UNC Lineberger Comprehensive Cancer Center

Cancer Lines

University of North Carolina School of Medicine & UNC Health Care

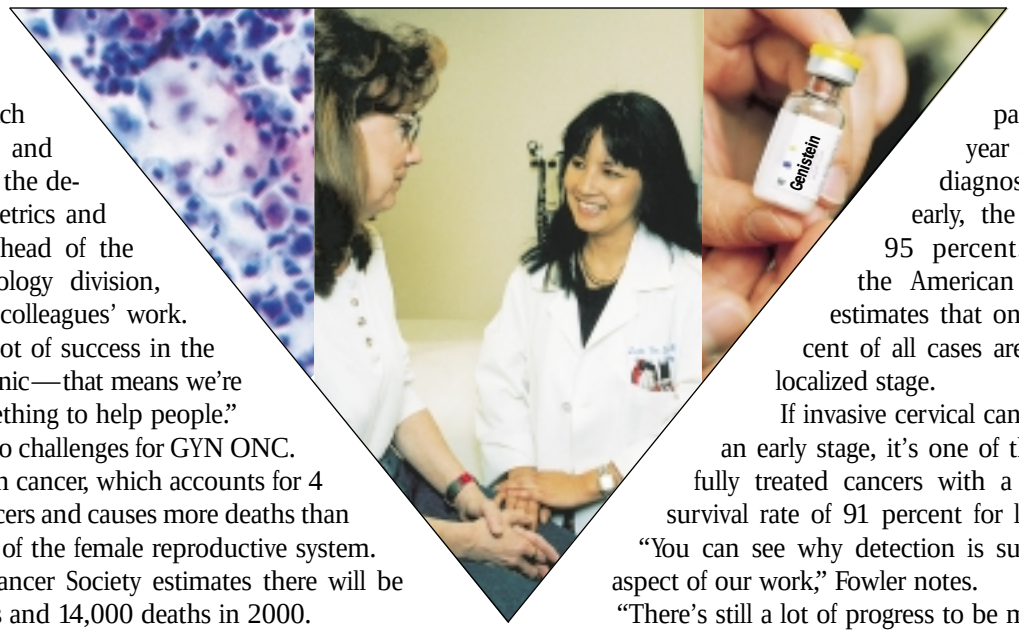
Summer 2000

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

the inside line . . . up

UNC Gynecologic Cancer Team:

Warm Care, Hot Science



"We're doing really great stuff."

That's how Butch Fowler, professor and associate chair of the department of obstetrics and gynecology and head of the gynecologic oncology division, characterizes his colleagues' work. "We're seeing a lot of success in the lab and in the clinic—that means we're really doing something to help people."

Fowler sees two challenges for GYN ONC. The first is ovarian cancer, which accounts for 4 percent of all cancers and causes more deaths than any other cancer of the female reproductive system. The American Cancer Society estimates there will be 23,100 new cases and 14,000 deaths in 2000.

"This disease presents in an advanced stage because we can't detect it very well in earlier more treatable stages," explains Linda Van Le, associate professor in the department of obstetrics and gynecology, division of gynecologic oncology. "Thus patients are already at a disadvantage. To detect the disease early and improve treatment and survival would be a major accomplishment for our patients."

The second is general prevention and detection. The two most prevalent gynecological cancers—ovarian and cervical—have good treatment outcomes if detected early.

Seventy-eight percent of ovarian cancer patients survive one year after diagnosis. If diagnosed and treated early, the five-year rate is 95 percent. Unfortunately, the American Cancer Society estimates that only about 25 percent of all cases are detected at the localized stage.

If invasive cervical cancer is detected at an early stage, it's one of the most successfully treated cancers with a five-year relative survival rate of 91 percent for localized cancers. "You can see why detection is such an important aspect of our work," Fowler notes.

"There's still a lot of progress to be made in here, and we're on the front lines doing some really innovative things in patient education and screening mechanisms," Fowler notes.

Here's a look at two ground-breaking research initiatives in the GYN ONC division.

Ovarian Cancer Prevention

There's further evidence that diet can play a significant role in cancer prevention, according to a study undertaken by Van Le. She and her team are studying genistein, a soy-derived isoflavone phytoestrogen currently popular for a

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Novel Therapies

New Ways to Attack Cancer

A preliminary study undertaken by Bob Orlowski, assistant professor in the department of medicine, division of hematology-oncology, may lead to a more effective chemotherapy option with few side effects for patients with hematologic malignancies such as acute and chronic leukemias, multiple myeloma, Hodgkin's and non-Hodgkin's lymphomas and certain myelodysplastic syndromes.

