

University Cancer Research Fund

Annual Report

2011–2012

Dear Members of the General Assembly,

One in three.

That's how many North Carolinians will be affected by cancer at some point in their lives. Survival rates for cancer are improving, but they still vary greatly by cancer type and stage at diagnosis. In North Carolina, almost 17,500 lives will be claimed by cancer this year.

Four to one.

That's the return on investment we are seeing from the state's landmark investment in cancer research. Our \$50 million annual appropriation from the state is helping us recruit and retain the best faculty and research leaders in cancer, create new jobs and companies, and leverage record amounts of research funding from outside North Carolina. In the four years since the University Cancer Research Fund was created, it has generated an economic impact of \$674 million — \$270 million this year alone — and created more than 5,000 new jobs for our state. Highlights include:

- The hiring and retention of 120 outstanding cancer research faculty;
- Continued increases in extramural funding directly attributable to UCRF investment: This year alone, UNC received \$69.2 million in new research funding from outside North Carolina directly attributable to UCRF;
- The launching of more than 10 new spinoff companies with private-sector jobs, adding innovation to the third-largest cluster of life science industries in the nation.

But cancer is about more than just numbers; it's about human lives. And as Chairman of the Cancer Research Fund Committee, I am pleased to share our annual report with you to highlight how North Carolina's investment in the UCRF is paying off — not just economically, but also in

terms of the tremendous research progress we are making in hopes of fighting this disease and saving lives.

As Dr. Ian Davis, one of our outstanding pediatric cancer researchers, says, UCRF "is fueling research that I believe will impact some of our youngest cancer patients, who deserve to have a shot at reaching their full potential in life."

UCRF funds are being used to develop large-scale projects to better understand North Carolina's cancer problems from the genetic to the community level. It's also supporting new innovations in cancer therapy, drug delivery, and cancer outcomes research that will help pave the way for better cancer care.

After UCRF was created in 2007, we developed a strategic plan to guide our priorities and maximize the benefits of this landmark investment. In this report you will find stories of compelling research, being done by Dr. Davis and others, that fall under the key elements of our strategic plan. You'll find more details on the economic value the UCRF has brought to our state. And hopefully, you will find — as I have — hope on the horizon for the families who have been and will be touched by this disease, in North Carolina and beyond.

Sincerely,



Holden Thorp, PhD
Chancellor, UNC-Chapel Hill
Chair, Cancer Research Fund Committee

Cancer is the leading cause of death in North Carolina.

- The N.C. Central Cancer Registry Estimates that 55,444 North Carolina citizens will be diagnosed with cancer this year — more than 150 each day.
- 20,000 North Carolinians will lose their lives to cancer this year — more than 50 each day.
- More than 40 percent of North Carolinians will be diagnosed with cancer during their lifetime.
- Lung cancer accounts for almost one-third of cancer deaths in North Carolina. Prostate cancer for men and breast cancer for women are also major causes of death, along with colorectal cancer for both genders.
- North Carolina's age-adjusted death rate for cancer is higher than the U.S. average.
- On average, each North Carolinian who dies of cancer will lose more than 10 years of his or her expected lifespan.
- In addition to costing lives, the annual economic cost of cancer to North Carolina is estimated to be about \$6.1 billion, including almost \$4 billion for lost productivity due to illness and premature death.

The University Cancer Research Fund (UCRF) is a nation-leading investment to promote innovation in cancer research, improve cancer diagnosis and treatment, and reduce the incidence of North Carolina's deadliest disease.

In 2007, the year cancer became the leading cause of death in North Carolina, the General Assembly created the UCRF to provide ongoing state support for cancer research. The UCRF will receive \$50 million annually, and complements two major state investments in cancer facilities — the NC Cancer Hospital and the Biomedical Research Imaging Center, a research facility that will open in 2013. Together, these investments make a synergistic approach to fighting this disease.

Goal

To create a nation-leading cancer research effort and to reduce North Carolina's cancer burden. UCRF is achieving these goals through:

- **Discovery** to better understand the causes and course of cancer;
- **Innovation** to create new and better ways to prevent, diagnose and treat cancer; and by stimulating
- **Delivery** of improved cancer care, screening and prevention across the state.

Strategic Plan

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

- **Understanding the Role of Genetics in Cancer Causation and Treatment** — to discover the genes that predispose families to cancer and that predispose cancer patients to poor treatment outcomes — particularly by looking for the mutant genes in specific cancer subtypes that lead to cancer therapy failure.
- **Developing Novel Therapeutics** — to devise new therapies targeted to the specific vulnerabilities of treatment-resistant cancers, and to develop new ways of delivering drugs and therapies to reduce toxic side effects for patients.
- **Optimizing NC Cancer Outcomes** — to build population-based data to track the occurrence and treatment of cancer across North Carolina in order to initiate research aimed at improving community prevention and early detection of cancer, and to enhance the quality of oncology and survivor care across the state.

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

Cancer Genetics

Cancer genetics — the study of the genetic changes that determine how and why cancer develops — plays a role in early detection, treatment, prevention and prognosis. The field is helping doctors identify which treatments work best for each patient, avoiding ineffective treatments and adverse side effects. UNC has emerged as a national leader in this fast-growing area of research.

Whole genetic sequencing targets unknown cancer risks

Imagine knowing that you are going to get cancer, even though you don't display any outward predispositions or symptoms. What, if anything, would you do differently in your life? Groundbreaking genomics research at UNC has led to a high-technology examination of the genetic detail that can help assess an individual's risk of getting cancer, as well as how doctors can use that information responsibly when communicating with their patients.

James Evans, MD, PhD, and Jonathan Berg, MD, PhD, recently received a \$6.4 million grant that makes UNC one of only five U.S. centers for cancer genetics analysis designated by the National Institutes of Health. Their research, called whole exome testing, allows scientists to look at a patient's entire exome (22,000 genes in that patient) instead of just the genetic markers that are known to be associated with disease.

