knowing the problem is an important part of any solution. The University Cancer Research Fund is partnering with the North Carolina Central Cancer Registry to make sure we know just how big North Carolina's cancer problem is.

"North Carolina has been a national leader in cancer surveillance and research, in large part due to our state's outstanding cancer registry," says Dr. Shelley Earp, director of UNC Lineberger. The challenge, explains Karen Knight, director of the NC Central Cancer Registry, is keeping up with the changing patterns in medical care. "In 1947, North Carolina was an early leader in making cancer a reportable disease. At that time and years after, cancer was almost always diagnosed in hospitals. But, times have changed. Many cancers, particularly melanoma and prostate cancers which are of particular concern to North Carolina, are being diagnosed in outpatient physician practices and may get missed by traditional reporting systems," says Knight. "UCRF support will add staff and electronic reporting software that will help us reach out past the hospitals and make sure we identify all the cancer cases."

"Enhancing the Registry will strengthen cancer research in North Carolina, not only at UNC," says Barbara Rinner, dean of the UNC School of Public Health. "Over the past 15 years, the Registry has made possible cancer research studies at UNC, Duke, and Wake Forest that have led to important revelations about cancer as well as successful competition for federal grant funding.

"The Carolina Breast Cancer Study, for example, has created a unique opportunity by combining epidemiologic, genetic, and clinical data from more than 20 counties across North Carolina. Findings from that study helped identify a type of breast cancer that occurs most often in younger African-American women that may help explain important disparities in breast cancer deaths. "Without the Registry," said Rinner, "that study could never have been done. Enhancing the Registry's capabilities to collect high quality treatment data and to code cancer cases by geographic location will make possible even more innovative studies. What's really important, though, is the opportunity to improve care for patients through improved understanding of cancer."

Cancer Survivorship: From Clinics to Communities, UNC is There

For many cancer patients, the end of active treatment creates a lot of uncertainty. After long periods of regular treatments and doctor visits, the routine changes. But concerns, challenges, and potential health problems remain.

Cancer survivors in North Carolina will now receive wide-ranging post-treatment care. Earlier this year, the Lance Armstrong Foundation (LAF) invited UNC Lineberger Comprehensive Cancer Center to join the LIVESTRONG Survivorship Center of Excellence Network. UNC Lineberger is now one of only eight centers in the nation designed to address the needs of the growing number of cancer survivors.

The LIVESTRONG Survivorship Center of Excellence at UNC Lineberger is charged with developing survivorship programs and services through the NC Cancer Hospital and partnering sites around the state. The Center benefits from the advice and expertise of a large Community Advisory Board made up of cancer survivors and advocates from around the state.

"In the past the focus has almost entirely been on treatment and 'beating' the cancer," explains Marci Campbell, the Center's principal investigator and professor of nutrition at UNC's School of Public Health. "These cancer survivors need services to help them deal with long term health issues including possible late effects of their cancer, and they are concerned about wellness issues such as healthy eating, exercise, weight control and quitting smoking in order to prevent other chronic diseases. They also need psycho-social support and may have concerns about employment, insurance, etc."

Researchers and clinicians will develop clinical survivorship programs for specific cancers at the N.C. Cancer Hospital, as well as education and outreach programs at UNC and its community based centers in Greensboro, Newton Grove, and Wilmington. In addition, the Center of Excellence will share its clinical and outreach programs with colleagues at East Carolina University in Greenville, Rex Hospital in Raleigh, and other interested sites. The team also will work with Walter Shepherd, director of the State of North Carolina Comprehensive Cancer Program in Raleigh, to expand the reach of survivorship programs and education to every region of the state.

"Working together, Network members will be able to establish best practices for survivor care. One of the innovations we hope to bring is experience working with community partners to develop health services," says Dr. Paul Godley, associate dean of medicine and the Center's co-principal investigator.

The Center also represents a commitment to support cancer patients throughout their cancer journey, not just while they are undergoing treatment. "We are dedicated to helping them through the transition to life after treatment," Godley says.
Fertility Preservation: Options for the Future

Due to advances in cancer diagnosis and treatment, an increasing number of young people with cancer are surviving their illness and many have not yet attempted or completed childbearing. Unfortunately, current cancer treatments, including aggressive chemotherapy and radiation therapy, frequently cause ovarian and testicular failure, leading to the inability to have children. Moreover, because treatment for most cancers begins immediately after diagnosis, most such patients have little opportunity to pursue or to preserve their fertility before treatment.

Although sperm banking provides men with an effective means to preserve their fertility when it is threatened by illness, young women in similar circumstances have had few, if any, options until now with recent advances in reproductive technologies and cryobiology.

At the new UNC fertility preservation clinic, patients may be referred by their physician and are seen quickly, usually within 48 hours. "When a patient is diagnosed with cancer, treatment is often begun rapidly, so consideration of fertility issues has to be given before therapy begins," explained Jennifer Mersereau, M.D., assistant professor of obstetrics and gynecology and clinic director. "During a consultation, we counsel patients about their risk of losing fertility and discuss options to preserve their fertility," she said. As part of this protocol, patients are offered an in vitro fertilization (IVF) cycle or ovarian tissue freezing. Patients also meet with a psychologist to discuss the psychological aspects of fertility issues.

Due to recent advances in reproductive technologies and in cryobiology, women with cancer have viable new options to protect and preserve their fertility - oocyte and ovarian tissue cryopreservation.

Most infertility services are not covered by insurance. A financial counselor is available to patients to explore options and, because this is a research study, services are offered at a significant discount.

Using Image Analysis Techniques to Battle Melanoma

Funded by a UCRF Innovation Award, a new collaboration among UNC melanoma researchers, the Renaissance Computing Institute (RENCI), and researchers from the departments of computer science, epidemiology, biostatistics, and statistics and operations research at UNC aims to use image analysis techniques to aid doctors in the fight against melanoma, the most serious form of skin cancer.

