

25th
anniversary

Cancer

University of North Carolina School of Medicine & UNC Hospitals – UNC Health Care

25TH ANNIVERSARY ISSUE



North Carolina: The State of Discovery in Breast Cancer

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Breast cancer is the second leading cause of cancer death for all women, and the leading cause of cancer death in women between the ages of 40 and 55. This year, a breast cancer will be newly diagnosed every three minutes, and a woman will die from breast cancer every 12 minutes. It's also a small threat to men — almost 1,600 will develop the disease this year.

With compelling statistics like this, it's no wonder that researchers, clinicians and public health specialists at UNC and the Lineberger Center are working diligently to find new ways of detecting, treating and preventing this disease. Their work begins with the National Cancer Institute-funded **Specialized Program of Research Excellence (SPORE) in Breast Cancer**, one of six in the country.

"The purpose of this SPORE is the integration of public health, clinical and molecular sciences to better investigate etiology, prevention and early detection in breast cancer and to devise ways to reduce breast cancer mortality," explains Shelton Earp, Lineberger's director and the SPORE's principal investigator.

The SPORE has four components:

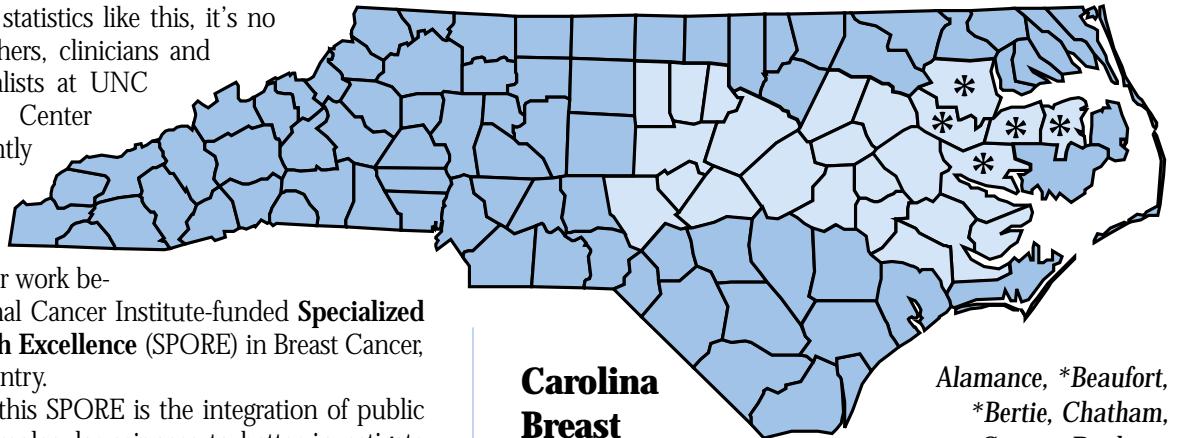
- **Public Health Intervention:** strives to increase the use of mammography in under-served African American populations

- **Molecular Epidemiology:** seeks to identify the environmental and genetic causes of breast cancer

- **Gene Discovery:** identifies new molecular markers of breast cancer that can be used for early diagnosis and treatment

- **Clinical/Developmental:** Projects that produce innovative ideas for novel therapies or diagnostics.

"I think the two most important features of the UNC SPORE are depth and flexibility," notes Bob Millikan, associate professor of epidemiology, and an investigator in two SPORE projects. "Depth because we address breast cancer at



Carolina Breast Cancer Study Counties & North Carolina Breast Cancer Screening Program Counties*

Alamance, *Beaufort, *Bertie, Chatham, Craven, Durham, Edgecombe, Greene, Harnett, Johnston, Jones, Lee, Lenoir, *Martin, Moore, Nash, Orange, Pamlico, Pitt, *Tyrrell, Wake, *Washington, Wayne and Wilson.

many levels — social, behavioral, genetic, environmental — and flexibility because we have been responsive to the needs of the North Carolina community in the design and implementation of our studies."

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Great NEWS

UNC Lineberger's plans for growth over the next five years received an enthusiastic response from the National Cancer Institute.

The Center submitted its 1,283 page, five-year core grant proposal to the National Cancer Institute early last year, followed by a visiting team of 25 experts from universities and cancer centers across the U.S. to review our plan and its financing. They recommended an extraordinary increase in

UNC Lineberger's annual budget—from \$1.7 million to \$3.3 million per year, a 94 percent increase, moving us into the top 10 in core grant funding in the nation.

Significant increases were given for:

- **Clinical Research**, to support development, evaluation and monitoring of new therapies;

- **Cancer Prevention and Control Research**, to support population-based studies using molecular techniques to understand the interplay among genetics, environmental exposures and lifestyle factors that may lead to cancer;

- **Basic Science Research**, to develop animal models that mimic the development of cancer in humans so we can better understand cancer's mechanisms and how best to target new therapies and preventive measures. ●



Dr. H. Shelton Earp, III

Did you know that the nation's oldest public university also houses one of the nation's leading cancer centers? With this special issue of *Cancer Lines*, we invite you, our co-workers and colleagues, to learn more about how the UNC Lineberger Comprehensive

Cancer Center fights cancer in the clinic, in the laboratory, and in our communities.

In the United States there are 6,021 hospitals. Most, if not all, have cancer centers or serve cancer patients. But, only 37 centers nationwide, including the UNC Lineberger, can call themselves National Cancer Institute (NCI) designated Comprehensive Cancer Centers.

NCI Comprehensive Cancer Centers are national leaders. They combine high quality, technically advanced, and compassionate patient care with outstanding research, community service, and training. The UNC Lineberger keeps excellent company. Name a famous Cancer Center—M.D. Anderson, Fred Hutchinson, Memorial Sloan-Kettering, Dana-Farber, the Mayo Clinic. We are all NCI-designated Comprehensive Cancer Centers. And yes, our colleagues at Duke and Wake Forest also share the designation, making North Carolina and California the only states with three such centers of excellence.

This designation is great publicity, but what does it mean for you?

Quality. At our Center, physicians, nurses, other medical experts, counselors, and support staff work together in multidisciplinary teams (including several featured in this

issue). Their collective wisdom produces state-of-the-art treatment in a supportive atmosphere: the best medicine and the best care.

Access. Sometimes even the best standard of care is not good enough. When this happens, our own teams of clinicians and scientists make available new and innovative therapies being tested in high-quality clinical trials. Through these trials, our teams offer leading edge treatment, diagnostic tools, and prevention methods not available in many community practices and hospitals.

Knowledge. UNC-Chapel Hill ranks in the top 15 universities nationwide in both biomedical and cancer research. UNC Lineberger researchers leverage substantial national support and their own intellectual capital to develop novel ways to treat cancer, find it early, or prevent it altogether. The constant interchange between our laboratory scientists, clinicians, and public health practitioners creates ideas and strategies admired throughout the world of cancer research. What we learn today will help you and your family tomorrow.

Being an NCI Comprehensive Cancer Center helps us but, you are our greatest asset. We succeed because we are part of the University and the UNC Health System.