Drs. Berg and Evans are using next-generation sequencing to sequence all the genes of these family members, and are evaluating other patients suspected to have genetic errors at the root of their disease. Their goal is to find new genes that can determine which people are predisposed to cancer. The grant also funds a team investigating patient, family, doctor and societal response to the information gathered.



James Evans, MD, PhD, and Jonathan Berg, MD, PhD, lead one of only five centers for cancer genetics analysis designated by the NIH.

Discoveries like this will have worldwide significance, opening the door for allowing a person's full gene profile to serve as a diagnostic tool to forecast their disease risk. This type of testing could be helpful for disease prevention, but also could have unintended consequences for a patient who previously had no idea he or she is likely to become ill.

"We can anticipate that whole exome sequencing will discover things about a person that they might not have wanted to know, such as being at high risk of an untreatable disease like dementia," Evans says. "Whole exome sequencing is a technology with the power to help, hurt, and confuse. We need to develop best practices for handling it in the most beneficial way for patients and society."

Drs. Berg and Evans recently co-authored an editorial in the Journal of the American Medical Association calling for responsible regulation of whole exome tests that might be offered directly to consumers.

UCRF funds were used to recruit Dr. Berg in 2009, effectively doubling UNC's capacity to deliver cancer genetics consultation for families with multiple cancer cases. UCRF also helped retain Dr. Evans, who had been offered the position of Deputy Director of the National Human Genome Research Institute at NIH, but stayed at UNC due in part to UCRF's support for his forward-looking program. UCRF leveraged the \$6.4 million NIH grant and the center designation.

Teamwork tackles pediatric cancer genetic discoveries

To help solve complex health problems, UNC works to bring doctors together in collaborative efforts that span various research disciplines. One successful team approach has led to recent discoveries that have promise for stopping Ewing's sarcoma.



Ian Davis, MD, PhD is working on treatment targets for Ewing's Sarcoma

This disease strikes children, adolescents and young adults with tumors that grow in bones or soft tissues. "Unfortunately, all too often we lose these patients, a tragedy for them, their families, and society as we lose their potential," said Ian Davis, MD, PhD, a pediatric oncologist and researcher.

Ewing's sarcoma is caused by changes in the tumor's DNA structure, which allows bone and soft tissue cells to grow uncontrollably and metastasize to distant sites in the body. Last year, Davis's lab made an important breakthrough: specific proteins made of pieces of different genes fused together to set off a chain reaction of uncontrolled cell growth. Dr. Davis' group showed that these "hybrid" proteins bind

to unexpected sites on the genome of cancer cells, beginning the genetic pathway to this devastating childhood cancer.

Thanks to UCRF-funded laboratory equipment, Davis and his colleagues developed a new way to analyze marks left by these "fusion proteins". This provided the ability to rapidly evaluate large numbers of potential chemicals that could become drugs to treat this disease.

Additionally, UCRF has been responsible for recruiting and retaining key members of the interdisciplinary research team: Steven Frye, PhD, and Bill Janzen at UNC's Center for Integrative Chemical Biology and Drug Development, and Jason Lieb, PhD, in the Department of Biology. Their preliminary results have convinced several private foundations and the NIH to invest through grants totaling more than \$1.6 million, including a \$130,000 grant from the V Foundation for Cancer Research in honor of ESPN broadcaster and UNC alumnus Stuart Scott and \$100,000 from Hyundai Hope on Wheels.

Says Davis: "UCRF is fueling research that I believe will impact some of our youngest cancer patients, who deserve to have a shot at reaching their full potential in life."

UNC houses resource for worldwide genetic research

Sixteen thousand cages of genetically manipulated mice may sound like the backdrop for a sci-fi thriller, but the real thrill of the Collaborative Cross — the most ambitious mouse genetics program ever devised — is the great potential it holds to fuel scientific discovery worldwide.

The Collaborative Cross, housed at UNC, puts North Carolina at the forefront of genetics research. This "library" of genetic material, including 450 strains of mice and a DNA database, aims to mirror the diversity of human genetics in the laboratory mouse population. About 95 percent of the genetic material in mice is the same as in people, which means test results on mice should be easily translatable to humans, but traditional lab mice have become so inbred that they lack the natural genetic diversity of the human population.

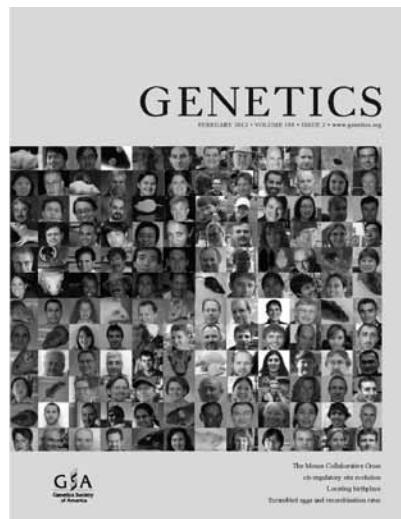
Fernando Pardo-Manuel de Villena, PhD, of the UNC Department of Genetics, is leading this international project with N.C. State geneticist David Threadgill, PhD, and Gary Churchill, PhD, at the Jackson Laboratory.

The Collaborative Cross is enabling systematic genetic mapping and analysis that will allow researchers to better understand human disease, develop new treatments, and move those ideas from the lab to the patient more quickly.

For example, potential medicines may be abandoned because normal laboratory mice have an adverse reaction — but when tested in a large, diverse population, these drugs may actually work for most individuals with a particular disease. The Collaborative Cross allows new, effective drugs to be tested in the lab in a more realistic way and provides the genetic data to make drug reactions completely avoidable.

Dozens of institutions are part of the Collaborative Cross consortium, and UCRF was the major initial funding source. New NIH grants totaling more than \$5.6 million have recently been awarded to UNC as a result of the project.

