UNC Lineberger Comprehensive Cancer Center

cancer Lines

The Cancer Program of UNC-Chapel Hill & UNC Health Care

Winter 2007

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LINEBERGER COMPREHENSIVE CANCER CENTER

the inside line . . .

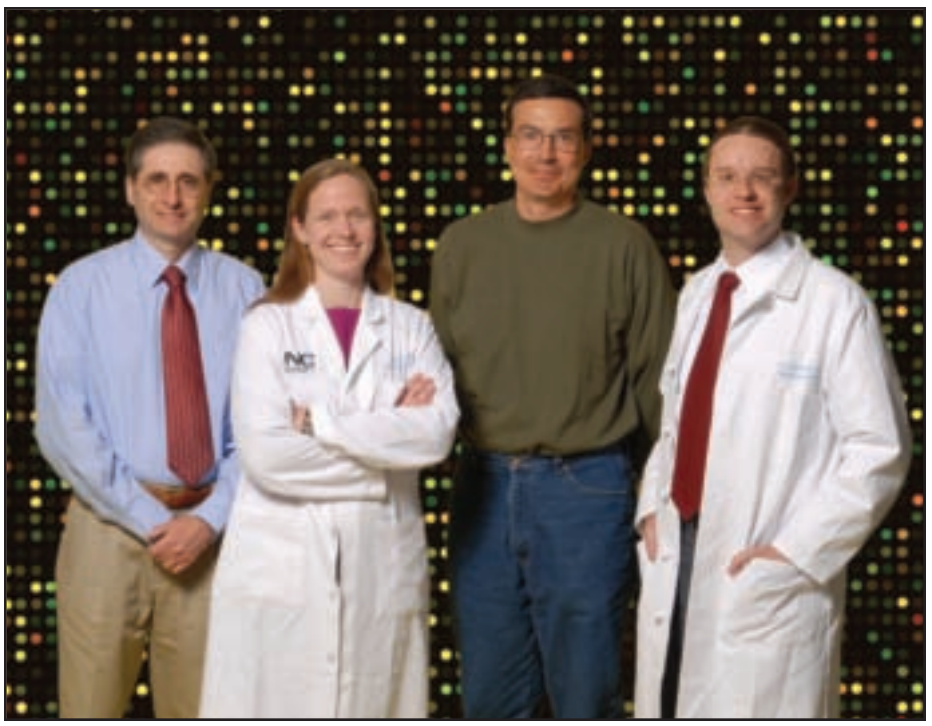
New Technologies Enable "Personalized" Medicine

"Today, most medical decisions are based on historical data compiled from groups of patients who, in general, appear to look like the patient under consideration for therapy," explains Neil Hayes, assistant professor of medicine in the division of hematology/oncology in UNC's School of Medicine. "We frequently practice medicine by the law of averages - on average a therapy should work for a given patient."

The study of cancer genetics is changing that by allowing physicians to go directly to more effective therapies for every patient sooner. And in those cases where no therapy appears likely to help, researchers can turn their attention earlier to developing newer and more tailored treatments.

"Personalized medicine is a movement away from treatment based on averages, and more based on data derived from the person seeking therapy," continues Hayes, a Lineberger member. "This information can assist us in making more accurate predictions about what events a patient is at risk for, such as rapid recurrence versus low likelihood of recurrence, specific sites of recurrence, the probability of responding to any therapy or to specific therapies. And it can aid in the selection of therapies."

Adds Michael Topal, professor of pathology and biochemistry/biophysics and a Lineberger member: "It's medicine that is fine-tuned to the genomic background of the individual and, in the case of cancer, to the tumor."



UNC Lineberger genetic researchers in front of a microarray, a key genetic tool: Drs. Michael Topal; Claire Dees; Chuck Perou; and Neil Hayes.

Technological Advances

In methods pioneered by Lineberger member Chuck Perou, "the ability to screen a high quantity of genes and gene products in large patient populations have revolutionized human genetics - and the way genetics is used in cancer research," Topal says.

Dramatic improvements in optics, robotics, microcomputing, and the dissemination of the human genome sequence set the stage for advances in modern medicine. "These developments have allowed for the 'profiling' of tumors and normal tissues for differential expression of genes and proteins, as well as for specific mutations and other genetic events," says Hayes.

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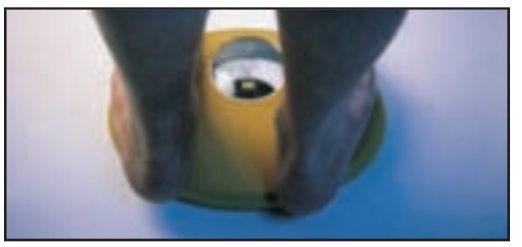
Weight Linked to Cancer Incidence, Survivability

Marilie Gammon, professor of epidemiology and a Lineberger member, has a serious message for people battling their weight: It could be a matter of life and death.

That's because excess weight increases the risk of developing cancers. Estimates from the International Agency on Cancer indicate that approximately 10 to 40 percent of selected cancers can be attributed to excess weight, making obesity one of the most important causes of cancer, after cigarette smoking.

Postmenopausal breast, colon, endometrial and kidney cancers, plus esophageal adeno-carcinoma, are most affected by weight, the research shows.



Breast Cancer & Obesity

The data on the relationship between breast cancer and obesity are particularly clear, Gammon says. "Women who gain about 45 pounds after the age of 18 are twice as likely to develop breast cancer after menopause than those who don't."