"Based on laboratory and animal testing," Orlowski says, "it seems possible that PS-341, the first of a new class of drugs called proteasome inhibitors, can be combined with standard chemotherapy to improve the benefits of this treatment, offer an alternative treatment to people who have not been cured with standard chemotherapy, and cause smaller side-effects than the drugs which are currently used."

Orlowski, an expert in proteasome research, is part of a collaborative effort at the Cancer Center, including Al Baldwin, Jim Cusack and Claire Dees. This group is devising several new ways to amplify chemotherapy's effectiveness. Orlowski designed this study for patients with hematologic malignacies to discover what side effects this new agent has, and to identify the maximal dose that can safely be given to patients. This step is the first in determining if a new drug will be useful in cancer chemotherapy. Once the maximal dose has been identified, a subsequent trial will apply it to determine its potential anti-tumor effectiveness.

New Treatments and Cures

Laboratory studies using both cells in culture and animal models have shown that proteasome inhibitors can induce the death of certain lymphoma and leukemia cells at a much

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Director's Message

Dr. Shelton Earp

Imagine this.

Late one night I walk into one of the many active laboratories in the Lineberger building. An excited group shows me two tissue culture dishes. I am startled. In the dish containing cancer cells, the cells are dead or dying. In the dish containing normal cells, the cells are alive and growing. As we switch our scientist's garb for the physician's white coat and go to the clinic, do we give the new substance to our cancer patients?

The answer, of course, is 'no.' Tissue culture dishes are not people. Experiments using tissue culture cells only give hints as to whether or how this new 'drug' will work in humans. The substance might work, but it could make things worse. The doctor's primary credo is *Primum non nocere* — first, do no harm. We are excited, but the evidence is not yet strong.

To learn more, we give the 'drug' to mice who have cancer. Mouse models of human cancers are not people either, but their genetic make-up, physiology, and immunology are similar enough for them to be good, but imperfect models. After our new treatment, the mice's tumors shrink and in many cases disappear altogether. We then test it for toxicity in other animal models. Now do I give the new drug to many patients?

The answer is both 'no' and 'yes.' No, we don't use the new agent to treat many patients. The evidence that the 'drug' is effective is now much stronger, but there is still much that we don't know about how it will affect humans. But, yes, it is time to give the 'drug' to some patients with advanced disease to see if it can be suitably formulated for human use. Can it be given orally or intravenously? Will it harm our patients? Now it is time for a clinical trial.

Clinical trials guard the gateway that leads from the laboratory to the bedside. In a series of steps or tests, these trials separate the truly effective treatments from the merely promising ones. First, in a very small number of patients whose disease is advanced and has resisted all attempts with current treatment. This Phase I trial (mentioned above) identifies the maximum doses that could be effective but that are also not toxic. Second, in a larger but still small number of patients, Phase II trials tell us whether the treatment is effective without serious side effects. Finally, with a large number of patients, Phase III trials tell us whether the new treatment is better than the current treatment. Only after a new treatment has passed all three tests do we let it move from the laboratory to clinical practice and the bedside.

Clinical trials are essential to improving not only cancer treatment but also diagnosis, screening, and prevention. Virtually every recent advance in cancer has passed through the clinical trial gateway, which is the best way to assure that what we do to fight cancer is effective, safe, and ethical.

Discovery is happening so fast. Literally hundreds of drugs are moving toward and through the clinical trials gateway. To find out if these very promising drugs really work, many thousands of volunteer patients and their physicians will need to participate in clinical trials. Right now, only three percent of all cancer patients join a clinical trial. Participation is even lower among older patients and many ethnic groups. Low participation means that trials take longer to complete. These delays lengthen the already long time currently needed to translate new discoveries into practice. Perhaps President Clinton's recent announcement that Medicare will cover the cost of clinical trials will stimulate the entire health insurance industry to do the same, thus increasing participation.

We need to raise awareness about the importance of clinical trials with practicing physicians and encourage patients to consider joining. Large comprehensive centers such as UNC Lineberger need to provide networks for performing complex trials at UNC and less complex trials in cooperation with physician practices. The molecular genetic discoveries — like the one described on page 1 of this issue of *Cancer Lines*—hold great promise for treatments that work better and/or have fewer side effects. But, we can't know until we test them. And, for now, clinical trials are the best way to assure that our treatments are safe and effective.