Ned Sharpless, MD, UNC Lineberger's associate director for translational research, is using the Collaborative Cross on breast cancer studies and says, "The Collaborative Cross provides the best means to understand why certain genes are linked to certain diseases."



The journal cover's photo mosaic reflects the genetic diversity replicated in the Collaborative Cross.

Developing New Cancer Treatments

One-third of the nation's cancer patients will die with advanced disease that eventually becomes resistant to treatment. Scientists are working to spot the unique vulnerabilities in cancer cells and develop new drugs and delivery methods that will kill the tumor while sparing normal tissues. But it takes more than a decade to go from discovery to drug development to total completion of drug testing, and only one in 20 drugs enduring this lengthy process receives FDA approval. Investments from UCRF support UNC's work to find a shorter, more effective path from discovery to market.

Startup earns \$3 million grant to make cancer treatments less toxic

Ned Sharpless, MD, from Greensboro, NC, wears many hats at UNC: scientist, doctor, administrator, teacher. In 2008, he added another: company founder. Dr. Sharpless — UNC Lineberger's associate director for translational research and professor of medicine and genetics — founded G-Zero Therapeutics, a startup company located in the Research Triangle Park, to commercialize technology he developed that protects patients from cellular damage caused by radiation or chemotherapy. Dr. Sharpless now sits on its advisory board.

Radiation and chemotherapy are common cancer treatments, but their side effects can affect quality of life for patients. In research efforts funded partly by UCRF, Sharpless' lab team discovered that certain treatments can cause specific

bone marrow cells to stop dividing temporarily — a phenomenon they called "pharmacological quiescence" or PQ — making them resistant to agents that damage DNA, like radiation and chemotherapy.

G-Zero holds the license to PQ, which has been shown to protect mice from a lethal dose of radiation even up to 20 hours after radiation exposure. In addition to helping cancer patients, PQ could prevent organ damage even after accidental radiation exposure, such as the nuclear reactor failure after the Japan tsunami.

G-Zero's goal is a simple, non-toxic pill. Last fall, the company received a \$3 million Phase II Small Business Innovation Research grant to further its work. The grant is being used to fund four employees and additional contractors to continue development of these drugs on a larger scale. This will allow G-Zero to apply for grants from the Food and Drug Administration and Homeland Security to begin testing on humans — the next step to manufacturing a viable drug that can help cancer patients and others who are exposed to radiation.

The market for drugs like this could be in excess of \$4 billion.

Nanoparticles could boost radiation therapy effectiveness

Research led by UNC Lineberger's Andrew Wang, MD, has shown the potential of nanoparticles as a way to target cancer at the molecular level, making chemoradiotherapy treatment more effective and avoiding damage to normal cells.

Docetaxel is a proven drug for head and neck cancers that often causes adverse side effects. Wang and colleagues developed a biodegradable nanoparticle version of docetaxel that targets the folate receptor, which is overexpressed in some tumors. They found that the folate-targeted docetaxel is more effective than the traditional drug, more effective than a non-targeted nanoparticle version, and has fewer side effects.

Dr. Wang, who was recruited to UNC from Harvard with UCRF support, had similar success developing a nanoparticle therapy for ovarian cancer through collaboration with his UNC colleagues and Duke University. The group used nanoparticles to deliver doses of chemo- and radiotherapy specifically targeting metastasized ovarian cancer cells, eradicating the cancer in mouse models lessening the side effects typically associated with the treatment.

"Our study demonstrates the proof of principle of engineering 'smart' therapeutics that can preferentially deliver chemotherapeutic treatment to cancer," Dr. Wang says. "Such therapeutics were not possible until the development of nanoparticle therapeutic carriers. These tiny devices can be precisely engineered to carry therapeutic cargo and be targeted to cancer cells."

In addition to developing these targeted therapies, Dr. Wang is also engineering nanoparticles that will target and identify multiple disease markers at the same time. This work, funded in part by a \$100,000 grant from the National Academies Keck Futures Initiative, is developing nanoparticles to deliver detailed information that can be used to improve tumor staging and evaluate how well a therapy is working.

Improving pancreatic cancer detection, treatment, prognosis

Pancreatic cancer is one of the most lethal types of cancer. More than 38,000 people in the United States die of this disease each year.



Jen Jen Yeh, MD, is working on better diagnostics for pancreatic cancer.

UNC research teams are working to improve pancreatic cancer outcomes in a variety of ways: a newly discovered molecular "signature" could better inform treatment decisions and improve prognosis. A nanotechnology project pairs imaging and drug delivery to not only detect tumors earlier, but better target treatment. And an isolated protein could become the key to blocking pancreatic cancer growth.

Jen Jen Yeh, MD, Associate Professor of Surgery and Pharmacology, is involved in all three of these efforts. Dr. Yeh has led UNC's initiative to establish state-of-the-art model of in pancreatic cancer, transplanting tumors directly from patients she operates



Norman E. Sharpless, MD, developed the technology behind G-Zero, Inc.

on who have given their consent, into mice designed not to reject human tumors. This innovative technique has the goal of finding new therapeutic targets for cancer treatment.

Pancreatic cancer is often not diagnosed until it is in advanced stages because the most common tumor type rarely causes early noticeable symptoms.

With support from a UCRF innovation award, Yeh and her colleagues have identified a six-gene “signature” associated with the risk of metastatic disease — showing for the first time that molecular differences in pancreatic cancer can be identified at earlier stages, and that these differences can predict future disease behavior. If this finding is verified in clinical studies, it could help patients and doctors make more informed decisions about treatment and spur further research on potential therapeutic targets.

“If we can better stage patients’ disease, we can better determine those who may benefit most from chemotherapy before surgery or from surgery alone,” says Dr. Yeh.