Over time, the work could lead to new tools for outcome prediction, thus assisting doctors in determining best treatment approaches.

Nancy E. Thomas, M.D., Ph.D., an associate professor of dermatology in the School of Medicine, will lead the project which will examine imagery from more than 1,300 melanoma patients worldwide, including 214 from North Carolina. Researchers will develop algorithms that can identify cancerous and healthy tissue in high-resolution images. Once cells in the images are identified as cancerous or healthy, the researchers will collect information on physical details, such as cell size, shape, and color of melanoma cells. All these details will be used to develop evidence-based models of melanoma cell descriptions.

Tamoxifen: Finding the Dose That Works

Lisa Carey, M.D., medical director, UNC Breast Center and Howard McLeod, Pharm.D., director, UNC Institute for Pharmacogenomics and Individualized Therapy, are working to help physicians better treat women with breast cancer.

Medicine has traditionally been a "one size fits all" field. For example, several hundred patients may be studied to determine one single drug dose that is then applied to all patients. However, modern technology has identified that there are many inherited variations in the genes that control how our bodies handle drugs, so the 'right' dose for one person may be the wrong dose for another.

This is illustrated by the drug tamoxifen. Tamoxifen is a drug that has been used in hundreds of thousands of women to prevent or treat breast cancer. However, the drug itself is inactive; it requires the action of enzymes in the liver, in particular one called CYP2D6 to convert it to the active form. Like all drugs, tamoxifen is given at the same dose to all women; however it is known that genetic variability in these enzymes results in large differences in the actual levels of the active drug.

This project asks a simple question: Can we use genetic knowledge to determine tamoxifen dose? Women receiving tamoxifen for breast cancer treatment are providing blood samples to have their CYP2D6 gene tested at the Institute of Pharmacogenomics and Individualized Therapy (IPIT), a new UNC institute dedicated to developing our ability to personalize medical therapy. Those women with less effective genes will have their treatment dose decreased, and they will be monitored to see if their active drug level increases. If this is successful, it will promote a large scale effort to develop individualized medical therapy for this drug.

"The objective of this proposal is to utilize image analysis to uncover associations between the physical characteristics of melanoma, somatic mutations in melanoma, and survival," said Thomas. "But ultimately, our long-term goal is to help patients. We want to use image analysis to improve melanoma classification, which we would expect to improve diagnosis and guide treatment recommendations."

Leading-Edge Technology to Guide Cancer Treatment

Jason Lieb, Ph.D., an associate professor in the department of Biology and Carolina Center for Genome Sciences, conducts research on how genes are turned "ON" and "OFF" at the right place and time. Understanding these issues is very important to cancer, since having the wrong genes ON or OFF at the wrong time is characteristic of every cancer type.

Lieb is using a novel, low-cost technology developed by his lab that can identify precursors of DNA ON/OFF errors, which in turn can help identify different types of a given cancer -- even if they look the same under a microscope. They are testing this approach on 100 breast cancers. If the results turn out as they expect, they will submit a much larger proposal to the National Institutes of Health and work toward methods that can help make sure women receive the medicine that is most likely to work for their breast cancer type.

Being able to determine the entire DNA sequence of an individual's cancer - something that was only dreamed of five years ago - may soon be the basis for diagnosing cancer and guiding its treatment. Advanced sequencing that works rapidly and efficiently is expensive, and currently only the most "elite" hospitals and universities have been able to invest in this forward-thinking technology.

Thanks to UCRF support, UNC has purchased revolutionary, state-of-the-art high-throughput DNA sequencers. Lieb explained, "Using both sequencers we can sequence up to 6 million DNA bases per week, twice the number of bases in the human genome, which took 10 years to sequence. It's like the difference between a bullet train and a horse-drawn carriage."
Between January and May, UNC held five listening sessions across the state to gather community feedback on the UCRF and cancer research. Working through the NC Area Health Education Centers (AHEC), UCRF Leaders traveled to Greenville, Asheville, Wilmington, Raleigh, Greensboro, and Charlotte.

At each session, Dr. Etta Pisano, vice dean, UNC School of Medicine; Dr. Richard Goldberg, physician-in-chief, NC Cancer Hospital; and Dr. Shelley Earp, director, UNC Lineberger Comprehensive Cancer Center, briefly presented the goals of the UCRF and then asked for public comment. “We want to hear from you, specifically about the problem of cancer in your community and about how cancer research can improve cancer prevention, screening, and treatment throughout this state,” said Pisano.

Over 200 citizens, survivors, community groups, advocates, and health care providers attended the five sessions. Their feedback has been invaluable in planning and prioritizing UCRF initiatives. Full transcripts from the events can be found at www.unclineberger.org. Additional listening sessions will be scheduled in other areas of the state. To receive updates on UCRF initiatives, please subscribe at: www.unclineberger.org/lcccnewsletter/subscribe_enews.asp.

Listening and Learning Throughout NC

Established by the North Carolina General Assembly to be used “only for the purpose of cancer research under UNC Hospitals, the Lineberger Comprehensive Cancer Center, or both.”

The mission of the University Cancer Research Fund is to save lives and reduce suffering from cancer in North Carolina and beyond. The Fund will accomplish this through:

- **Discovery**
  Better understanding the causes and course of cancer.

- **Innovation**
  Using new knowledge to create new and better ways to prevent, find, and treat cancer.

- **Delivery**
  Improving cancer care, screening, and prevention across the state.

The Listening Tours are continuing via the internet! Go to www.unclineberger.org/ucrf/ and share your ideas, comments, and questions.