Our 500 staff and 200 plus faculty members represent more than 25 different departments concentrated in cancer research's traditional home base in Health Affairs. That's good, but we are working to extend participation in Academic Affairs—psychology, computer science, chemistry, biology, information and library science, journalism, business, and many others. These faculty have much to contribute, and we are developing new partnerships and programs to increase campus-wide participation in cancer research. Working together, this diversity in

knowledge offers the best opportunities for combating a complex disease with substantial societal impact.

Our partnership with the UNC School of Medicine, Hospitals and the Health Care System provides patients with the highest levels of expertise, experience, technology, and support. A visit to the NC Clinical Cancer Center or anywhere in the UNC Hospitals and Health Care System provides patients with all the resources and superb staff of an outstanding academic medical center.

With the School of Public Health, the School of Nursing, and others, we are finding better ways to help people in communities across North Carolina live healthily. We are also using new approaches to study the patterns of cancer in our communities and predispositions to cancer in their families. These approaches will uncover important clues about what causes cancer and what to do about it.

This year the Cancer Center reaches its silver anniversary. Over the past 25 years, the UNC Lineberger has grown from five to more than 200 faculty. Our members' grant funding has increased from \$250,000 per year to more than \$70 million per year. What was at first a small band of researchers has become a nationally recognized Comprehensive Cancer Center. Just last year, a rigorous National Cancer Institute five-year review confirmed our excellence and continued promise by doubling our federal core support grant funding.

Yet, when all is said and done, without the excellence, support, and resources of the University and the Hospitals, the UNC Lineberger could not have achieved all that it has and all that it hopes to accomplish. We are proud to be a part of the University of North Carolina at Chapel Hill and the UNC Health Care System. And, we want you to be proud of us. ●



UNC Lineberger is designated a comprehensive cancer center by the National Cancer Institute.

Cancer Lines is a semi-annual publication of the UNC Lineberger Comprehensive Cancer Center, The University of North Carolina School of Medicine at Chapel Hill.

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NC: The State of Discovery

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Here's an overview of some projects within the SPORC:

The North Carolina Breast Cancer Screening Program

Breast cancer can be successfully treated with greater than a 90 percent cure rate if it is detected early. But early detection through regular screening mammography is critical, and the message hasn't been as effectively delivered to some women as to others. Less than half of women age 50 and older in the United States have regular screening mammograms—and the number is even lower in the African-American community. In all women, breast cancer incidence increases with age, rising rapidly after age 40. Almost 80 percent of all breast cancers occur in women over 50 years of age.

The NC-BCSP is a long-term, comprehensive, multi-level community intervention program designed to increase breast cancer screening among older African-American women in five rural eastern

North Carolina counties. Its primary objectives are to:

- Increase initial and repeat mammography screening by black women ages 50 years and older
- Increase follow-up of positive screening mammograms
- Establish partnerships between health care providers and communities that will maintain increased breast cancer screening and follow-up once the grant ends.

These objectives are being pursued through three complementary intervention components: **OutReach**, **InReach** and **Access**. **OutReach** efforts emphasize providing social support to women within their social networks through 160 "natural helpers" trained as lay health advisors (LHAs); the **InReach** and **Access** components are directed at lowering organizational and structural barriers to breast cancer screening. **InReach** focuses on health care providers and organizations, while **Access** addresses factors such as cost, referral systems, and transportation.

The LHAs are one of the initiative's most innovative elements. "Our outcome evaluation suggests

that our LHA intervention—probably supplemented with our **Access** and **InReach** interventions—made a difference in the number of older African-American women who actually got mammograms in the past two years," reports principal investigator Jo Anne Earp, professor and chair of the department of health behavior and health education.

The Carolina Breast Cancer Study (CBCS) and The Carcinoma-in-situ (CIS) Study

These two projects are population-based case-control studies aimed at discovering new risk factors for breast cancer. Both invasive and in-situ (or non-invasive) breast cancer are identified among women in 24 counties of North Carolina. The two studies are run in parallel and enroll equal numbers of African-American and white women, and include women of other racial/ethnic groups as well.

The two studies seek to identify environmental and behavioral risk factors (using information collected from in-depth interviews) as well as genetic factors which influence breast cancer de-

velopment. “Our study is one of the first to treat breast cancer not as a single entity, but to consider subtypes defined on the basis of genetic changes that are acquired in breast tissue as tumors develop,” says Bob Millikan, principal investigator of the Carolina Breast Cancer Study. “The particular patterns of mutations may help to uncover causes of breast cancer.”

Two types of genetic markers are examined in the CBCS and CIS studies: inherited genetic alterations and acquired genetic alterations found only in breast tumors. Due to the complexity of and ethical issues surrounding genetic markers, the studies have involved advocates at several stages of the planning and implementation.

“We convened an advisory board of breast cancer advocates, many of whom have served on national advisory panels, to educate us about the personal side of genetic testing: the issues women face, the ramifications for their families, and the problems with insurance and confidentiality. We used their ideas as the basis for a detailed policy regarding genetic testing in our studies.”

Gene Discovery and Molecular Basis of Breast Cancer

To fully understand breast cancer, researchers must look at it on the genetic and molecular levels. “We’re trying to find new genes involved in signaling molecules or proteins that tell cells to proliferate, invade or metastasize,” explains Bill Cance, professor of surgery and one of the project’s principal investigators. His work centers on the focal adhesion kinase (FAK). “My laboratory was the first to identify FAK in human tumors and link it to cell death or apoptosis. We’re now trying to develop it as a target for molecular therapeutics so we can effectively program a cancer cell to kill itself,” said Cance, the Center’s associate director of clinical care.

Channing Der, professor of pharmacology, and Cance are collaborating on a project to develop a novel method to detect mutant genes important in breast cancer causation and progression. “Intraductal breast cancers have a lot of mutations in their genes — even at the early stage,” Cance says. “Our lab is making a pool of genes from breast cancers and then inserting them one at a time (by using a strategy involving viruses) into normal breast cells. In that way we can screen thousands of genes to see if they cause cancer,” explained Der.

Another gene-based research project focuses on BRCA1 and is led by Tony Leadon, professor of radiation oncology, and Beverly Koller, assistant professor of medicine. “If we can understand the function of BRCA1 (the first breast cancer gene discovered), we may be able to understand why women who carry this gene get breast and ovarian cancers. That in turn will help us develop a prevention strategy,” he explains. Leadon and Koller have made an exciting discovery linking defects in BRCA1 to defects in certain processes that repair DNA; this defect, which targets DNA repair to active genes, can compound errors, leading to a wider circle of mutant genes. Their finding, like many others of Lineberger researchers, was published in one of the top biomedical journals in the world — in this case, *Science*.

The faculty and staff of the SPORE projects have branched out into many aspects of the University

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“Making A Real Difference.”