Dr. Yeh is also working with Wenbin Lin, PhD, and Leaf Huang, PhD, as part of the National Cancer Institute’s Cancer Nanotechnology Platform Partnerships. Based on nano-materials developed in Dr. Lin’s lab, the UNC team will design and test nanoscale metal-organic frameworks — a new type of hybrid nano-materials that can carry both imaging and therapeutic technologies, or carry multiple drugs to amplify their effect.

“By developing a more targeted delivery system for imaging, we hope to be able to detect tumors earlier,” Lin says. “And by using the hybrid nano-materials to deliver drugs directly to the tumor, we could lessen side effects for patients.”

UNC received \$2.3 million from the NCI and was one of 11 institutions selected for this partnership.

Dr. Yeh is part of another group of UNC scientists who are taking a closer look at a protein called RGL2. Scientists have known for decades that a gene called KRAS is mutated in almost all pancreatic cancers, making it an important target for researchers looking for a way to stop tumor growth. But KRAS triggers cancer cell growth in many ways and through multiple cell signaling pathways. Scientists have had a hard time determining which pathway would be the most promising to block in designing an effective drug for patient treatment.

Channing Der, PhD, working with Dr. Yeh and Sharon Campbell, PhD, have demonstrated that RGL2 is overexpressed in pancreatic cancer. Der, who led the research, said the group has been investigating RGL2 as a pathway for more than five years. “We think it is an attractive target for achieving what has, to date, been impossible: making a KRAS-blocking drug,” he says.

Cell movement studies lend insights into metastasis

Cancer spreads, or metastasizes, in part by cell movement and migration. When, how, and how quickly these cells migrate are important questions for doctors who are trying to stop or slow the growth. UNC scientists are part of a team that has identified how certain proteins affect the movement of cells that cause melanoma, one of the only forms of cancer that is still on the rise.

Metastases are the major cause of melanoma deaths, but the research team — led by Channing Der, PhD, and Nancy Thomas, MD, PhD — found that mice lacking a protein called P-Rex1 are resistant to melanoma metastases. When they tested human melanoma cells and tumor tissue, P-Rex1 was elevated in the majority of cases. Their initial research was funded by UCRF.

A drug approved last summer, vemurafenib, is the first treatment targeted at a gene called BRAF, whose mutations affect the development of melanoma. The work by Drs. Der and Thomas suggests that P-Rex1 plays an important role in metastasis, leading them to believe that vemurafenib may work in part by blocking the elevation of P-Rex1.

“As a physician and a scientist, I know firsthand the frustration of having very limited therapeutic options to offer to patients with metastatic melanoma,” Thomas says.

Jim Bear, PhD, is focusing on another protein and its effects on cell migration: ARP 2/3. When that protein is present, a cell moves by forming a fan-shaped

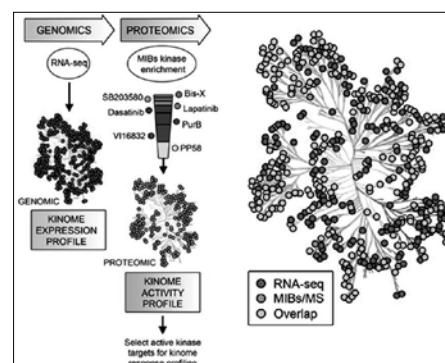
structure (called lamellipodia), at the front end to help it crawl. When ARP 2/3 is not present, cells instead move by forming finger-shaped structures (called filopodia), and move much more slowly.

After learning that ARP 2/3 plays a role in determining which form — finger or fan — a cell may use to help it move, Dr. Bear and his team tested how the two forms responded to environmental cues. Contrary to the widely held belief that cells need lamellipodia “fans” to respond to soluble chemical cues — important because of the many drugs that target cell behavior — Bear found that lamellipodia “fans” and filipodia “fingers” both respond to chemical cues the same way.

UCRF’s support of these discoveries enables future breakthroughs in areas requiring controlled cell migratory behavior, such as wound healing and tissue repair, cardiovascular disease, and cancer.

Dr. Bear, associate professor of cell and developmental biology and a Howard

Hughes Medical Institute Early Career Scientist, and has a personal connection to cancer: his father died of melanoma. “I want to do something about this disease to make it so that other people don’t have to go through this,” he says. This recent work was published in one of the world’s most prestigious journals, *Cell*.



Diagrams show how kinase activity changes with cancer treatment.

Broad-based kinase test could boost therapeutic success

A UNC research group led by Gary Johnson, PhD, has unveiled the

first simultaneous test on large numbers of protein kinases, giving investigators a glimpse of how cancers resist treatment so they can develop strategies to block that resistance.

Of the 518 known human kinases — proteins expressed in human tissues that play a key role in cell growth — about 400 are expressed in cancers. Despite the effectiveness of kinase inhibitors such as Herceptin®, Gleevec® and Tykerb®, most cancers eventually become resistant.

With the initial support of a UCRF innovation award, Dr. Johnson’s team, which includes UNC Lineberger Director Shelley Earp, MD, developed a test that can measure both the presence and activity of 60-70 percent of all kinases at the same time. This allows investigators to see how cancers evade treatment with kinase inhibitors, so that they can combine drugs to overcome that resistance and continue to effectively treat cancer.

“One of the most frustrating things as an oncologist is when a patient’s tumor develops resistance to a treatment,” says Lisa Carey, MD, who is working with Dr. Johnson on clinical trials using the test. The trials involve GlaxoSmithKline and Genentech. “We are excited about the ability to examine tumor samples before, during, and after kinase inhibitor treatment to see how the tumor kinase profile changes, and potentially respond to those changes using different inhibitors.”

A patent application has been filed for the testing technology.

Optimizing NC Cancer Outcomes

The third research priority for UCRF is to better understand and improve cancer outcomes in North Carolina. Through population-based studies and outreach efforts, UNC is working with communities across the state to understand how best to implement effective prevention and treatment strategies.