Weight gain after age 50 also is linked to about a 70 percent increase in the chance of developing

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Director's Message

Dr. H. Shelton Earp, III

Personalized medicine is a popular topic in the news today. But what does it mean? The vast majority of human DNA is the same in all of us, but the small differences may impact how we respond to certain treatments. As the field of cancer genetics advances and we understand genetic patterns and pathways better, we aim to develop tailored therapy that will give each patient the greatest benefit: what is the best therapy for an individual, who is more likely to have a toxic reaction to a drug, can we combine two therapies in this individual? The pace of discovery is swift.

UNC is one of the leading institutions for these advances and we are recognized nationally for our achievements in this area of research. Two of our faculty, Chuck Perou and Neil Hayes, were recently awarded a prestigious grant from the National Cancer Institute to UNC Lineberger to participate in the Cancer Genome Atlas. The Cancer Genome Atlas is a large-scale collaborative effort to systematically characterize the genomic changes that occur in cancer. We have become national leaders in this type of genome analysis and join the likes of Harvard, MIT, Stanford, and Memorial Sloan-Kettering in this new national discovery network.

The cover story describes several UNC research endeavors related to personalized medicine. Our physicians are enrolling patients onto the **T**rial **A**ssigning **I**ndividua**L**ized **O**ptions for Treatment **R**x (TAILORx) trial for breast cancer. This study will examine whether genes that are frequently associated with risk of recurrence for women with early-stage breast cancer can be used to assign patients to the most appropriate and effective treatment.

In the next issue we will include a second report on personalized medicine highlighting the work of one of our newest recruits, Dr. Howard McLeod, director of the new UNC Institute on Individualized Medicine based in the UNC School of Pharmacy. I am pleased to welcome Howard to UNC and the Lineberger Center. You will hear more about these groundbreaking efforts in the future.

In this issue, you will also read about our Cancer Genetics clinical program, led by Jim Evans, as well as a profile of a family who has used and benefited from this UNC program. The clinical cancer genetics team is an essential part of personalized medicine. Once we are able to know more about our DNA, we need someone to help patients understand what it means to them.

On the national scene, the big news remains the cutback in federal support for the National Institutes of Health (NIH). This represents a major threat to biomedical research in general, and to cancer research here at UNC Lineberger and at cancer centers nationwide. In the late 1990s, the United States ramped up its investment for discovery and novel therapies for cancer, putting our country firmly in the lead. That lead is now being eroded by almost five years of flat and now decreasing funding. In addition to slowing current discovery of new therapies, these cuts make it difficult for young faculty to successfully launch their careers in cancer research.

In my role as President of the Association of American Cancer Institutes, I am working with other cancer research organizations to educate both the administration and Congress on the amazing opportunities, the economic benefit, and the needs of cancer patients that call for reinvigorating our investment in the NIH. So far, our highly competitive Lineberger faculty have been able to sustain our overall research funding. Opportunities lost have been replaced with new grants, such as the Cancer Nanotechnology and Genome Atlas grants, but if we are not able to convince Congress of the wisdom of investing in what has been and should be the world's strongest biomedical research enterprise, we face serious consequences down the road.

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UNC Lineberger is designated a Comprehensive Cancer Center by the National Cancer Institute.

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

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2006 Oncology Excellence Awards

The UNC Lineberger Comprehensive Cancer Center awarded its 2006 Oncology Nursing Excellence Award and Clinical Services Excellence Award to four staff members. The awards are in recognition of the staff's extraordinary hard work, care and dedication that they bring to the center each day.

Nurses Linda Fowler, RN, OCN, and Sharon Cush, RN, OCN, won the Oncology Nursing Excellence Awards, and Susan Whorley and Tonya Thompson won the Clinical Services Excellence Awards.

Fowler has been at UNC since 1987 and is a nurse in the Gynecologic Oncology chemotherapy infusion room. Cush is a nurse clinician who coordinates the UNC Neuro-oncology Brain Tumor Clinic. She has been at UNC for 24 years.

Dr. Richard Goldberg, associate director of clinical research and physician-in-chief of NC Cancer Hospital, said that "both of the individuals chosen for the nursing awards are long-term employees who have distinguished themselves in both patient care and in training and supporting their coworkers."

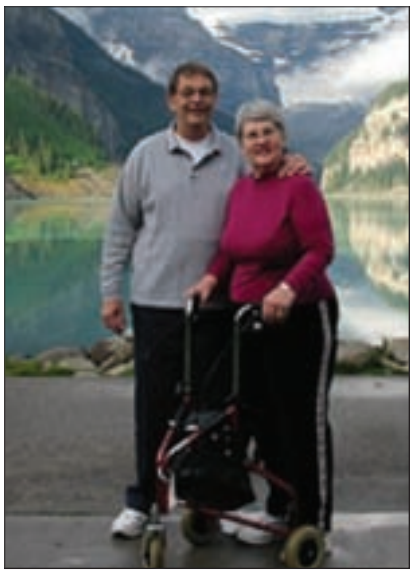
Susie Whorley has been at UNC for 14 years, the last 3 of which she has been a program assistant for the Multidisciplinary Oncology Programs.

Thompson is a social worker for the in-patient hematology/oncology services.