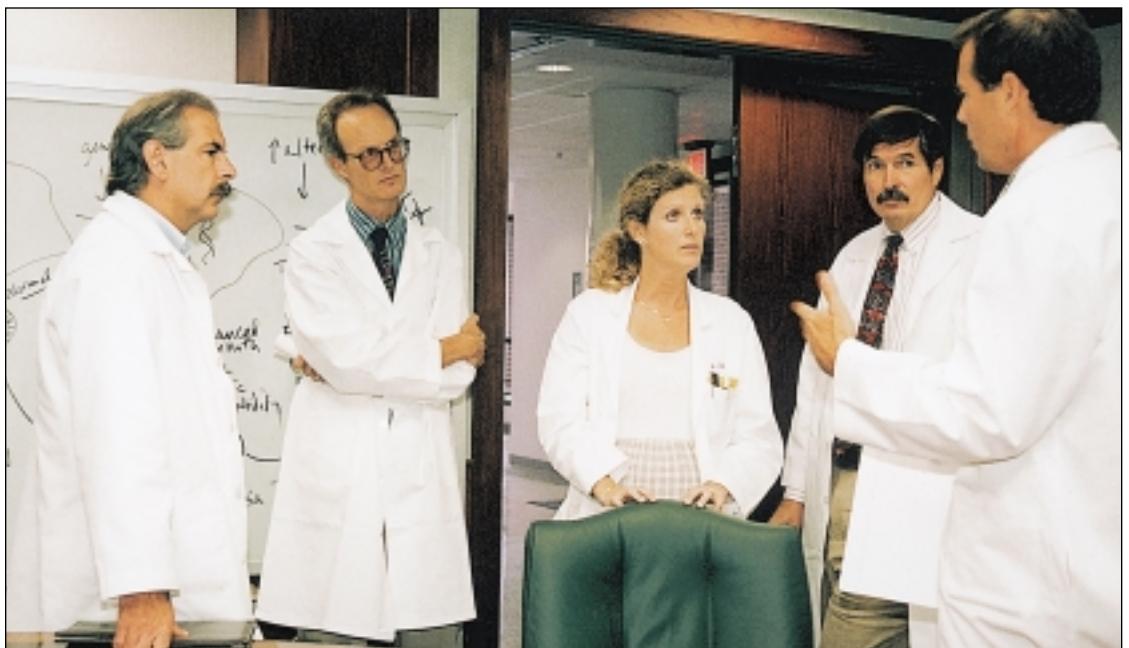
“During my recovery from cancer, I found out how therapeutic it was to talk to other cancer survivors. I now realize that education and advocacy are just two of the ways survivors can fight back. The NC-BCSP provides the opportunity for me to organize support groups and provide them with useful, authoritative information that will help all survivors gain back a sense of balance and control in their lives.”

Bernice McElrath (right), breast cancer survivor and leader, breast cancer support group, NC-BCSP shown here with support group member and survivor Nancy Barnhill. (pictured left top)



“As a survivor, I am excited to be involved with the Carolina Breast Cancer Study. We must find out why so many of our women are being diagnosed with this disease. Hopefully, this study will give us answers we desperately need to point us in the direction of a cure.”

Julie R. McQueen, director of education, Poe Center for Health Education; Co-chair, 1999 Komen NC Triangle Race for the Cure. (pictured left)



(Left to right) Drs. Tony Leadon, William Kaufmann, Lisa Carey, Shelton Earp and Bob Millikan discuss the role of DNA damage in breast cancer epidemiology.

Moving Science from the Bench to the Bedside

Translational research—moving laboratory findings to clinical application—is a major priority at UNC Lineberger. Effective collaborations between laboratory scientists and clinical scientists are what turn a promising scientific idea into a new treatment.

Available right now at UNC LCCC are a breast cancer vaccine developed at UNC, and a trial of a new drug for blood-borne cancers such as leukemia, lymphoma and myeloma, sponsored by UNC Lineberger as part of a collaboration with Proscript pharmaceutical company. Later this year, a clinical trial that uses a novel therapy developed at UNC will be started to treat patients with advanced stages of solid malignancies including breast, colon, lung, and pancreatic cancer as well as sarcoma.

Breast Cancer Vaccine

Researchers at UNC Lineberger are excited by the potential of a breast cancer therapy developed by a team led by Jon Serody, assistant professor of medicine.

“We’ve been working in my laboratory as well as in Jeff Frelinger’s and Ed Collins’ lab for over four years in evaluating ways to enhance immune responses to proteins,” Serody notes.

The result was a breast cancer vaccine — but it’s not a shot. In the world of tumors, a vaccine is a treatment designed to enhance the immune response to a tumor. “The treatment is designed to work by stimulating a patient’s lymphocytes to recognize and kill tumor cells,” Serody explains. “It would be delivered to the cells intravenously.



Drs. Ed Collins, Jon Serody and Jeff Frelinger (left to right) discuss dendritic cell biology.

“Current treatments are inadequate for women with metastatic breast cancer,” Serody says. “Often women with this disease have responses to treatment, but these are of brief duration and not durable.” So the research team is studying whether the vaccine can help these women’s immune systems make their own T-lymphocyte response to the proto-oncogene HER2/Neu (the normal switches used to control growth and tissue repair)—and whether that response can result in shrinkage of established tumors.

The treatment is available to any woman with breast or ovarian cancer that expresses the HLA 0201 allele, which is approximately 30 to 40 percent of the population. “We have extensive data in the laboratory using this approach to enhance T-cell responses and have FDA approval to begin the therapy in patients.

“We’re quite interested in this work because it brings together a strong collaborative interaction between basic scientists like Dr. Collins and Dr. Frelinger and a physician-scientist like me in an attempt to deal with a significant clinical problem,” Serody notes.

Although he’s one of the BMT attending physicians, Serody is focused predominantly on basic research. “In my lab, we have produced leukemia-specific lymphocytes for a clinical trial and are now talking about a trial to use lymphocytes to kill Hodgkin’s disease tumor cells.” He adds, “The breast cancer work is linked in that we transplant—with modest success—a large number of women with metastatic breast cancer.”

The trial is now open for accrual.

Novel Cancer Therapy

The new therapy for solid malignancies is based on UNC’s international leadership in understanding how to block a protein that allows cancer cells to resist chemotherapy and radiation therapy.

Successful collaborations between Dr. Albert Baldwin, UNC LCCC associate director for basic research, and Dr. James Cusack, co-director of the Center’s Multidisciplinary Gastrointestinal Oncology Program, facilitated the translation of the early findings in the Baldwin laboratory into a novel treatment developed in the Cusack laboratory. The new treatment provides a means of overcoming cancer cells’ defense mechanisms that protect them from the effects of chemotherapy. The clinical trial—in development and awaiting FDA approval—has captured the attention of several other national cancer centers as well as the National Cancer Institute.

Compound to Treat Blood-Borne Cancers

UNC is the one of the first to study this new drug for blood-borne cancers. Dr. Robert Orlowski, assistant professor of medicine, is directing the trial. Dr. Orlowski’s laboratory was the first to show

that a proteasome inhibitor, the type of drug being used in both clinical trials, caused preferential death of cancer cells compared with normal cells. He was the first to demonstrate that drugs of this class are able to decrease tumor growth in an animal model of human cancer.