The National Cancer Institute is partnering with the North Carolina Advisory Committee on Cancer Control and Coordination and the Cancer Information Services of the Carolinas to train ambassadors to share information about taking part in a clinical trial. The pilot project is taking place in two U.S. locations—Baltimore, Maryland and North Carolina. Training sessions are being held throughout the state of North Carolina.

The UNC Lineberger fully supports this effort to raise awareness about clinical trials. In addition, our Clinical Protocol Office (visit our website http://cancer.med.unc.edu or call 919-966-4432) can help answer your questions about the clinical trials available through the UNC Lineberger. They can also help direct you to other resources, such as the Cancer Information Service of the Carolinas, the National Cancer Institute, or the American Cancer Society.

New drugs and treatment are coming from UNC Lineberger researchers at an ever increasing rate. Our clinical trials apparatus must be ready to take advantage of these marvelous new opportunities.

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

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

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New Class of Drugs

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higher rate than similar normal cells. "If the same were true in people," Orlowski notes, "this suggests that it is possible to kill these cancer cells with much less impact on the rest of the body.

"Since none of the currently used chemotherapy drugs kill cancer cells in the same way as proteasome inhibitors, patients who have not been cured by these other standard drugs might derive a benefit from this new class of agents," he continues. "There is evidence that these inhibitors can be combined with drugs already used in chemotherapy to increase the number of cancer cells killed."

Working on the Molecular Level

Orlowski's work centers on molecular therapeutics, which allows researchers to develop a better understanding of what is involved in the process by which normal cells become cancerous at the genetic level. This knowledge will enable scientists to identify important steps that can be targeted for blockade, either by currently available or newly designed drugs.

"The more we understand the development of cancer," he contends, "the more we have learned that it is a complicated, multi-step process which can be very different even between two patients with the same leukemia. It is unlikely that, in the near future, we will have the resources to study each new patient as an individual and design a treatment that is unique for them. We must therefore identify targets in cancer cells which are specific enough to these cells that they are not present in normal cells, are important enough that their interruption will cause cancer cell death, but are present in a large enough proportion of patients that it will be feasible to use a relatively restricted number of treatment combinations in their therapy."

(Left to right) *Drs. Small and Orlowski are studying the ways in which this new class of drugs kills cancer cells in the laboratory, which will help to define how best to use them in human patients.*

Orlowski says a second challenge is using the information being generated on the biology of tumors and their biochemistry to design, test, and put into clinical practice new drugs that will have significant anti-tumor activity.

Looking Forward

Over the past few decades, great strides have been made to improve the care of patients with hematologic malignancies. For instance, patients with Hodgkin's disease — once a lethal malignancy — now have an excellent possibility of cure. But what's true for some cancers is not true of all. In many other hematologic malignancies — including some of the acute and chronic leukemias, and some of the non-Hodgkin's lymphomas — cure is much less likely, and a majority of patients eventually die of their disease.

"The biggest challenges in the field of hematologic malignancies are, therefore, to identify new agents with activity in these diseases that might improve our current cure rates, and to better understand the biology of these illnesses," Orlowski notes. "This insight might allow us to either make better use of the drugs we already have, or design new ones, and hopefully both."

Warm Care, Hot Science

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multitude of reasons, including its ability to abate hot flashes in women preferring to avoid hormone therapy.

The early research is exciting, Van Le says. "Genistein is not associated with major side effects, is inexpensive relative to major drugs and is readily available in health food stores."

Structurally similar to estrogen, genistein inhibits breast cancer cell growth in laboratory studies. "Coupled with the observation that endometrial cancer, usually a hormone dependent cancer, is less common in the Asian countries where soy plays a large part in daily diets, we undertook studies to determine if genistein inhibits growth of endometrial and ovarian cancers, as well. To date, our data appear encouraging."

While the public is fairly cognizant of ovarian cancer, cancer of the uterine endometrium is less well-known. However, it will result in approximately 6,500 deaths this year, with 36,100 expected diagnoses. Incidence rates are higher among white women (22.4 per 100,000) than among black women (15.3 per 100,000), though mortality rates are the opposite with nearly twice as many black women dying from the disease than white women.

Van Le is cautiously optimistic about genistein's potential. Though still being studied, she concedes that, "the results, if positive or encouraging, would mean ready access to this product since it is already on the market. Quality of life would not be impacted greatly since the side effects are minimal."

Cervical Cancer Detection & Prevention

Say "Pap smear" in a room full of women and you're likely to be met with reactions ranging from vague discomfort to dirty looks. But this much-maligned procedure can hold the key to early detection of cervical cancer, one of the leading gynecological cancers. In fact, since the advent of the Pap smear, the rate of cervical cancer has decreased markedly. Still, this year, an estimated 12,800 cases of invasive cervical cancer will be diagnosed and approximately 4,600 women will die of the disease.