Front row (left to right): Dr. Richard Goldberg, Tonya Thompson, Linda Fowler, Sharon Cush and Susie Whorley. Back row: Bobbi Marks, Dr. Shelley Earp, director, UNC Lineberger, and Dr. Matt Ewend, leader, Neuro-Oncology Program.

Bobbi Marks, administrative director of UNC Health Care Oncology Services, said, "Susie and Tonya are wonderful representatives of the best in caring attitude. To their patients, families and peers they are attentive to the details of the work to be accomplished, displaying a calm, efficient, and caring demeanor even in the face of urgency and anxiety."

The Oncology Nursing Excellence Awards are in their fifth year at UNC. Winners receive a $1,500 stipend along with the award to be used towards professional education activities. The award was named in memory of Charmayne S. Gray, an outstanding oncology nurse practitioner who died in an auto accident in 2002. The Clinical Services Excellence Awards are in their third year.



Ambrose and Alice Dudley of Raleigh, NC on vacation in the Canadian Rockies.

The Loving Caregiver: A Story of Faith & Courage

Ambrose Dudley and his wife, Alice, have been loyal supporters of UNC Lineberger since 1998. Ambrose says it best: "where else would you give your money but to the place that saved your life and made you feel like part of the family?"

Ambrose was diagnosed with Stage 3 multiple myeloma in 1997 and underwent a bone marrow transplant seven months later. It was a success, and he has been in remission for 9 years.

Twenty-six months after Ambrose's diagnosis, Alice was in a traffic accident that left her with a closed-head brain injury and many broken bones. Unconscious for three weeks, she recovered thanks to lots of therapy.

After these two major life-threatening events, they wrote a book sharing their story. Published this fall, *The Loving Caregiver* is a story of faith, courage and brilliant medicine and how two people faced back-to-back crises hand-in-hand.

The Dudleys are sharing the proceeds from the sale of their book with UNC Lineberger. To purchase a copy of their heart-warming story, contact Ambrose directly at adudley002@nc.rr.com.

UNC Women's Basketball Coach Sylvia Hatchell received the 2006 UNC Lineberger Outstanding Service Award. She was cited for her work to raise awareness of gynecologic cancers and for her fundraising, including proceeds from her blueberry patch near Black Mountain, NC. Dr. Shelley Earp, Director, UNC Lineberger Comprehensive Cancer Center, presented the award at the Lineberger Board of Visitors meeting in September.

Blue Cross Blue Shield of NC 2006-07 Leadership Partner for UNC Lineberger

Blue Cross Blue Shield of NC has generously supported UNC Lineberger as a lead sponsor of major special events this year. We are grateful for their partnership and their commitment to cancer care, prevention and research.

In the fall, the Blue Cross and Blue Shield of North Carolina Foundation unveiled its new, interactive Button Chair exhibit, an innovative art display designed to increase awareness of breast cancer, in hopes of saving lives. The purpose of the exhibit is to educate visitors about breast cancer, encourage women to get mammograms and to deliver messages of hope from survivors who have overcome the disease.

The new display is a dynamic, interactive experience highlighted by the glass enclosed Button Chair and four hands-on, educational kiosks. The exhibit's featured elements are video stories of hope, as five North Carolina women (representing Asheville, Durham, Greensboro, Raleigh and Wilson) share their stories of detection, treatment and survival. These uplifting accounts reveal how the disease has touched each woman's life, and the lives of their families. One of the stories is told in the survivor's native Spanish and all information featured on the touch screens is available in both English and Spanish.

The Button Chair was created in 1998 as a tribute to all women-as well as their families, friends and support networks-who have battled breast cancer in North Carolina. Every button represents a unique story of courage and strength, each having belonged to a breast cancer survivor or someone who lost their battle with the disease.

The Button Chair is available for display free of charge to North Carolina schools, businesses, hospitals, community groups and other organizations. It can be reserved online at www.bcbsnc.com/foundation/button_chair.html.

Left to right: Dr. Tom Shea, director, the UNC Bone Marrow Transplant and Hematologic Malignancy programs; transplant coordinator Betty Hinshaw; Senator Marc Basnight; UNC physician's assistant John Strader; and transplant coordinators Debbie Covington, and Sam Sharf, and Barbara Kok, BMT Clinic nurse. Not pictured:Bobbi Marks, administrative director, UNC Oncology Services.

Outer Banks Marathon and Bone Marrow Drive A Huge Success

Ten members of the UNC Bone Marrow Transplant and Hematologic Malignancy programs traveled to the inaugural Outer Banks Marathon on November 10-12 to hold a Bone Marrow Donor Drive for the National Marrow Donor Program (NMDP). With funding from UNC Hospitals and the support of the race organizers and residents of the Outer Banks, the Drive was held in the Dare County Convention Center which also served as race headquarters.

The Drive and the marathon were both huge successes with enrollment of 226 new donors and nearly 4000 participating runners.

UNC has been invited back next year and program members look forward to continuing to work with groups such as this to continually expand the donor pool in the NMDP so that all prospective patients who need a donor can find one.

Tickled Pink in Triplicate!

Dr. Paola Gehrig, Associate Professor of Obstetrics and Gynecology, Tickled Pink co-chairs Margie Haber and Missy Julian-Fox, and Dr. Carolyn Sartor, Professor, Co-Chair of the UNC Breast Center, and newly appointed Chair of Radiation Oncology.