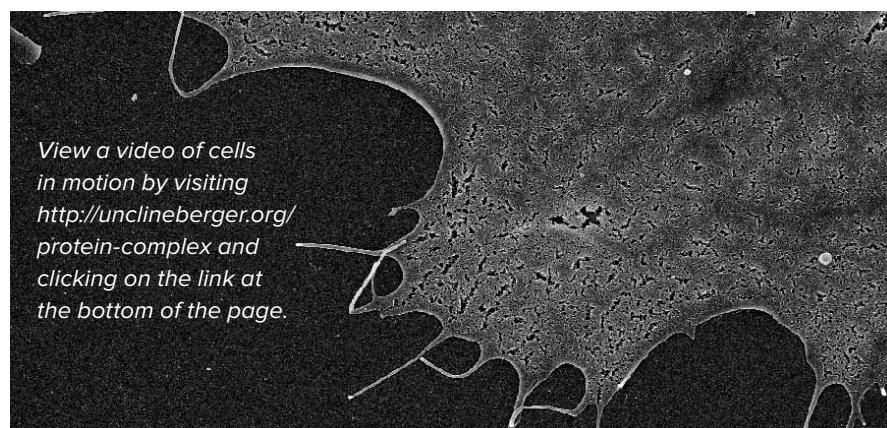
Comparative effectiveness tests performance of different therapies

When a new cancer treatment is developed, it endures a rigorous testing process in highly selected patient or subject populations before it can ever be commercialized for large-scale use. However, these activities do not often reflect the reality of being used on a more diverse patient population in a less controlled environment.

Just as policymakers often rely on evidence-based outcomes to make decisions, comparative effectiveness research is emerging as a practical way to evaluate the effects — both positive and negative — of health care interventions.

UNC and Harvard, which are collaborating on a comparative effectiveness consortium to for cancer treatments, published their first study this winter. They found that adding the drug oxaliplatin to the standard chemotherapy used for colon cancer is associated with better survival among patients receiving colon cancer treatment in the community. The drug had already been approved by the FDA because of its performance in clinical trials, but that population was younger, healthier, and less diverse than most people who receive chemotherapy for colon cancer.

“This research approach provides evidence for whether treatments work in the ‘real world’ — if they are as effective in a health care environment that



View a video of cells in motion by visiting <http://unclineberger.org/protein-complex> and clicking on the link at the bottom of the page.

Scanning electron micrograph of Arp2/3-depleted cell showing extensive filopodia

is less precisely controlled and has more patient diversity than a clinical trial, where treatments are initially tested,” says Hanna Sanoff, MD, a member of UNC Lineberger’s consortium group. Dr. Sanoff, who was a trainee at UNC, left to start a faculty career at the University of Virginia. She has just been recruited back to UNC with the help of UCRF. In addition to her research, she will treat North Carolinians with advanced colon and pancreatic cancer. Her mentor and collaborator, William Carpenter, PhD, was recruited to UNC with help from UCRF.

Ronald Chen, MD, knows all too well that evaluating therapies as they work in the “real world” can affect a patient’s healthcare decisions — not to mention their pocketbooks. Dr. Chen recently reported findings from a large comparative effectiveness study that examined three different therapies used to treat localized prostate cancer.

Chen and his colleagues at UNC Lineberger and the Sheps Center for Health Services Research compared conventional conformal radiation therapy (CRT) to intensity modulated radiation therapy (IMRT), finding that IMRT is better at reducing prostate cancer recurrence and lessening side effects than the more traditional CRT. He also found that proton therapy — which is growing in popularity but can cost at least twice as much as other prostate treatments — was no more effective than IMRT.

“Patients and doctors are often drawn to new treatments, but there have not been many studies that directly compare new radiation therapy options to older ones,” Dr. Chen said. “In the past 10 years, IMRT has largely replaced conventional conformal radiation therapy as the main radiation technique for prostate cancer, without much data to support it. This study validated our change in practice, showing that IMRT better controls prostate cancer and results in fewer side effects.”

Dr. Chen was recruited to UNC from Harvard with UCRF support. He takes care of patients with prostate and brain cancers.

Health-e-NC partners for on community-based pilot projects

Since it was created in 2007, UCRF has helped recruit more than a dozen new faculty members in cancer prevention and control. Their work has helped establish a community-based partnership for statewide cancer prevention called Health-e-NC (Health for Everyone in North Carolina). Health-e-NC aims to develop a state-of-the-art way to deliver and test interventions that:

- Reduce cancer risk factors (tobacco use, dietary behavior, physical activity, obesity);
- Increase cancer screening;
- Help people make more informed decisions about prevention and treatment options;
- Increase utilization and maintenance of proven prevention, treatment and survivorship programs and strategies.

Health-e-NC partners a series of pilot projects in multiple counties. “We challenged our faculty to design forward-looking projects focused on the state’s biggest needs,” said Shelley Earp, MD, director of UNC Lineberger. “We then asked a group of national experts in the field to select the best. The result puts outstanding ideas to the test in North Carolina communities.”

One pilot project for tobacco prevention is Health-e-NC’s partnership with the N.C. Community College System to identify evidence-based interventions for cancer prevention. The state’s 58 community colleges serve residents in all 100 counties, and their broad reach means they have high potential as a setting for effective prevention programs.

“The results of this partnership with UNC will provide our colleges with the tools they need to help students, employees and citizens make life changes that will ultimately reduce their risk of cancer,” said Community College President Dr. Scott Rawls. “Since our colleges provide the education and training for the majority of North Carolina’s nurses and allied health professionals, it is fitting that they would also be involved in working with UNC to promote healthy lifestyles across our state.”

Colorectal cancer is the third most common cancer diagnosis and second leading cause of cancer deaths in the United States. Although overall rates of colorectal cancer screening have gone up, screening rates among low-income, uninsured, less educated, minority, and rural residents are lower than the rest of the population.