The drug is being tested with solid tumors (breast, colon, lung) at other institutions. Advantages of the new therapy being evaluated are: possibly fewer side effects and increased sensitivity of

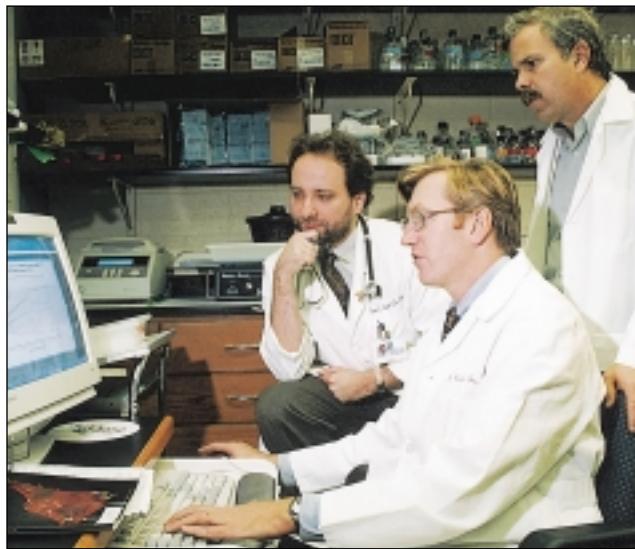
cancer cells to these compounds, suggesting that the drug may target cancer cells while having minimal effect on normal cells.

This Phase One trial will include 20-30 cancer patients to determine the highest doses they can receive without developing side effects.

Others involved in the trial are Drs. Beverly Mitchell, UNC LCCC associate director and division chief of hematology / oncol-

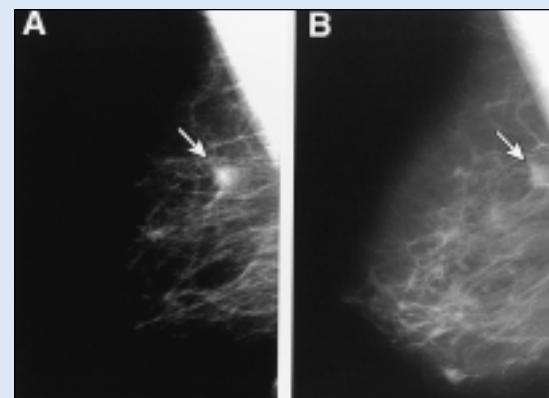
ogy, and Tom Shea, director of UNC’s bone marrow transplantation program.

For information about any of these new therapies, please call the UNC Protocol Office at (919) 966-4432. ●



(Left to right) Drs. James Cusack, Robert Orlowski and Albert Baldwin examine data on the efficacy of proteasome inhibitors.

Advantages for Patients of a Multidisciplinary Team Approach



UNC has high-tech diagnostic tests for many types of cancer. For breast cancer, the newest screening technology is digital mammography, shown in A. This gives more precise information than conventional x-rays (B), leading to fewer callbacks for false positive or unclear results.

Smoke-Free Kids

Old habits are hard to break. That's why Christine Jackson, associate professor, Department of Health Behavior and Health Education at the UNC School of Public Health, initiated a program called Smoke-Free Kids designed to prevent young children from smoking.

"The younger the age at which a child starts smoking, the more likely he or she is to become a habitual smoker during adolescence and adulthood," Jackson says. About 20% of children first try smoking while in elementary school, though most school-based anti-smoking programs begin in middle school—after a fifth of the student body has taken its first puff. "Once they've started, smoking prevention messages are much less effective."

According to a comparison of prevalence estimates across several studies, Jackson found that the group of early initiators breaks down like this:

- 10% of 3rd graders
- 18-23% of 5th graders
- 25-40% of 7th graders

The 1993 North Carolina Youth Risk Behavior Survey found that 30% of all 9th and 12th graders first smoke a whole cigarette prior to age 13. Another study, *Monitoring the Future*, showed that 40% of 8th-grade students reported retrospectively that they first tried smoking in the 4th to 7th grades.

A Unique Approach

Smoke-Free Kids is unique because it aims to modify smoking-specific socialization processes that affect children in households where parents smoke cigarettes. "That's never been done before," Jackson notes. "Most anti-smoking campaigns exclude par-



Smoke Free Kids investigator Dr. Christine Jackson explains some of the program's publications.

ents; ours focuses on parent-child communication, decision-making and consequences."

To do that, the program targets the preparation stage—when children learn the social meaning of smoking. It's one of the few programs in the nation that targets children under 12. And it's the only one that's home-based, getting parents who smoke involved in lowering their children's risk of smoking.

Parental Involvement

Smoke-Free Kids directly and extensively involves parents who have the potential to make a strong impression on their children's decisions about smoking. "Compared to adolescents, elementary school-aged children are strongly influenced by their parents and less so by their peers," Jackson says. "Yet few parents realize that smoking prevention should begin with children at this age. Most wait until adolescence before worrying about tobacco or other substance abuse."

It's no secret that children of smokers are more likely to take up the habit. That's why Jackson's first goal is to create a program that prevents early smoking initiation by children whose parents smoke. Twenty-one percent of 3rd-, 4th- and 5th-grade children of smokers had started smoking, according to a study by Jackson. Only 9.8 percent of children of non-smokers did.

A secondary goal is to provide a complementary program to school-based prevention efforts by involving parents. "We're aiming to engage parents who smoke in countering their pro-smoking influence by getting them involved in anti-smoking socialization activities," Jackson explains. "This is an innovative and potentially powerful way to break the link between parental and child smoking."

Smoke-Free Kids will help smoking parents take steps to reduce the likelihood that their children will start smoking:

- Talk to your child about smoking and its consequences
- Eliminate the home as a source of tobacco
- Monitor smoking behavior of your child and friends
- Establish and communicate the disciplinary consequences of smoking

For parents who smoke, Jackson adds that they should reduce smoking in the home to further strengthen the message. The program focuses mostly on mothers, since most children spend more time with their mothers—almost one-third of American children live with single parents and 81% of single parents are women.

The program is currently under way in 30 school districts in North Carolina, South Carolina and Colorado. Jackson will begin contacting parents and children in the spring to evaluate their participation and results. Annual follow-up calls will be placed for three years. The program will be evaluated by measuring whether fewer children try smoking after participating in Smoke-Free Kids versus those receiving fact-based programming.

"The premise of this project is that children learn to smoke long before they ever puff on a cigarette," Jackson notes. "If the parents participating in Smoke-Free Kids can change what their children learn about smoking, perhaps they can avoid passing on to their children the life-threatening habit of smoking." ●

- The best care based on individual patient's case evaluation by a team of experts to determine the optimal treatment plan
- Ready access to a full array of physician experts, clinical services and treatments
- Coordinated care as patients make transitions among medical specialties and different phases of treatment

Treatment at UNC Means Access to:

- Clinical trials developed at UNC LCCC and through national clinical trials cooperative groups
- Support programs and services from support groups to Internet searches, and individual counseling to wig and turban "banks"



Genetic counseling and evaluation are available.



Each patient's case is thoroughly discussed by a team of experts at a case conference, and an individual treatment plan is designed based on their conclusions.



A young patient turns the tables on his oncologist, Dr. Stuart Gold.

Chromosome loops offer clues to cancer & aging

Scientists at UNC Lineberger and Rockefeller University appear to have solved an important and long-standing mystery in cell biology. The puzzle is why cells' internal repair machinery doesn't mistake the ends of chromosomes for broken DNA and either "fix" or destroy them. Their findings have generated articles in publications ranging from the *New York Times* to *Popular Science*.

Working together, the researchers have discovered that mammals' chromosomes end in loops. Under intense magnification, those chromosome ends, or telomeres, look something like lassos.