Tickled Pink 2006 was a series of three totally pink events to benefit women's cancers. This past October, women of all ages attended two fun and funky, all pink luncheons, which were held for the third consecutive year at Squid's Restaurant in Chapel Hill and for the second year at Galloway Ridge in Fearrington. Everything in sight was pink, from the creative decorations, right down to the dressing on the salads.

A third event, "Tickled Pink at Twilight," was introduced at Top of The Hill Restaurant in downtown Chapel Hill. This totally pink co-ed event complete with feather boas and pink drinks was a fun way to bring men and women of all ages out to support research for women's cancers.

Tickled Pink 2006 raised $63,000 and had over 530 people in attendance. The total money raised for women's cancers at UNC Lineberger since Tickled Pink's creative beginning three years ago is $161,000.

Our thanks go out to all of our sponsors, our wonderful committee members, Squid's/Chapel Hill Restaurant Group, Top of The Hill and Galloway Ridge in Fearrington.

Profile

Even as a child, John Boggess wanted to teach. "So I'm living the dream," says the associate professor of obstetrics and gynecology. But his secret passion is movie production and special effects.

"If I weren't doing this, I'd make movies with George Lucas," he quips. "I'd be knocking his door down. 'You wouldn't have to pay me.'" He creates digital special effects on his home computer, just in case Lucas is hiring.

Boggess is one of those lucky people for whom vocation and avocation meet. By practicing leading-edge medicine, he teaches others and uses video production techniques to spread his educational reach. And the Newport Beach, Calif., native gets to work with one super high-tech toy that would make even the creator of *Star Wars* green with envy: the da Vinci Surgical System, a robotic "surgical assistant" manufactured by Intuitive Surgical.

Leading-Edge Technology

Purchased in February 2005 to support the Urology Oncology program, the da Vinci System gives surgeons better dexterity and allows more control than open surgery. It also allows high-resolution 3-D visuals that improve precision and reduce trauma to surrounding tissue. And it's all done through quarter- to half-inch incisions.

Impressed, Boggess wanted to explore its use in gynecologic oncology. "There was no description of how to do that," he recalls. "So we started blazing a new trail. We were the first people to document robotic procedures for cervical and uterine cancer." (UNC Hospitals purchased a newer version of the robot, the only one of its kind in the state, for the Women's Hospital in July 2006.)

While the technology is exciting, the real value of robotics is improved patient outcomes. "Robotics improves quality of life," he notes. "Using the robot, there's much less blood loss and patients get faster recovery times. Most of our patients having any type of hysterectomy (radical for cervical cancer, endometrial staging, large fibroids or simple hysterectomy) go home in less than 24 hours with no IV pain meds. This compares to 3-4 days for open procedures. As importantly, we have never transfused a patient for a robotic hystectomy and have done now over 130 of them. The average recovery is only 1-2 weeks to feel 90 percent normal compared with 8-12 weeks with open surgery. We are doing a better cancer operation and this translates into better survival."

Dr. John Boggess

Big Ideas

Boggess came to UNC after completing his residency at the University of Washington in 1994. "One of my interests is in developing new ideas," he says. He was attracted by the opportunity to do fellowship training in less-invasive surgical techniques, like laparoscopy. "The program at UNC suited me."

Three years later, he joined the faculty and started the minimally invasive surgery program. "It's a privilege to be exposed to robotics at the right time and be able to run with it," he says.

"I'm very proud of our hospital staff and leadership, particularly the nurses and the OR techs," he continues. "I'm involved with people who are overwhelmingly talented; it's humbling to work with them. Everyone took to this with a lot of enthusiasm, so we've had more success. What we've done in a year and half has blown me away. We really followed through on this mission and it has paid off for our patients."

John's wife, Dr. Kim Boggess, is an associate professor of maternal- fetal medicine, and they live in Chapel Hill with their two children, Emma, age 8, and Mason, age 9.

Briefs

Drug Combination Slows Treatment-Resistant Bone Marrow Cancer

Combining a newly formulated drug with a proven standard treatment slows the progression of multiple myeloma, an advanced cancer of the bone marrow cells, according to a clinical trial led by Robert Orlowski, Lenvel Lee Rothrock associate professor in the division of hematology/oncology at the School of Medicine, and Lineberger member. Orlowski reported his findings at the annual meeting of the American Society of Hematology in December 2006.

The phase III trial included 646 patients with relapsed or refractory multiple myeloma, a condition in which cancerous cells continue to multiply despite treatment. Patients in the trial were randomly assigned to receive the drug bortezomib (Velcade), standard therapy for relapsed multiple myeloma, or a combination of Velcade and Doxil, a chemotherapy drug (doxorubicin) delivered via liposomes, or microscopic fat bubbles.

An interim analysis revealed that participants receiving the combined treatment had a 9.3-month median time to progression - the time interval between the response to treatment and the time the disease starts to show evidence of growing or recurring. Those on Velcade alone progressed after 6.5 months. The interim analysis also showed an early trend toward increased survival for patients taking the combination treatment.

"It does provide some added hope for patients and their families," Orlowski says.

New Lung Tumor Subtypes Identified in DNA Profiling Study

A new study led by researchers at UNC Lineberger identified three subtypes of non-small-cell lung cancer tumors. The discovery may provide valuable clinical information about patient survival in early- or late-stage disease, how likely the cancer is to spread and whether the tumor will prove resistant to chemotherapy.