The Gynecologic Cancer Team. Front row (left to right)*: Ann Dunlap; Dr. Leslie Walton; Susan Godfrey; Dr. Dan Veljovich; Dr. John Boggess; Juanita Moore.* Back row (left to right)*: Mary Horton; Dr. Wesley Fowler; Dr. Linda Van Le; Dr. Tom Morrissey.*

Despite that, however, few women get regular check-ups that include this minimally invasive, inexpensive screening test.

"The last 10 patients I've seen with advanced cervical cancer did not have a Pap smear in 10 years," Van Le notes. "If all women could undergo screening regularly, cervical cancer would not be such a problem."

John Boggess, assistant professor, obstetrics and gynecology, mirrors Van Le's passion. He's leading the charge by undertaking a combination of clinical and basic scientific research to find new ways to detect and prevent cervical cancer.

Boggess has identified a potential biomarker that would enable a more accurate Pap smear. "We know that human papilloma virus (HPV) causes cervical cancer—but it's overwhelmingly common in women who don't develop the cancer."

What happens to HPV to spur cancer growth? DNA integration. The HPV breaks open and becomes a part of a woman's chromosomes and causes abnormal cell cycling. This, in turn, promotes the expression of telomerase, an enzyme which is activated in almost all cervical cancers.

"If we can detect telomerase in the cervix, we know the patient has a high risk lesion that's more likely to become cancer," Boggess explains. So he and his team are attempting to integrate telomerase testing with Pap smears to increase accuracy, reduce abnormal results and avoid unnecessary biopsies. The new and improved Pap is currently in a 120-woman trial.

Boggess also is collaborating with Jo Ann Earp, chair of health behavior and health education at the UNC School of Public Health, to develop a community-based outreach program to promote Pap smear screening. The program will be structured similarly to Earp's ground-breaking breast cancer screening program *(see story, page 5)*.

"Getting more women to have Pap smears is important," Boggess says, "but it's a challenge. These tests and issues are sensitive. However, we have a great model to follow in Dr. Earp's work with breast cancer, so we're very encouraged."

The Team Approach

This cross-department collaboration is a huge benefit to researchers and patients alike. "Lineberger is a wonderful place to work because I have the clinic, the molecular lab, epidemology, outreach efforts and treatment trials right here," Boggess says. "That kind of interaction among areas is truly exciting."

Van Le agrees. "We have a team approach to all gynecologic cancers that integrates new findings clinically. We are equipped, by virtue of our clinical trials office, to initiate new promising treatments quickly. With this infrastructure in place, we can offer patients new, more promising treatments expeditiously. We also have a great team! We have two dedicated chemo nurses, a devoted clinic staff, and offer a compassionate attitude towards all of our patients with cancer."

All this bodes well for the future of cancer research at Lineberger. "Nineteen-ninety-nine was a very productive year for us," Fowler notes. "I'm looking forward to more great developments this year."

Photo montage on cover includes a conventional pap smear (left).

Gynecologic Cancer Awareness Month

UNC Lineberger observed the first national Gynecologic Cancer Awareness Month in September with a special exhibition of quilts made by North Carolina women, honoring friends and family members who have been affected by ovarian and other gynecologic cancers, as well as quilts made by members of the National Ovarian Cancer Coalition. Standing in front of the quilt given to UNC are: (left to right) *Dr. Wesley Fowler, chief, gynecologic oncology division; Karen Binder, ovarian cancer survivor and chair of the Triangle N.C. Ovarian Cancer Connection, and Marie Owens, ovarian cancer survivor, hold a proclamation from Governor Jim Hunt declaring September as Gynecologic Cancer Awareness Month.*

Profile

Pediatric Oncologist Stuart Gold Learns Life's Priorities from His Patients

Even while growing up in Savannah, Ga., Stuart Gold knew his future would involve children and medicine. "My uncle was an old-fashioned pediatrician," recalls Gold, associate professor of pediatrics, in the hematology oncology division. "He made house calls, he was warm and compassionate. And he was a great role model."

Between playing tennis, running, sailing and taking pictures, Gold was learning the personal, compassionate aspects of patient care at his uncle's side. "He'd even take me with him to the public health clinics in Atlanta," Gold remembers.

Decades later, Gold takes care of children, too — kids with cancer and blood disorders including sickle cell disease and hemophilia/clotting disorders. Chatting with him, it's clear he embodies the very characteristics he admired in his uncle.