Michael Pignone, MD, and Stephanie Wheeler, PhD, MPH, are hoping to pinpoint factors that influence underserved populations to pursue colorectal cancer screening, and devise strategies and potential policy decisions that could help increase screening rates and improve health outcomes in disadvantaged communities.

Another pilot, a home-based exercise study whose goal is to get breast cancer survivors active through a progressive walking and resistance training program.

“The fact that most cancer survivors don’t have access to exercise programs is unfortunate,” Denise Spector, PhD, post-doctoral fellow at the UNC Gillings School of Global Public Health and study co-investigator, said. “A high percentage of breast cancer survivors are not meeting current physical activity recommendations. The percentage is even higher among African-American breast cancer survivors.”

Health-e-NC also facilitates *Cancer Transitions*, a six-week free program

developed by the Cancer Support Community and LIVESTRONG that offers cancer survivors individualized advice and information on issues such as exercise, nutrition, emotional health, quality of life, and medical concerns after cancer treatment ends. Survivors often find that transitioning out of treatments raises many questions about how to stay healthy, how to cope with long-term



Buddy Coppersmith’s goal is to get back to fishing on his commercial boat (shown here).

side effects, and other issues. This spring, UNC partnered with eight cancer treatment centers across the state to hold *Cancer Transitions* workshops. The researchers used telemedicine technology to train community healthcare professionals to conduct the program. In this way, UNC is helping other centers across the state provide cancer support services for survivors.

Navigation eases “the most difficult thing I’ve ever done”

Wiley “Buddy” Coppersmith of Manteo, NC, knows what it’s like to be the patient in the middle of patient-centered cancer care. He has doctors at East Carolina University’s Leo Jenkins Cancer Center and at UNC’s N.C. Cancer Hospital. Thanks to the UNC Cancer Network’s nurse navigators, he’s getting true collaborative care.

Studies show that patients who work with nurse navigators have better long term outcomes than those who don’t, but Buddy says that they really make a difference in the middle of cancer treatment. He was diagnosed with colon cancer in July, 2011 and referred by his friend, Joe Jenkins, MD, to surgical oncologist Ben Calvo, MD, at UNC.

“Dr. Calvo recommended that I get radiation and chemotherapy before I consider surgery,” said Buddy, “so I went to ECU to see Dr. Lepera and Dr. Biswas.” There, he was introduced to UNC Cancer Network outreach nurse navigator Judy Koutlas, who works with patients with gastrointestinal cancers. “She is an angel,” said Buddy. “She coordinated with the doctors so I could get chemo and radiation in Greenville, which isn’t as far to drive. She’s great for moral support, really responsive when I call her with questions and is very practical and reassuring.”

A commercial fisherman specializing in tile fish and other North Carolina delicacies, Buddy values the personal touch. “That’s the whole key to this program. You don’t have to fight cancer alone, there are people helping me every step of the way.”

While in treatment in Greenville and Chapel Hill, Buddy was introduced to outreach nurse navigator Deborah Parsons, who works in Nag’s Head with UNC Cancer Network’s Dare County Program. Now when he sees his doctors, he comes to see Parsons a few days later.

“I have given her permission to get my records and she helps me understand them and what the doctors are thinking about my treatment. She is really compassionate and understands what I am going through,” he adds.

Because the navigators work as a team, they have helped Buddy avoid unnecessary driving between treatment centers. He is now waiting to let the course of radiation he had do its work before doctors make a decision about surgery.

“I just want to work on my boat and get back to fishing,” he says, “This is the most difficult thing I have ever done, I have never been sick. It’s great to have so many people helping me along the way.”

About UNC Lineberger

The UNC Lineberger Comprehensive Cancer Center continues to thrive as one of the nation’s premier matrix comprehensive centers. One year after achieving an “exceptional” rating in its National Cancer Institute review, the Center continues to grow. Directed by Dr. Shelley Earp, Lineberger comprises 322 faculty members from across a great state university. These individuals, along with extraordinary support from the institution and the State, make the Center one of the best places to train students and postdoctoral fellows and perform integrated basic, population, translational, and clinical research. In the last year, the Cancer Center has maintained outstanding cancer research funding in a difficult economic period. As of September 30, 2011, UNC Lineberger members hold \$69.9M (total cost) in NCI funding and \$212.8M (total cost) in cancer-related total extramural funding. For more information, please see unclineberger.org/ucrf.

Statewide Projects:

Cervical Cancer-Free North Carolina (CCFNC) aims to eliminate cervical cancer in North Carolina. Led by researchers at the UNC Gillings School of Global Public Health, this collaborative effort unites public, private, academic and community partners in promoting HPV vaccination, cervical cancer screening, and improved testing and treatment.

Counter Tobacco Youth Engagement Program engages youth and young adults in tobacco policy advocacy and FDA enforcement via a new modular store audit system called Counter Tobacco. The Counter Tobacco customizable store audit form will be pilot tested via web-enabled mobile device in late Spring, 2012, and could ultimately be deployed as a local- and state-level point of sale surveillance system. The first generation FDA compliance store audit form was developed with support from **Health E-NC**; funds were leveraged to secure an additional grant from North Carolina Alcohol Law Enforcement and the NC Division of Mental Health, Developmental Disabilities and Substance Abuse Services.