"We are frequently surprised with the range of responses that our patients' non-small-cell carcinomas have. Some are very responsive to treatment, some metastasize early, and we have no way of sorting this out up front," explains study lead author David Neil Hayes, assistant professor of medicine in the division of hematology/oncology in UNC's School of Medicine and a Lineberger member. The study results were published in the November issue of the *Journal of Clinical Oncology*.

Hayes and his colleagues used a relatively new technology, DNA microarray analysis, which allows researchers to identify a tumor's genetic pattern. "We see evidence that these genetic patterns are associated with significant differences in tumor behavior, which could not be anticipated by any conventional testing method," he says.

The tumor subtypes, named bronchioid, squamoid and magnoid, according to their genetic pattern, also correlated with clinically relevant events, such as stage-specific survival and metastatic pattern. "If we can pigeonhole these tumors right from the start, then we can become much more rational in our decision making for treatment and our ability to tell patients what to anticipate in terms of their risk, likelihood of recurrence and response to therapy," Hayes says. "That's the goal."

Tumor Suppressor Gene is Key to Celluar Aging

A gene that suppresses tumor cell growth also plays a key role in aging, according to Norman Sharpless, assistant professor of medicine and genetics at the UNC School of Medicine and a UNC Lineberger member. Researchers from the UNC-Chapel Hill, University of Michigan and Harvard University found increasing concentration, or expression, of the gene p16INK4a in older pancreatic islet cells and brain and blood stem cells. An author or co-author on all three studies, Sharpless' results were published in the September 2006 issue of *Nature*.

The findings indicate that disparate cell types share a common aging mechanism and suggest that aging-related diseases such as diabetes result from a failure of cell growth. "The studies indicate that certain stem cells lose their ability to divide and replace themselves with age as the expression of p16INK4a increases," Sharpless says. "This suggests that if we could attenuate p16INK4a expression in some way in humans, it could lead to enhanced islet re-growth in adults and a possible new treatment for diabetes."

Leslie H. Lang contributed to this section.

Fast Break Event Doubles Support for Cancer Research

Roy Williams' 2nd Annual *Fast Break Against Cancer* was held on the floor of the Dean E. Smith Center on Friday, October 13th. There were 400 people in attendance at this year's lively event, which raised over $200,000 for cancer research - doubling the goal of $100,000! This seated breakfast benefited UNC Lineberger Comprehensive Cancer Center and the American Cancer Society.

This year's event was a "who's who" of Carolina basketball. Coach Williams and his entire coaching staff, former Coaches Dean Smith and Bill Guthridge were in attendance, as were many former players including several from the 1957 National Championship team. Guest speaker and former Tar Heel player Michael Norwood, shared his family's personal experience with cancer at the event (see side story).

Coach Williams and "Voice of the Tar Heels" Woody Durham closed the event with a very spirited auction. By far, the hottest item was the chance to sit on the bench with Coach Williams and the team during a non-conference game - truly a once in a lifetime experience! Coach also personally donated two items autographed by former Tar Heel great Michael Jordan and Coach Williams.

Special thanks to presenting sponsor, PPD and our other lead sponsors: Atlantic Corporation, Blue Cross Blue Shield of North Carolina, Curtis Media Group, GlaxoSmithKline and Long Beverage, Inc.

Next year's Fast Break Against Cancer is scheduled for Friday, October 12. Mark your calendars now!

Coach Roy Williams and Emcee Woody Durham help John Morgan, a cancer survivor from Hillsborough, NC, celebrate his 13th birthday while all 400 attendees sang "Happy Birthday"!

Remembering Nell

The guest speaker at this year's *Fast Break Against Cancer* event was former Tar Heel basketball player Michael Norwood. Michael shared his family's personal experience with cancer and the importance of ongoing support for cancer research. Michael and Caroline Norwood's young daughter Nell was diagnosed with rhabdomyosarcoma when she was 2 ½.

Nell endured 14 months of treatment, spending long hours, days and sometimes weeks in the hospital. To keep Nell busy, her parents would bring crafts to the hospital for Nell to work on to pass the time. Stringing beads became a wonderful way for Nell to interact with family and friends while she was in the hospital-and a wonderful way to help Nell continue working on her shapes and colors.

In the summer of 2002, Michael and Caroline Norwood were told Nell would not survive her illness. She had lost her sight to the disease and her illness was advancing rapidly. Nell was taken home to be with her family and friends. Her family hosted a small jewelry making party for Nell after she returned home from the hospital. As it turned out, the jewelry party was the last day Nell was full of zest, and she passed away less than a week later.

Shortly after Nell's death, a friend of the Norwoods from church asked if she and other church members could make beaded jewelry to sell at a church festival. The Norwoods agreed to the idea. "Nell's jewelry" can now be found in stores and at events in the eastern part of the state. The money raised has exceeded $10,000 and is used to help other families in need. Caroline Norwood continues to make "Nell's jewelry" and can be reached at cpnorwood@suddenlink.net.

Weight

continued from page 1

postmenopausal breast cancer. "Thus, as a breast cancer risk reduction strategy, it is never too late to watch your weight," she adds.

Decreased Survivability

A recent study, led by former UNC School of Public Health graduate student Page Abrahamson, found that excess abdominal fat can affect breast cancer survival by tracking 1,254 women ages 20 to 54 who were diagnosed with invasive breast cancer between 1990 and 1992. Those with waist-to-hip ratios higher than 0.80, an indicator of larger concentrations of abdominal fat, were 52 percent more likely to die of breast cancer in the next nine years.