A report on the findings appeared as the cover story in the journal *Cell*. Lead authors were Drs. Jack Griffith, professor of microbiology and immunology at UNC, and Titia de Lange, professor and head of Rockefeller's Laboratory of Cell Biology and Genetics.

"We think this work is highly important because it should provide a whole new way of thinking about basic molecular mechanisms related to cancer and to control of aging in cells," Griffith said.

Genetic information in cells is stored in 46 long thread-like molecules called DNA, and each is packaged into a rod-shaped structure called a chromosome, he explained. When cells are exposed to X rays or other insults that break DNA molecules, the repair mechanisms stitch the broken ends back together. If too many breaks occur, then a cellular suicide response kicks in, and cells die.

"The question has been why natural chromosome ends, of which there are 92 per cell, do not trigger that response," the scientist said. "We believe we've found the answer.

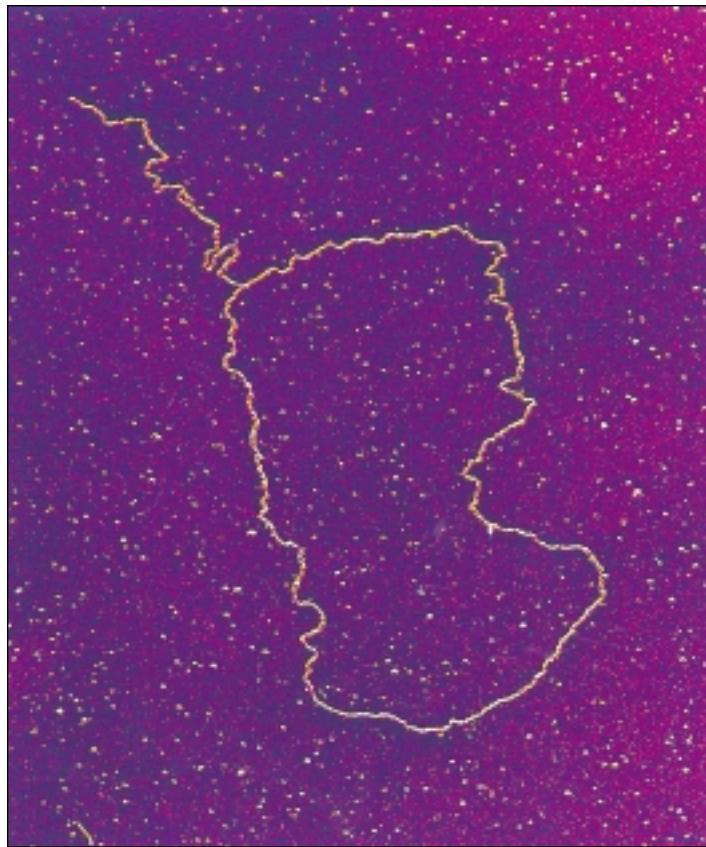
"The first clue came from studies by Dr. de Lange's group of one of the proteins they had discovered," said Griffith, whose laboratory employs electron microscopes to investigate the architecture of DNA molecules. "When this particular protein was functionally removed from the cell, the cell suicide response was triggered, which implicated the protein in masking the chromosome ends."

That finding encouraged the Rockefeller and UNC-CH teams to carry out experiments to examine how the protein might arrange DNA molecules containing genetic sequences typical of telomeres, he said. Resulting electron microscope images showed DNA molecules arranged into the lasso-like structures.

"DNA typical of the chromosome end, or telomere, was looped back around and attached to a distant internal site on the DNA and held there by the added protein," Griffith said. "The loop thus formed disguised the DNA end, keeping it cloaked or hidden from the sensors that trigger the cell suicide response."

Researchers then clipped DNA away from the ends of both human and mouse chromosomes, revealing very large loops, he said. While those structures appeared huge in photographs, they measured only 1/3000th of an inch around and comprised only 1/1000th of the chromosomes' total DNA.

Because chromosomes shorten as people age, many scientist believe telomeres play some un-



End of a human chromosome visualized in the electron microscope seen in the form of a giant lasso.

explained central role in the body's lifelong biologic clock, Griffith said. Thus, telomeres may be some kind of regulator of cell death.

"Very rarely these days in science does a new result emerge from ongoing research, loop around, bite you from behind and make you say 'Hey!'" wrote Dr. Carol Greider of Johns Hopkins University in an accompanying editorial in *Cell*. "But this is just what has happened in the telomere field. These results will make us re-think the classical view of telomere function that has emerged over the past 20 years and give a context in which a new synthesis will emerge."

The National Institutes of Health supported the research at both laboratories. ●

UNC Melanoma Program

The ABCDs of Melanoma

Asymmetry. *One half doesn't match the other half.*

Border irregularity. *The edges are ragged, notched or blurred.*

Color. *The pigmentation is not uniform. Shades of tan, brown and black are present. Dashes of red, white and blue add to the mottled appearance.*

Diameter. *Greater than six millimeters (about the size of a pencil eraser). Any growth of a mole should be of concern.*



The UNC Melanoma Team: An Image-Minded Group

“It’s time to find your place in the sun.”

When Pablo Cruise made that song popular in the mid-1970s, people were just starting to consider the adverse effects of unprotected exposure to the sun. Today, you can still find your place in the sun, according to UNC Lineberger surgeon and Melanoma program leader Benjamin Calvo, but just make sure you slather on the sunscreen.

That’s because anybody can get melanoma, the most serious form of skin cancer. “Those most at risk are people of northern European descent who live in southern latitudes like the Sunbelt states,” Calvo notes. “The one preventive measure to take is to avoid sun burns early in life and throughout life. So always use sunblock.

“North Carolina is a Sunbelt state and the number of melanoma patients is rapidly rising,” he adds. “To better serve the citizens of North Carolina and the nation, we are very interested in prevention, treatment and research of all aspects of melanoma.”

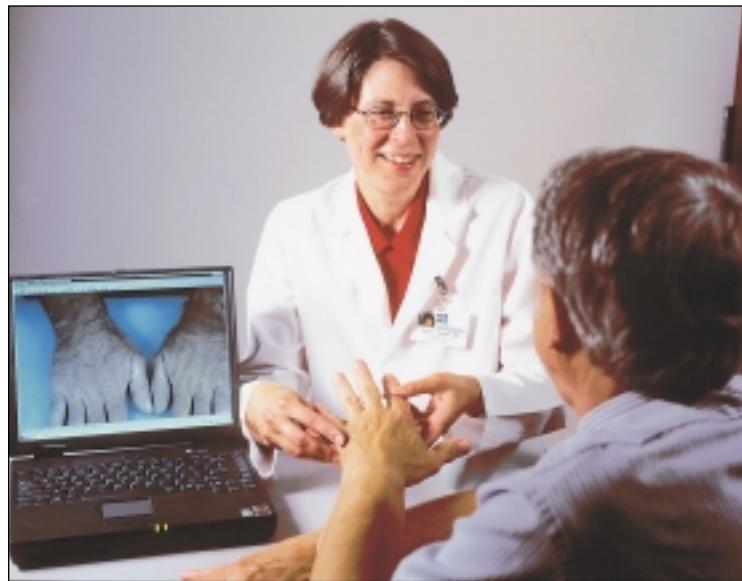
Vital Statistics

Melanoma can appear without warning or develop from or near a mole. It’s most often found on the upper back, but can occur anywhere including nail beds, soles of feet and skin between toes. Most melanoma is found on skin—about 90 percent—with only 5 percent found in eyes and 1 percent in the mouth or anus. If left untreated, malignant melanoma can spread to organs and cause death.