Regional Evidence Academies

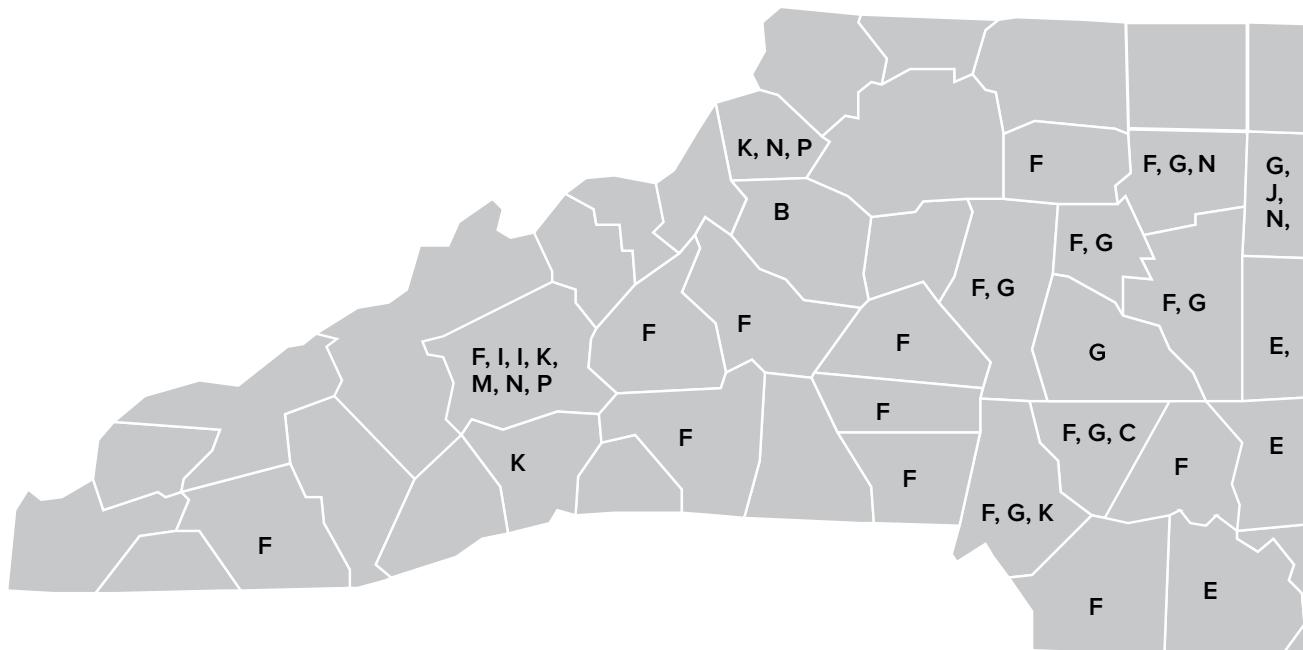
We partnered with state and local organizations to deliver Evidence Academies in different regions of North Carolina. These conferences are designed to disseminate evidence-based guidelines and findings from new research, as well as stimulate partnerships between academic and community settings. In 2011, we held two evidence academies titled “Moving Tobacco And Lung Cancer Knowledge (TALK) into Action.” Conference sponsors included the NC TraCS Institute, the Mountain and Southeastern Area Health Education Centers, the North Carolina Comprehensive Cancer Program, the UNC Center for Health Promotion and Disease Prevention, the NC Center for Health and Wellness, Mission Hospital and Zimmer Cancer Center.

Expecting Excellence: Perinatal Smoking Cessation and Smoking Cessation during Pregnancy

We worked with obstetrics, gynecology, and family practice residents in Western North Carolina to improve the delivery of tobacco screening and treatment services for pregnant and post-partum women. We partnered with MAHEC and You Quit Two Quit to provide training, technical assistance on office systems changes, and North Carolina-specific resources for providers and their pregnant patients who want to quit.

Health E-NC is aimed at finding out what really works in the areas of cancer prevention, detection, diagnosis, treatment and survivorship. Health-E-NC provides pilot funding to support leading-edge research that focuses on the development, implementation, evaluation, or dissemination of interventions that will reduce the cancer burden in North Carolina. A web portal will serve as a venue for testing interventions as well as for sharing evidence-based tools, materials, and information.

The N.C. Cancer Hospital Nicotine Dependence Program (NDP) provides comprehensive tobacco treatment services to NC Cancer Hospital patients from across the state. Quitting tobacco use after a cancer diagnosis is associated with reduced treatment complications and decreased risk of disease recurrence and development of secondary tumors. A tobacco treatment specialist works with patients to develop individualized quit plans, including cessation medication when appropriate, and provides follow-up support through the quitting process. Since 2009, NDP has served nearly 300 patients from 40 counties. NDP



has provided consultations on development of tobacco treatment programs to a number of cancer centers across the country. In collaboration with other leading cancer centers, NDP is developing research projects designed to improve the delivery of tobacco treatment services to cancer patients and their family members.

NC Cervical Cancer Resource Directory helps connect North Carolina women and girls who are uninsured or underinsured to free or low-cost cervical cancer screening and HPV vaccination services. The online resource is available at <http://www.ccreourcedirectory.org/>.

NC Tobacco Retailer Mapping Website highlights the results of regulatory compliance checks of tobacco retailers. The North Carolina Alcohol Law Enforcement (NC ALE) agency visits thousands of retail establishments annually to conduct compliance checks to reduce illegal tobacco sales to minors; additional underage buys and advertising and labeling inspections will be conducted beginning in 2012 as part of a new contract with FDA. Compliance check data is useful for local and state grantees, policy advocates, and the general public and will now become easily accessible. Site users will see the tangible work of government and be able to map tobacco retailer locations, proximity to schools and parks, and violation patterns and trends.

NC TraCS Community Workshop Series
UCRF funding facilitates collaboration in a series of workshops sponsored by NC TraCS CARES (Community Resources for Engaged Scholarship). These workshops are intended to build capacity for community members, organizations, and health care providers to facilitate research and foster partnerships to improve health. We are involved in the development and delivery of specific topics including Participatory Approaches to Research, Translational Research, Program Evaluation, Communicating Health Information, and Evidence-Based Interventions.