"I could not imagine a field more exciting than this," he says. "Working with incredible kids and families, being able to provide continuity of care and watching these kids grow up and have families of their own." Somberly he adds that the most challenging part of his job is "helping families deal with the hardships of cancer diagnosis, and unfortunately sometimes death." Happily, about 70 percent of childhood malignancies are now curable.

"Working with kids is fun," Gold says. "The key is not to treat them as if they are ill, to treat them as normal. They teach me a lot — especially about my priorities in life."

While he loves the patient interaction, there also is research value to working with kids. "This group of patients gives clues to the genetic basis of cancer — and hopefully clues to help all types of cancer." Kids with cancer can help researchers identify certain malignancies that run in families or have been identified with certain genes/chromosome abnormalities. "That's helped identify tumor related genes."

Gold also is a member of the Children's Cancer Group and is the principal investigator for the group's North Carolina section. "I have worked on several of their treatment protocols as a member of their committees for acute leukemia and brain

tumors."

Gold did his undergraduate work at Vanderbilt, majoring in math with a minor in chemistry. He medical school there. He did his pediatric and subspecialty training at the University of Colorado Health Science Center from 1981 to 1989.

When he's not working with kids, Gold enjoys rose growing, running and cooking. In fact, his dream is retiring and tending to his garden, which he claims is "the best rose garden around" with more than 100 rose bushes.

Briefs

Study shows black churches can help improve healthy behaviors

Black churches, long a source of spiritual comfort and community for their members, can also help improve people's eating habits and other behaviors to make them healthier, according to a major new study involving a dozen researchers, three Triangle universities and state health experts.

The study—the largest of its kind ever done—was conducted by Marci Campbell, assistant professor of nutrition in the schools of public health and medicine, and colleagues. It was intended to determine whether church-related activities could change ingrained eating habits.

Nutrition and other health experts now believe reducing dietary fat and increasing fruit and vegetable consumption can cut cancer risks, which are higher and increasing among blacks, while providing other significant health benefits as well.

"We found we could boost the amount of fruits and vegetables people in the study consumed by about a serving a day," said Campbell, leader of Lineberger's cancer prevention and control program. "One serving equals a half cup of fruit or cooked vegetables, a cup of salad or six ounces of 100 percent fruit juice. That doesn't sound like a lot, but when you think of this amount of change across the large sample of 2,500 people involved, that everyone was surveyed regardless of their level of participation and that the effect has lasted for at least two years, it's actually pretty impressive."

The study's results provide good news, showing that eating patterns can be changed and that church activities are among the most effective ways of doing that. Similar efforts through schools and work sites have shown smaller effects on behavior.

NCI awards UNC-CH $5 million for unique prostate cancer studies

UNC researchers received $5 million from the National Cancer Institute and the National Institute on Aging to investigate prostate cancer, the second leading cause of cancer deaths among men in the United States. Scientists will investigate mechanisms responsible for reappearance of hormone-independent prostate cancer in patients following treatment to remove the source of androgen. They also will investigate why black men develop prostate cancer twice as often as white men. Answering these questions should provide solid clues to the illness that will benefit both races, the scientists say.

"Prostate cancer requires male hormones known as androgens both to develop and to grow, and the same is true for benign prostate tissue," said James Mohler, associate professor of surgery. "One big difference is that cancer can spread, which obviously can make it fatal. Researchers want to determine how the cancer can grow without male hormones. Such information might enable them to effectively cure prostate cancer just by preventing its re-growth," the surgeon said.

"A particular focus will be on how this process is different in Caucasians and African-Americans, who are twice as likely to die from prostate cancer, even after accounting for possible differences in health care," he said.

Co-principal investigators are Frank French, professor of pediatrics and director of the Laboratories for Reproductive Biology, and Gary Smith, professor of pathology and laboratory medicine. Others involved in the project are: Elizabeth Wilson, professor of pediatrics and biochemistry; Sharon Presnell, assistant professor of pathology and laboratory medicine; Desok Kim, research associate at the Lineberger Center, and Christopher Gregory, postdoctoral fellow in pediatrics and the Laboratories for Reproductive Biology.

Scientists find protein in Epstein-Barr virus causes B cell lymphoma in laboratory mice

An international team of scientists from UNC and Japan has proven that a protein called latent membrane protein 1 in Epstein-Barr virus causes a form of cancer known as B cell lymphoma in mice. The work is important, the scientists say, because it shows the protein's central role in Epstein-Barr virus' ability to change normal cells into cancerous ones. That virus already is known to cause infectious mononucleosis in humans and has been associated with such malignancies as Burkett's lymphoma, Hodgkin's lymphoma and nose and throat cancer. It is especially hazardous to AIDS patients and other patients whose immune systems have weakened.