The first sign of malignant melanoma may be a flat, mottled, dark blemish with irregular borders. It can be a quarter-inch in size and may turn red, blue or white, develop a crust on the surface or bleed. Because it’s harder to see in dark skinned people, there’s a common misconception that people with darker skin including African Americans are at no risk. On the contrary, says Calvo, “Their tumors are frequently detected later and have a worse prognosis.”

Multidisciplinary Approach

Treating any cancer, including melanoma, requires a multidisciplinary team of medical professionals. “Obviously different specialists bring into focus different areas of expertise which are important to the global treatment of any cancer,” Calvo asserts. “As is true of any other human endeavor, teams frequently think better than individuals.”



Dermatologist Dr. Nancy Thomas evaluates a patient in the Pigmented Lesion Clinic, which uses whole-body photography to create a pictorial record to follow any changes that may occur.

The Melanoma Program takes a cross-functional approach to diagnosing and treating patients with malignant melanoma. The program provides the expertise of physicians from Dermatology, Nuclear Medicine, Surgical Oncology, Head and Neck Surgery, Reconstructive Surgery, Pathology, Radiation Oncology, and Medical Oncology.

Treatment modalities are available through the whole gamut of melanoma tumors. “From screening to treating very early (thin) tumors to very late metastatic tumors,” he says, “our treatment modalities include all aspects of surgery (sentinel node), chemotherapy, melanoma vaccines, radiation therapy and basic science studies.”

“Patients frequently require more than one type of treatment—operations, chemotherapy, vaccine therapy, radiation therapy,” Calvo explains. “The order of the treatments and the timely, seamless

transition from one modality to another has to be planned and executed well in order to obtain maximal benefit for the best outcome.” Charmayne Gray, MSN, is the nurse practitioner who coordinates the multidisciplinary melanoma program. “Patients quickly learn what an important and personal resource Charmayne is,” Calvo notes.

Detection

Once a person has developed melanoma, he or she is at increased risk for developing other melanoma lesions. “It becomes very important to raise our vigilance about other pigmented lesions in that person,” asserts Robert Briggaman, Chair of Dermatology at UNC.

To do that, the Department of Dermatology developed the Pigmented Lesion Clinic, which uses whole-body photography to create a pictorial record from which the team can follow any changes in lesions throughout the whole body. This augments observations by physicians and patients. “In people with many—sometimes hundreds—of pigmented lesions or moles, a photographic record becomes critical to early detection,” Briggaman notes. And it’s a very inexpensive procedure, costing less than a typical set of dental X-rays.

Another detection device is sentinel node biopsy. In approximately 20 percent of patients with melanoma, the disease spreads to the regional lymph nodes. “This approach allows us to determine if tumors have traveled to lymph nodes with minimal discomfort to the patient and is vital to determining the aggressiveness of a tumor,” explains David Ollila, a surgical oncologist who has conducted important research on sentinel node biopsies. “Tumors that have the ability to travel to lymph nodes are much more likely to come back in some other part of the body. So patients with these types of tumors need treatment beyond surgery alone.” The team began using the biopsies three years ago.

Another tool for detecting melanoma is genetic counseling. Melanoma patients can undergo genetic tests to determine if they have a genetic predisposition to melanoma. If so, the team is alerted to not only watch pigment lesions such as moles on the patient, but on his/her family members as well.

“If a person has a genetic predisposition to melanoma, then siblings and children potentially may be at increased risk for developing it, too,” cautions James Evans, chief of the Genetic Counseling Service. “In

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UNC Melanoma Program team members: front (left to right) Dr. Tom Hensing; Charmayne Gray; Dr. David Ollila; Protocol Office staff Leah Sansbury, Rachael Hajnal, Denise Ritchie; back row (left to right) Dr. John Woosley; Dr. Jim Cusack, Dr. Bill Cance, Dr. Michael Zenn, Dr. Stephen Falen and Dr. Ben Calvo. Not pictured are Drs. Robert Briggaman, James Evans and Nancy Thomas.

Profile

research interest has to do with developing and evaluating interventions that are based on theories of behavior change, and testing them in populations at risk for cancer.”

It's Simple: Eat Well and Be Active!

When talk turns to the “study of the week”—the latest hot-shot preventive for cancer or other dread diseases—Marci Campbell rolls her eyes. “The media keep pushing the latest findings of various epidemiological studies that actually don’t prove causation or lack of causation,” she says. “But all these conflicting media stories do cause more confusion and skepticism among the public about what to eat.”

For instance, there’s been a lot of talk in the media about supplements.

Although vitamins and compounds such as beta carotene are important, Campbell, a nutritionist at UNC-CH’s School of Public Health, says, “Supplements do not have the same beneficial effect as fruits and vegetables. And, in the case of beta carotene, some scientific findings indicate that supplemental doses actually increased cancer risk,” she asserts. Her advice: eat more fruits and vegetables and avoid eating a lot of high-fat foods.

People looking for a magic bullet preventive are tilting at windmills. “It may not be possible to look at one aspect of health and say that’s the one thing to do,” Campbell says. “Nutrition and exercise work together to create better overall health that reduces the risk of cancer, cardiovascular disease and other diseases.”

Basic & Social Sciences. Campbell’s work centers on helping people improve their health and maximize their natural resistance to disease. “My

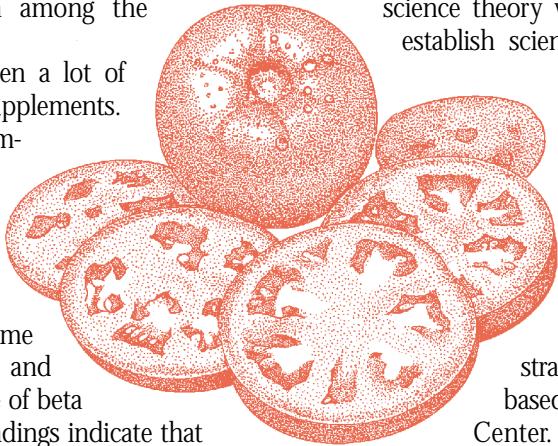
To do that, Campbell blends a strong grounding in biological science with a healthy dose of social science theory. As a botany major at Duke University, Campbell grew an interest in nutrition. Later, she earned a Master of Public Health degree at UNC in 1977 and went on to earn her PhD from UNC in Health Behavior and Health Education in 1992.

The combination of skills allows Campbell to devise effective interventions based on solid social science theory with credible evaluations that establish scientific merit. “Having a strong biological science background has given me an appreciation for rigorous research and designing studies carefully and thoughtfully so they stand up to scientific scrutiny,” she says.

Improved Nutrition.