The research also noted that obesity (a body mass index of 30 or higher) adversely affects survival rates for breast cancer patients. Study participants with BMIs over 30 were 48 percent more likely to die during the nine-year study period than women of ideal weight. Even more startling: Women enrolled in the study who were both overweight (a BMI greater than 25) and had waist-to-hip ratios over 0.80 increased their risk of dying from breast cancer by 92 percent.

Professor of Epidemiology Marilie Gammon

"We don't know whether weight loss can really reduce your risk of developing breast cancer," Gammon admits. "However, weight maintenance - in other words, avoidance of weight gain - will help women to avoid the increased risk in developing breast cancer, or the increased risk of dying once diagnosed, that has been associated with adult weight gain."

Charles and MeMe Briley graciously hosted a Lineberger event at The Cypress of Charlotte last December. Dr. Shelley Earp spoke to a group of about 60 people on the increasing personalization of cancer care. The Brileys (left) and Dr. Earp (right) are pictured here with Alice Lineberger Harney, member of the UNC Lineberger Board of Visitors.

Running the Numbers

Looking for more data besides what your scale tells you? Ask your doctor or check out these online resources:

A waist-to-hip ratio calculator is available at www.healthcalculators.org/calculators/waist_hip.asp

The Centers for Disease Control and Prevention offers a body mass index calculator for adults and children at www.cdc.gov/nccdphp/dnpa/bmi/index.htm

what do *you think?*

We want to know your thoughts about cancer*Lines*.

Do you find this newsletter useful? Whether you're a new or longtime reader, please share your opinions by completing the brief online survey by March 9, 2007 at http://unclineberger.org/lcccnewsletter

Genetics Helps Doctors, Patients Understand Susceptibility

Technological advances that help scientists understand the genetics of cancer have made it possible for physicians to better predict patients' susceptibility.

It's been recognized for 2,000 years that we've been missing a significant component of medicine," says Jim Evans, director of Clinical Cancer Genetics and The Bryson Program in Human Genetics at UNC, and a Lineberger member. "It's only recently that we've begun to acquire the tools to figure out why if you have two people who smoked for 20 years, one gets lung cancer and another doesn't. We are finally accruing the tools to begin to solve that equation."

Cancer Genetics Program members study a family tree, one of the tools they use to assess the risk of developing cancer. Pictured (left to right): Lisa Susswein; Dr. Jim Evans, program director; and Cecile Skrzynia.

Right now, most doctors don't treat people, they treat diseases, Evans says. "We give the same medicine and doses to everyone and hope it works well ….and doesn't cause adverse affects." Knowing who has genetic predispositions for developing cancer allows physicians to offer patients better options and treatments. "We're starting to guide our choice and dosing of drugs by one's genetic constitution," he continues. "The impact of that could be profound."

Genetic Testing

Genetic testing is a catch-all phrase for tests that directly or indirectly uncover a patient's particular and unique genetic status. Sequencing DNA is the most common genetic test. Sequencing allows researchers to determine the exact order of the base pairs in a segment of DNA for comparison with others. This helps identify anomalies or mutations that could lead to higher susceptibility.

"It's startlingly simple at its most basic," Evans says. "DNA is a digital code - and that's not a metaphor. Our ability to analyze that code and do so cheaply has given us an emerging ability to get prodigious amounts of data on lots of individuals in lots of health states and correlate that information."

Breast Cancer

The most common genetic tests currently are for breast cancer. Two of the genes that are associated with familial breast and ovarian cancers, BRCA1 and BRCA2 can be analyzed with DNA sequencing. UNC's High-Risk Breast Cancer Clinic offers this kind of testing to about 650 patients a year. Lineberger funds have been used to offer tests to patients who cannot afford to pay.

"Genetic testing for cancer predisposition is not something offered to all patients at this point," explains certified genetic counselor Lisa Susswein. "But all individuals can have their personal and family history assessed by a genetic counselor to see if testing is indicated."

If a mutation is found, doctors and the patients can take preventative action. Susswein explains: "A woman who is diagnosed with breast cancer might be a candidate for lumpectomy (breast conserving therapy). However, if she is found to carry a gene mutation that puts her at greatly increased risk for another cancer, she has the opportunity to choose bilateral mastectomy instead. Women who have not had cancer also have the choice to have preventive mastectomies. Furthermore, all women with a BRCA mutation are advised to have their ovaries removed since ovarian cancer is difficult to detect."

Other Cancers

There are several other genes associated with cancers in other organs. "Colon cancer, for example, can be due to alterations or mutations in so-called mismatch repair genes," explains assistant professor Cecile Skrzynia, who also is a certified genetic counselor. "Testing is available for families that show familial clustering of colon cancer and specific other cancers such as endometrial and gastric."

Other genes associated with more rare cancers, such as thyroid or renal cancers can also be tested. "Our team consults with any person concerned about cancer in their family," she continues. "Frequently we can be reassuring as to the possibility of an inherited pre-disposition to developing cancer. In many other cases we are able to pinpoint the exact change in the gene of interest and provide valuable information for the family and the treating physicians."

The breadth of genetic counseling services available at UNC is rare, Evans says. "We are one of the few centers that provides integrated care," he says. "We have medical geneticists, a team of counselors and an integrated lab to evaluate patients from the get-go. We can decide on whether to test, do the test and help navigate insurance. From the basic science to the clinic, UNC is at the forefront."