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NC-BCSP Successfully "Breaks the Silence" about Breast Cancer

Breast cancer is fairly easy to detect—often at an early, treatable stage. Surprisingly, however, less than half of women age 40 and older in the United States have regular screening mammograms—and the number is even lower in the African-American community. The incidence of breast cancer increases in all women as they grow older.

Those facts contributed to the creation of the North Carolina Breast Cancer Screening program (NC-BCSP), a long-term, comprehensive, multi-level community intervention project designed to increase breast cancer screening among older African-American women in five rural eastern North Carolina counties. The program intended to increase initial and repeat mammography screening by black women ages 50 years and older and increase follow-up of positive screening mammograms. To do that, it deployed 160 lay health advisors (LHA), local women who provided social support for mammography to women within their social networks.

"In general, the increase of mammography screening nationwide is pretty strong," notes Jo Anne Earp, professor and chair of the department of health behavior and health education and principal investigator of NC-BCSP. "It was a surprise to find that black and white women, starting from more than a 20 percent point differential in 1994, had essentially the same screening rates in some of these counties at the end of just three years of our intervention."

Earp and her fellow researchers are currently gathering data from the study's second follow-up to see whether the early progress was sustained over a five- or six-year time period. "I am betting that it will be, as least for two or possibly three of our five counties where the lay health advisors continue to be extraordinarily active," Earp predicts.

NC-BCSP community outreach specialists past and present, and program staff. Front, left to right: *Lucille Bazemore; Georgia O'Pharro; Eva Hill; Bernice McElrath; Barbara Leary.* Back, left to right: *Linda Mayne, regional coordinator; Survilla Cherry, Dr. Jo Anne Earp, program director; Judy Ruffin; Dr. Eugenia Eng, program co-director; Helen Guthrie; Evelyn Neptune.*

Not only did the study show that interventions like the LHAs could "break the silence" about the importance of breast cancer screening in the older, rural African American community but, more importantly, it closed the racial gap that existed in breast cancer screening before NC-BCSP began, Earp says.

The study also uncovered another interesting finding. "What appeared to be a racial gap in physician recommendation for mammography screening turned out to be an income and education gap," she explains. "Women who saw their doctor more often—who were younger, had higher incomes, and more education—were more likely to receive a recommendation from physicians to go for their annual screening mammogram than were women of the opposite characteristics—the very women who are dying more often of breast cancer. Such a disparity in screening recommendation was very surprising and more than a bit unsettling."

The Lasting Impact

The NC-BCSP shows that adapting interventions for the communities, populations and groups most in need of them, and targeting many groups in a community, can "get the job done" in a way that fits the norms and values of the community in which it's happening. "We can see movement towards a healthier, better screened population even on a sensitive issue such as breast cancer screening," Earp comments.

Geni Eng, a colleague on the project and professor of health behavior and health education, says what really made the difference is "tireless efforts by the women who were the living statistics contributing to the higher breast cancer mortality rates among black women in these counties. If we can have this effect in these very poor, rural, poorly educated counties of eastern North Carolina, surely others in urban ghettos and rural areas elsewhere in the United States can also mount programs that will make a difference in the public's health."

Spreading the Word

But to be successful they not only need an example, they need money to pay for screening from Centers for Disease Control and state governments, and money for treatment where breast cancer is found.

To that end, Earp, Eng and the rest of the NC-BCSP team are working to get the word out about how natural helper lay health advisors have been successful in increasing breast cancer screening rates in eastern North Carolina.

There's still work to be done, however. "While nationally we need more efforts aimed at reaching vulnerable communities where screening rates are still low—for example the Latino community or some Native American or Asian communities—our prevention efforts may be best targeted at health professionals to get them to examine and change their behavior," Earp urges. "Certainly health care providers should be sent the message as much or more than the communities in need."

More to Come

These answers are just the beginning, Earp says. So she and her team continue to ask questions. "Why do certain community interventions work, or work in certain populations and not others, or work some of the time but not the rest of the time? The important questions need much more attention paid to them than the amount of money currently being put into prevention social science research," she notes.

"The success of this project, at the highest level, is important because it may convince more policy makers to fund more generously evaluations of prevention intervention efforts and that will be a good thing!"