Currently, she is using these strategies in two projects primarily based out of the Lineberger Cancer Center. The WATCH (*Wellness for African Americans Through Churches*) Project, funded by the American Cancer Society, and PRAISE (*Partnership to Reach African Americans to Increase Smart Eating*) program, funded by the National Cancer Institute, center on eastern North Carolina, a target area for other health promotion projects as well. The region was chosen because, she says, “We’ve wanted to get out in rural communities where there is a higher minority population and the cancer rates are above average.”

WATCH and PRAISE both work through churches. “PRAISE is focusing on increasing fruit, vegetable, and fiber intake, and decreasing fat



intake. We try to reduce total fats, but there are some good fats, such as mono-unsaturated fats like olive oil. The WATCH project focuses on nutrition, but also stresses physical activity and screening for colo-rectal cancer.”

Another of Campbell’s projects, Black Churches United for Better Health, was funded by the National Cancer Institute and was also based in rural eastern North Carolina. Fifty churches participated with a goal to see if a community-based intervention could help participants to improve overall health and decrease the risk of certain types of cancer. The main message of the project was to encourage consumption of five servings of fruits and vegetables each day, since they are foods that are full of cancer-preventing anti-oxidants such as vitamin C, folic acid and beta carotene.

Education. “There’s a lot of conflicting and contradictory advice coming out in the media and it’s a huge problem for health educators,” Campbell adds. “We really don’t know absolutely that a healthy diet and activity will prevent cancer, but evidence is mounting that eating well and being active can have many health benefits including psychological ones. So get out there and enjoy!” ●



NC: The State of Discovery

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and indeed the State, says Shelton Earp. “Since the SPORE was first funded in 1992, the Center has become one of the best places in the country for integrated breast cancer research; national funding for breast cancer projects has increased eight-fold — just one mark of the esteem the nation has for our faculty.

“The opportunities and new ideas that emerge from our SPORE, mixing behavioral, epidemiologic, molecular and clinical scientists both astound and delight me — this intellectual melting pot will make a difference.” ●

by Margot Carmichael Lester

Early detection through mammography can save lives and UNC Breast Cancer SPORE funds have helped lay the groundwork for major grants to study technical innovations. For example, Dr. Etta Pisano, chief of breast imaging in the department of radiology, is leading an international consortium to evaluate the efficacy of computerized digital mammography versus conventional x-ray mammography. Other projects examined a woman’s perception and response to the mammographic experience, e.g. (left to right) Drs. Etta Pisano and Jo Anne Earp have studied whether false positive mammograms keep women from getting subsequent screening mammograms.

Improving Cancer Diagnostics

Diagnosing cancer early can mean less invasive treatment and a better chance of recovery. UNC Lineberger offers several new diagnostic procedures and techniques to cancer patients.

Sentinel Node Biopsy

For breast cancer and melanoma patients, determining if the tumor has spread beyond the local tumor to the lymph nodes is critical to determine what type of therapy, in addition to surgery, is necessary. For breast cancer patients, this used to mean removing nearly all the lymph glands under the arm, a procedure that could cause persistent numbness and tingling in the armpit and, in some patients, cause permanent swelling of the arm. Now, a procedure called sentinel node biopsy can help. Sentinel lymph node biopsy involves removing the first “sentinel” lymph node(s) into which cancerous cells might drain.

Sentinel node biopsy candidates receive an injection of radioactive tracer material around the primary tumor. In the operating room, blue dye is injected into the same area. Surgeons can locate and remove the sentinel node by visual inspection as well as with a handheld gamma probe to trace the radioactivity as it travels through the lymphatics to the sentinel node. If no cancer is present, then removing other lymph nodes isn't necessary. Less surgery, more knowledge.

Sentinel node biopsy is technically challenging to perform. Dr. David Ollila, assistant professor of surgery, cautions patients to ask their surgeons about the “false negative rate.” “Doing so can reduce one's risk of being told that the biopsy results were negative—that the cancer has not spread—when, in fact, it actually has. A false negative result could mean that patients' disease isn't properly staged so they don't get the proper therapy.”

UNC has conducted a “validation trial” of the procedure. In this trial, 80 breast cancer patients underwent the

sentinel node procedure followed by complete removal of the lymph glands. The UNC team was 100 percent accurate in identifying the sentinel node with no false negative diagnoses.



Top photo: Dr. Boggess evaluates enzymes which may signal malignant transformation. Bottom photo: Conventional white light bronchoscope (left); LIFE bronchoscope shows area of abnormality (right).

Improving Pap Smears

Pap smear is the gold standard for cervical cancer screening, but many of the abnormal results it produces do not lead to an increased risk of cancer. UNC researchers are studying the value of a new biomarker for improving cervical cancer screening.

The clinical trial will examine cervical smears for a protein whose presence in cervical cells removed during Pap smear testing may help predict those women who are at greater risk for developing cancer.

According to Dr. John Boggess, assistant professor of obstetrics and gynecology, “A lot of women undergo expensive testing and painful procedures only to find out they've got something that doesn't need treatment or is unlikely to become cancer.” The findings that the specific protein can be detected in a Pap smear is not new, but its use as a biomarker for cervical cancer development is new.

To make Pap smears yield more precise information, Dr. Boggess is testing a new biomarker developed in collaboration with Dr. William Kaufmann, professor of pathology and laboratory medicine, who conducted the laboratory research that provided the scientific underpinnings for the trial.

“To women who express the protein in their Pap smears, we can say ‘you have genetically altered cells in your cervix, which can be treated.’ But if she is not expressing the protein, we can say with greater certainty that other treatments might not be necessary.”

Detecting Lung Cancer Earlier

LIFE, or the Lung Imaging Fluorescence Endoscope created by XILLIX, is a new device that uses clearly detectable red or green light-waves to detect lung cancer more accurately and at earlier stages than the conventional X-rays or sputum tests. Physicians at UNC, the only facility in North Carolina with the device, have

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The UNC Melanoma Team

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this case, we advise family members to take prevention measures such as sun-screen. We would also recommend they be followed carefully by screening tests such as total body photography.”

Treatment

Patients in the melanoma program benefit from the exchange of knowledge and opinions among team members. “Because we discuss cases and perform multi-specialty patient evaluations, we can create a comprehensive treatment plan designed specifically for each patient,” Calvo says.

Treatment may include surgery, radiation, chemotherapy or a combination of these modalities. When a large amount of skin needs to be removed or a difficult area of the body such as face or lips is affected by melanoma, the reconstructive surgery team makes possible the best cosmetic re-

sults. These specialists have the ability to graft skin for another part of the body or rotate skin (flaps) to cover defects left by the melanoma resection.

Radiation is sometimes used to treat local recurrences of melanoma that cannot be removed surgically. UNC and Wake Forest University jointly run a radiation treatment modality used to treat melanoma metastatic to the brain.

Chemotherapy includes conventional biologic agents such as interferon, or the FDA-monitored melanoma vaccine—CancerVax.[®] This vaccine doesn't kill melanoma cells directly, but it stimulates the patient's own immune system to identify and destroy any present melanoma cells. The vaccine is currently in clinical trials at UNC. “If this study shows the vaccine is effective,” Ollila explains, “we'll be able to offer patients a treatment option that is less toxic than conventional drugs.”