Should You Consider Genetic Testing?

The likelihood that breast cancer is associated with BRCA1 or BRCA2 is highest in families with a history of:

Breast cancer under age 50
Multiple cases of breast cancer
Ovarian cancer
Male breast cancer
Ashkenazi Jewish heritage

If you meet any of these criteria, you should consider working with a genetic counselor to determine whether genetic testing is right for you. For more information, contact the Genetics Clinic at 919-843-8724.

The Gene Girls

Carlyle, Rivka and Courtney From

For Rivka From and her daughters Carlye and Courtney, genetic testing at UNC provided them with "an opportunity to live an amazing life," Rivka says.

A Raleigh-based life coach, From was diagnosed with an aggressive form of breast cancer in 2004. Because her mother had died of ovarian cancer, doctors recommended a test for the BRCA mutation before beginning treatment.

"If I tested negative, the treatment would be chemo or radiation," Rivka recalls. "If it came back positive, they suggested a mastectomy. When the test came back positive, I had a bilateral mastectomy and oophorectomy. Cleaned me right out."

But the result did more than impact her treatment. "It was a no-brainer for my daughters," she says. "We had to get them tested." Both have the mutation.

"Screening for the BRCA mutation was, in my mind, mandatory for me," says Courtney, who also lives in Raleigh. "I want to know what is going on with my body to be able to take careful preventative actions. My mother and grandmothers did not have the opportunity for testing and all developed cancer - fortunately Mom is alive and thriving today but I was never blessed with the opportunity to meet my grandmothers as they passed in their 40s."

For Carlye, a student at Meredith College, the results helped her take action that will help improve her overall health - and lower her cancer risk. In addition to regular screening and exams with her doctor, Carlye made some lifestyle changes.

"I eat organic foods at home and choose healthier options when I'm at school," she says. "I have changed my 'college lifestyle' of socially drinking every weekend to an occasional drink once a month. I have started exercising regularly with a friend and using the workout facilities on campus. I started a low dose birth control because it reduces my risk of developing ovarian cancer. Since the test I have also been focused on minimizing the amount of stress in my life. I use this test as a wake-up call to make overall healthy choices for myself."

The Froms have become activists for genetic cancer screening, calling themselves The Gene Girls. They speak at events and find any opportunity to spread the word.

"To live with the not-knowing for us would be far more painful than the actual knowing of it," Rivka says. "Honey, if we're on this earth we've all got something - some genetic mutations. We are blessed to know about this vulnerability. If you know, you can go about taking care of yourself.

"It's not always happy stuff that you hear," Rivka notes, "but it really matters if you want to live. And bottom line honey, I want to live."

Personalized Medicine

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DNA microarray analysis is one of the most powerful tools scientists use to learn more about cancer genes.

"Knowledge of how a patient's many genes, or genome, respond to disease and therapy provides a profile or fingerprint for correlation with clinical outcomes," Topal explains. "This knowledge also provides us with information about which genetic pathways are turned on or off in response to stimulus such as disease or treatment. That, in turn, enables comparisons between different patients and how they respond to therapeutic regimens both clinically and genomically."

Thanks to these technological breakthroughs, more effective diagnostics, preventives and therapies for cancer are possible as researchers learn not only how cancer works, but how it differs among patients.

Hayes and Topal are co-principal investigators with principal investigator Chuck Perou of a newly funded genome characterization center, one of seven grants awarded by the National Cancer Institute and the National Human Genome Research Institute. Perou is associate professor of genetics and pathology, and a Lineberger member.

The UNC team is part of the Cancer Genome Atlas project, a national effort to characterize and chart the molecular changes in specific types of cancer. The Cancer Genome Atlas is a collaborative three-year, $100 million pilot project to test using large-scale genome analysis technologies to identify important genetic changes involved in cancer. Launched in December 2005, the cancer atlas will map the genomic changes associated with lung, brain and ovarian cancers. The seven genome characterization centers will operate as a network, with each center using advanced genome analysis technologies to identify major changes in the genomes of these cancers. Read more about this at http://www.unc.edu/news/archives/oct06/genome101606.htm.

Lung Cancer Genetics

The ability to look into the genetic make-up of cancer cells is changing the treatments given to patients with certain types of lung cancer.

Currently, lung cancer treatment is based mostly on the size and location of the tumor, and whether it has metastasized. Almost 80 percent are identified as non-small-cell carcinoma (NSCLC), a catch-all diagnosis. Some patients respond well to treatment, while others metastasize early. No existing technology gives any meaningful insight into why patients have such different outcomes.

But DNA microarray analysis enabled Hayes and the research team to look at the genetic pattern of specific tumors. The result: The scientists discovered three subtypes of adenocarcinoma, where only one type was observed before. Their findings were published in the 11/01/06 *Journal of Clinical Oncology* (see *Briefs* page 4).

"In patients who have tumors that look similar under a microscope, there are dramatically different gene expression patterns," Hayes says. "There is evidence that these patterns are associated with significant differences in tumor behavior that couldn't be anticipated by any conventional testing method."

Categorizing the tumors early enables doctors to more accurately target treatments, improving patient outcomes.

Breast Cancer Genetics

The development of new biomarkers, and genomic analyses using gene expression, genetic variation single nucleotide polymorphisms, help Lineberger researchers understand breast cancer better.