1999 Patient Education Symposium

Organizers of the 1999 Patient Education Symposium (left to right): *Anne Washburn, coordinator, Cancer Patient Education and Support, symposium chair; Dr. Shelton Earp, Lineberger Center director; Sharon Cush, neuro-oncology nurse and symposium research update sessions chair; Karen Binder, quilt display; Dr. Jeff White, keynote speaker, Director, Office of Cancer Complementary and Alternative Medicine, National Cancer Institute. Over 300 patients and family members attended the day-long meeting which included research updates for all cancer sites, a luncheon speaker on nutrition, and breakout sessions on acupuncture, massage, music therapy, nutrition and relaxation.*

Lineberger

Wit. The cast and director of the Playmaker's production of "Wit," the play about an English professor who is diagnosed with Stage Four ovarian cancer, visited with Lineberger faculty and staff to discuss issues and ideas of the show. *(Left to right)* UNC gynecologic oncology surgeon, Dr. John Boggess, "Wit" director Drew Barr;"Wit" lead actress Tandy Cronyn; Dr. Wesley Fowler, chief, gynecologic oncology division.

Outstanding Service. Board of Visitors members *(left to right)* Missy Julian-Fox and Sue Moore received the Outstanding Service Awards. Sue Moore, a breast cancer survivor, was honored for her leadership in breast cancer advocacy. Missy Julian-Fox, a breast cancer survivor, was cited for her extensive work on behalf of the Center.

Golf Event. The Fountain Odom golf tournament was held in October in Charlotte. *(Left to right)* are: Sen. Odum; Center director Dr. Shelton Earp; and Senator Tony Rand. The event raised close to $17,000 for UNC Lineberger.

2000 Club Brunch. Corporate sponsors from Wachovia Bank *(left to right)* Scott and Tricia Faircloth and Carol and Jud Franklin, whoop it up with Ramses at the 2000 Lineberger Club Brunch and basketball game.

Briefs

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"We have shown for the first time that Epstein-Barr virus clearly can cause cancer," said Nancy Raab-Traub, professor of microbiology and immunology, and leader of the Lineberger's virology program."Now we can go after the specific protein that is responsible and perhaps one day stop that protein function and prevent the cancer from growing.

A National Cancer Institute grant to Raab-Traub supports the research.

Chromosomes found to end in big loops

The puzzle surrounding why cells' internal repair machinery doesn't mistake the ends of chromosomes for broken DNA and either "fix" or destroy them appears to have been solved by a team of researchers who 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 a cover story in the journal *Cell*. Lead authors are Jack Griffith, professor of microbiology and immunology at the UNC-CH School of Medicine and Lineberger faculty member, 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.

"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."

Because chromosomes shorten as people age, many scientist believe telomeres play some unexplained central role in the body's lifelong biologic clock, Griffith said. Thus, telomeres may be some kind of regulator of cell death. The National Institutes of Health supported the research at both laboratories.

Scrapbook

Walk for a Cure. North Carolina Central University students participated in "Walk for a Cure." The event, sponsored by the business club Phi Beta Lambda, Inc., raised over $800 for the UNC Breast Center. *Pictured (left to right) front:* Sonya Scott, student advisor to Phi Beta Lambda, UNC LCCC director Dr. Shelton Earp; *second row:* Algenon Conyers, Felicia Taylor, Hulon McIver, Jr., Melanie Bishop; *fourth row:* Quincy Bess.

Vitale Visit. Sports announcer Dick Vitale visited UNC on Thursday, February 3, to talk to cancer patients and families. With Nick Valvano, CEO of the V Foundation, he presented a check from Papa John's Pizza and the V Foundation to the Thoracic Oncology Program. During his hour-long stay, he autographed pictures and signed basketballs. *(Left to right):* Papa John's Pizza representative Mike Smith; V Foundation for Cancer Research CEO Nick Valvano; Thoracic Oncology program members Dr. Patricia Rivera; Dick Vitale; Dr. Mark Socinski; clinical nurse Ann Steagall; Dr. Frank Detterbeck.

Fellows & Preceptors. 1999 Lineberger Fellows with their preceptors. Fellows receive a $3,000 supplementary stipend to recognize the excellence of their research activities. The awards, begun in 1987 encourage promising new cancer researchers. This year's fellowships were made possible by Best Distributing Company in Goldsboro, NC, and the Cancer Research Foundation of America in Arlington, VA. *(Left to right):* Preceptor Dr. Mark Peifer, Fellow Rob Cavallo; Fellow Jun Nakamura; Preceptor Dr. Eng-Shang Huang; Fellow Robert Johnson; Fellow Linda Gorman; Preceptor Dr. Ryszard Kole; Fellow Anneclaire De Roos; Preceptor Dr. Andrew Olshan.