The Melanoma Program also provides access to other new cancer treatments through affiliation with national clinical trials groups and participation in clinical trials developed at UNC through the

Lineberger Comprehensive Cancer Center. The Program offers clinical trials to treat Stage III and Stage IV melanoma.

In cases in which the disease has spread to other parts of the body, patients can undergo treatment with chemotherapy. “We're committed to the development of improved treatments for all patients with melanoma and are currently studying a novel chemotherapy approach for these patients,” explains Tom Hensing of Medical Oncology.

Better Results

“We link aspects of prevention—genetic counseling, whole body photography—and treatment—state-of-the-art surgical techniques, chemotherapy, vaccine therapy, radiation therapy,” Calvo says. “Relevant research results and measurable clinical outcomes ultimately lead to increased prevention, new treatments and for the majority of patients with melanoma, a cure.” ●



Celebration. At an earlier cancer patient/family reunion, patients gather around a celebratory cake for the group photo. For the past two years, the fall symposium has featured research updates for all cancer sites, educational sessions on complementary therapies such as massage, music and yoga therapy as well as keynote and luncheon speakers. These meetings attract close to 300 patients, their family members and friends and Lineberger doctors, nurses and healthcare staff.

Improving Cancer Diagnostics

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been using this tool, which detects pre-malignant cancers, for the past year.

“It’s 50 percent more sensitive than the traditional white-light bronchoscopy for pre-cancerous lesions,” explains Dr. M. Patricia Rivera, assistant professor of medicine and a member of UNC Lineberger’s Thoracic Oncology program.

Traditionally, physicians relied on white light illumination to diagnose lung cancer. “With the white light method, even an experienced bronchoscopist can miss a lesion,” she explains. “LIFE uses a different wavelength from the white light illumination method. With LIFE, areas of normal cells appear bright green, and all areas that are abnormal appear red or brown-red.”

Using the combined procedures means that patients receive the most accurate detection and diagnosis of lung cancer. This improved sensitivity

means physicians can encourage patients who are found to have pre-malignant lesions to adopt new and healthier life habits.

“By catching tumors that are pre-cancerous, we can make interventions and also encourage patients to stop smoking. We know that some pre-malignant lesions may regress if patients stop smoking.

“There is a lot we still don’t know about lung cancer,” she admits, “but this technology will help us begin to answer some of these questions, which means we have the potential to save lives.” ●



(Left to right) Dr. David Ollila performs a sentinel node biopsy observed by Dr. Lorraine Corwell, Senior Resident, and assisted by Dr. Bill Cance, associate director of UNC Lineberger.

Scrapbook



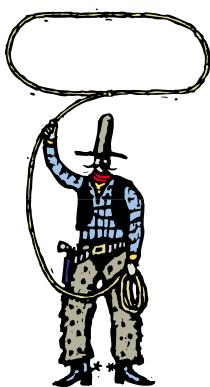
UNC Students. A newly formed UNC group called Carolina Cancer Focus (CCF) strives to get college students involved in the fight against cancer through “informing, serving, and supporting.” CCF is comprised of an administrative board as well as the education, service and fundraising committees which enhance cancer awareness on campus and in the community as well as assist in cancer education programs for patients and families. They give their time and energy to help patients and raise money for Lineberger. (Left to right, seated): Joanna Pearson; Robert Botkin; Brennan Bouma. (Left to right, standing): Cameron Jackson; Anne Washburn, UNC Lineberger Patient/Family Resource Center coordinator and CCF advisor; Eric Johnson.

Race for the Cure.

UNC Lineberger and UNC Healthcare annually enters a team (last year’s largest) in the Susan G. Komen Breast Cancer Foundation’s Race for the Cure. Doctors, nurses, scientists and cancer center staff take



part. Here, UNC Breast Center Advisory Board members (left to right) Mary Beck and Linda Brown pause for a photo. This year, we look forward to running along with the large contingent from the Rex Cancer Center.



Roundup for a Cure.

Chapel Hill downtown business association members, 95-strong, participated in the event, held March 27 in 1999 and March 25, 2000. Shoppers were offered the chance to “roundup” their purchase total for cancer research; i.e. from \$15.20 to \$16.00 or even \$20.00. Some businesses matched the contributions from shoppers. (Left to right): Chris Rice, owner, Carolina Brewery; Missy Julian-Fox, owner Julian’s and Julian’s Home; Kathleen Lord, owner Emma’s and 1999 chair, Downtown Commission; Carol Richards, Director of Promotions, *The Chapel Hill News*; “Robby Roundup” Robert Humphreys, Executive Director, Chapel Hill Downtown Commission.



Dialogue. Postdoctoral fellows in the clinical, laboratory and public health sciences interact at UNC Lineberger Comprehensive Cancer Center. (Left to right): Drs. Minnie Holmes-McNary, postdoctoral fellow in nutrition; Hank Van Deventer, fellow in medical oncology; Denis Guttridge, fellow in cancer cell biology.



Leadership. UNC Lineberger laboratory science leaders review faculty recruitment and delivery of molecular technology to UNC labs: (left to right) Dr. Jenny Ting, cancer immunology; Dr. Beverly Mitchell, Center associate director and molecular therapeutics; Dr. David Lee, cancer cell biology; Dr. Nancy Raab-Traub, virology; Dr. Al Baldwin, Center associate director.

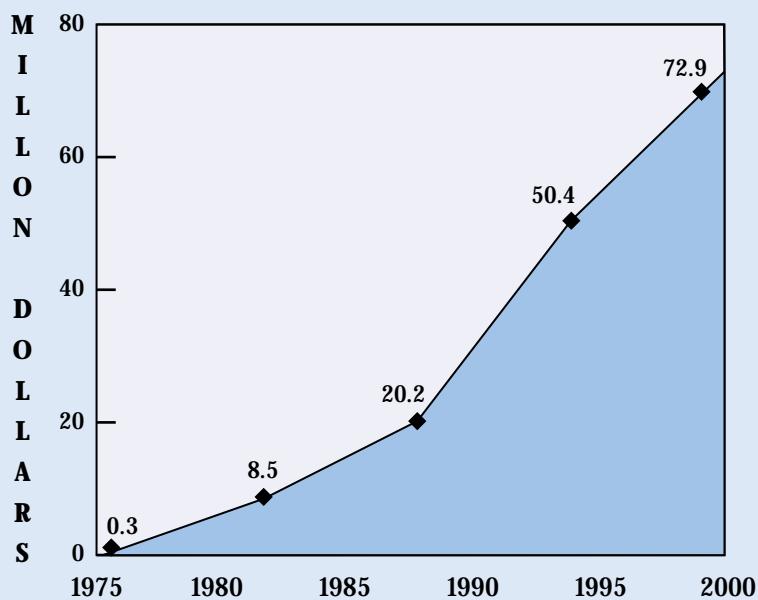
The Patient/Family Resource Center offering help for patients & their families

- Internet access to cancer information
- Support groups
- Massage therapy
- Individual counseling
- Videos, book loan collections, pamphlets/brochures



25 years of growth

UNC Lineberger Faculty Members' Grant Funding 1975-1999 (Direct \$)



Over the past 25 years, the UNC Lineberger has grown tremendously, both in size and in excellence. The dramatic increase in faculty members' grant funding is one measure of the Center's growth.

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