"We know that breast cancer isn't one disease, but several," explains Perou. "We hope this will enable us to give patients more specific therapies that are targeted to their tumor biology. This will increase efficacy."

It also decreases toxicity. "We tend to over-prescribe to be safe," he says. "But we're learning to be more precise in what we give. Knowing which drugs they need and which they don't, toxicity will go down and their survival will go up."

For example, breast cancer patients who over-express the HER2 protein represent 20 to 25 percent of all breast cancer patients. They respond particularly well to Herceptin®, a drug that inhibits the activity of the HER2 protein, while those with other tumor types do not respond.

"If you give Herceptin® to everyone, it 'fails'," he says. "But if you give it just to those who have the target, it adds a survival benefit. We are developing more diagnostics that will help identify these patients so they will get this particular treatment."

Looking Ahead

While more personalized therapies mean better patient outcomes, Perou is cautiously optimistic.

"It's a double-edged sword," he admits. "New diagnostics and drugs are quite promising, but we still need to be patient and to properly evaluate them. That just takes time and patient participation in clinical trials. That's the most critical thing patients can to do help advance treatment. Without clinical trials and money, none of these things will get implemented."

The effort is worth it. "Personalized diagnostics and therapies offer the promise of earlier detection of cancers because of greater knowledge of the risk factors for that patient," Topal says. "Earlier detection offers treatment at a time when the cancer is more susceptible to therapy. In addition, knowledge of the genomic background of the patient and the cancer will mean greater ability to design the most effective therapy against the particular cancer in that patient. This will mean more effective screening, more effective therapy, and at a lower cost for society."

Personalized Medicine Today

UNC Lineberger clinical researchers are participating in a new treatment trial investigating individualized therapy and designed for women with node-negative estrogen-receptor positive, HER 2 negative breast cancers. In this study, patients are randomized to receive chemotherapy or not based on a recurrence score calculated from the expression of genes in their particular tumor.

Called TAILORx (**T**rial **A**ssigning **I**ndividua**L**ized **O**ptions for Treatment **R**x), the study is part of the NCI-sponsored Program for the Assessment of Clinical Cancer Tests (PACCT) and is designed to determine whether adjuvant hormonal therapy with chemotherapy is better than adjuvant hormonal therapy alone in a particular group of patients who have intermediate risk of recurrence. Over 4,000 patients will be randomized in this study at cancer centers all over North America.

"Oncotype DX™ is a new assay which looks at the expression of 21 genes in a person's tumor and from that expression pattern calculates a risk score," explains Claire Dees, MD, assistant professor of medicine in the Division of Hematology and Oncology, and leader of the Developmental Therapeutics Working Group at UNC Lineberger. "This study will investigate whether adding chemotherapy helps people whose recurrence risk scores are in a middle range. Patients whose tumors have a score between 11 and 25 are randomized to be treated with either endocrine therapy only or with endocrine therapy plus the adjuvant chemotherapy that they and their oncologist have planned." About 44 percent of node-negative ER positive breast cancer patients have a recurrence score in this range.

The findings will help personalize breast cancer treatment further by giving doctors patient-specific information that will help them optimize care plans for each patient.

"Current guidelines and practice patterns include use of chemotherapy in great numbers of node negative patients, many of whom may not benefit from it," Dees explains. "This is a way to try to make better individualized judgments about which patients in this group will benefit from chemotherapy in addition to endocrine therapy."

Patients who think they might be eligible and are interested in knowing more should call the Clinical Protocol Office at 919-966-4432 or visit http://unclineberger.org/ct/ or http://www.cancer.gov.

Photo of UNC Cancer Patient Wins Top Award and Prize

This photograph taken by Morganton, NC, resident Anne Wilson, the mother of UNC cancer patient Katherine Wilson, won a national award and a monetary prize of $10,000 for cancer research at the UNC Lineberger Comprehensive Cancer Center. The prize was presented by Eli Lilly and Company in partnership with the National Coalition for Cancer Survivorship (NCCS) at an awards finale in New York City in December 2006. Anne and John Wilson and thoracic oncology program nurse coordinator Ann Steagall attended the event hosted by Regis and Joy Philbin.

Anne Wilson took the award-winning picture of Katherine and her father, John, and titled it "This Is Not A Dress Rehearsal."

Judges for the contest, called Lilly Oncology on Canvas: Expressions of a Cancer Journey International Art Competition, selected Wilson's photo as Best of the United States 2006 from over 490 entries. The picture shows Katherine and her father, John, standing side by side, hats in hands and both sporting bald heads, Katherine's due to cancer therapy, and her father's due to his head shave in support of her. Katherine died in 2005 of small cell lung cancer.

Said Wilson, "One of Katherine's greatest concerns was the tremendous need for more cancer research, especially lung cancer research. This wonderful gift from Lilly to the UNC Lineberger Comprehensive Cancer Center can make a difference in this much needed research."

Shown left to right: Dr. John C. Lechleiter, president and COO of Eli Lilly and Company, Regis and Joy Philbin, Anne Wilson, and Michael Bergin, COO of the National Coalition for Cancer Survivorship.

calendar of events

April 2007

14th Fourth Annual Beach Ball, University Mall, Chapel Hill, NC

20th UNC Lineberger Board of Visitors Meeting, Chapel Hill, NC

24 - 25th 31st Annual Scientific Symposium. Chapel Hill, NC

June 2007

9th Komen Race for the Cure NC Triangle Affiliate, Raleigh, NC

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