Dedication. The Big Rock Blue Marlin office in the Lineberger building was dedicated at the February Board of Visitors' meeting. *(Left to right):* Ben and Sue Moore, members of the Board of Directors of the Big Rock Blue Marlin Tournament and of the UNC Lineberger Board of Visitors; and Dr. Albert Baldwin, Associate Director of Basic Research.

Floyd Relief. Lineberger faculty and staff supported our research team in eastern North Carolina who were impacted by Hurricane Floyd. Bags of food were delivered during the holidays. Photo shows delivery to Newton Grove. Other funds donated were used for shoes, grocery, coupons, utility maintenance and additional needs.

Theta Chi. Jonathan Fulcher, a cancer survivor and member of Theta Chi Fraternity (Theta Omega chapter) from Appalachian State University, joins his fraternity brothers in delivering baseball caps for pediatric oncology patients.

Clinical Trials Underway

For information about any of these clinical trials, please call 919-966-4432.

Chronic Myeloid Leukemia (STI571-102) This is an open-labeled pharmaceutical Phase II study for Philadelphia chromosome-positive CML patients in myeloid blast crisis.

The study is designed to evaluate the anti-leukemic activity and safety of once daily oral administration of STI571, a protein-tyrosine kinase inhibitor. Secondarily, the study will look at duration of response, overall survival, cytogenetic response, symptomatic improvement, possible mechanisms involved in resistance to this drug, and signal transduction inhibition in vivo.

Nationally the target accrual is 100 newly diagnosed patients who have not received previous therapy for the accelerated and blastic phases of the disease.

Limited enrollment is available for patients who have received previous therapy for CML in blast crisis. This population will only be evaluated for response. Statistical considerations are based on the previously untreated patient population only. *PI Thomas Shea, M.D.*

Melanoma (UCHSC98-533) Colorado Health Sciences is sponsoring this multi-center Phase III study of neoadjuvant CVD/IL-2/IFN in patients for Stage III Malignant Melanoma.

Patients will receive two cycles of cisplatin, vinblastine, decarbazine, IL-2, and interferon followed by lymphadenectomy. Post-operatively, patients will receive an additional two cycles of this biochemotherapy regimen. Patients will be hospitalized for 5 days during the administration of all biochemotherapy.

Eligibility requires patients present with at least one measurable lymph node and be biochemotherapy naïve.

One hundred patients will be enrolled in a two-year accrual period. The primary objective is to determine the disease-free duration and overall survival in Stage III melanoma. Cutaneous melanoma is one of the most rapidly increasing rates of any cancer in the US. *PI Thomas Hensing, M.D.*

Hematologic Malignancies (LCCC 9834) This is an investigator initiated Phase I study using a novel drug (PS-341) in patients with hematological malignancies refractory to all standard therapy.

PS-341 is a proteasome inhibitor. Studies have shown that the proteasome is absolutely necessary for cell survival and proliferation. Disruption of this pathway has been shown to lead to apoptosis, or programmed cell death.

Patients are treated at the General Clinical Research Center twice weekly for four weeks followed by a two-week rest period. If stable, patients can continue for more treatment.

Correlative laboratory studies are looking at plasma pharmacodynamics of PS-314, proteasome inhibition, interleukin 6 levels (multiple myeloma patients), and extent of apoptosis in peripheral blood mononuclear cells.

Candidates must be refractory to conventional therapy, or have a disease for which conventional therapy is not recognized. *PI Robert Orlowski, M.D., Ph.D.*

Breast Cancer (LCCC 9925) This is a Phase I/II investigator initiated trial investigating Herceptin® as a potential radiosensitizer in patients who have not had a complete clinical response to neoadjuvant chemotherapy, or presenting Stage IV, T4d, and N2 breast cancer.

Herceptin® will be administered weekly while patients receive external beam radiotherapy daily for five weeks. Effective radiosensitizers enhance radiation-induced cell kill. Pre-clinical studies indicate the potential of Herceptin® as a radiosensitizer in the treatment of HER2 overexpressing breast cancer. The epidermal growth factor receptor (EGFR) family consists of HER2.

Herceptin® was developed to interfere with HER2 signaling. Inhibitors of growth factors in concert with DNA damaging agents may serve to increase tumor cell kill. *PI Carolyn Sartor, M.D.*

calendar of events

OCTOBER

13th Board of Visitors Meeting.
Lineberger Cancer Center, Chapel Hill, NC.

UNC Lineberger Comprehensive Cancer Center
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