UNC Health Registry/Cancer Survivorship Cohort
A recent report by the Institute of Medicine, part of the National Academies, notes that many cancer patients are “lost in transition” from treatment to survivorship. Primary care physicians and other health care providers are seeking more information about the consequences of cancer and want more explicit

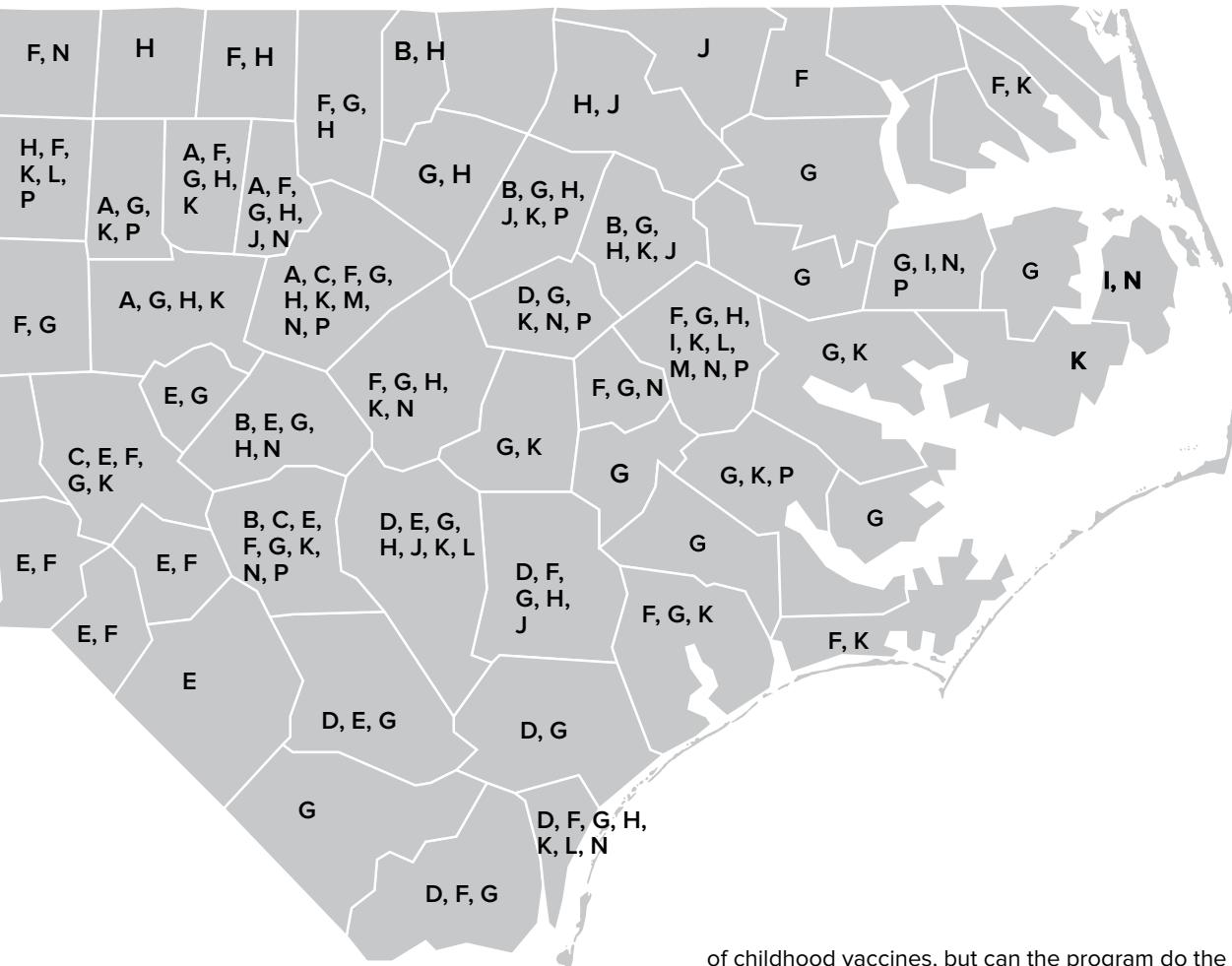
guidance from oncologists. The UNC Health Registry/Cancer Survivorship Cohort enrolls, monitors and collects biologic and clinical treatment information on consenting patients at UNC Health Care clinics. UCRF initiated the enrollment of 10,000 patients into the UNC Health Registry/Cancer Survivorship Cohort in 2010. The data collected will help researchers determine methods for improving cancer outcomes and quality and length of life after treatment.

Regionally-focused projects:

A — Barbershop Physical Activity intervention Study (FITShop) meets African American men in barbershops — community-based locations that can be centers for social and peer interaction. One of the key contributing factors to high cancer rates among African American men is lack of physical activity. UNC and NCCU investigators will test the effectiveness of a multi-level intervention aimed at increasing physical activity among African American men. Partnership with shop owners, barbers and the BEAUTY & Barbershop Advisory Board, and approximately 14 barbershops and 560 shop customers will be enrolled into this research study. Since barbershops are located in all communities, if effective, this intervention can reach and impact many individuals here in North Carolina and nationally.

B — Improving Rates of Colorectal Cancer Screening
We are partnering with the North Carolina Community Health Center Association and three Federally Qualified Health Centers to study the implementation of a toolkit for improving rates of colorectal cancer screening. The toolkit, based on a product by the American Cancer Society, was tailored with input from health center providers and staff across the state. We incorporated the toolkit into a grant proposal to the National Cancer Institute which was funded in September, 2011.

C — Community Wellness & Cancer Prevention (CWCP) North Carolina’s high rates of obesity and smoking are important, and potentially reversible, factors contributing to high cancer rates. Both problems are associated with low socioeconomic status and more prevalent among ethnic minorities. CWCP works with four Kate B. Reynolds Charitable Trust grantees to develop and implement evidence-based approaches designed to increase physical activity and reduce



obesity and smoking rates. The four partner agencies are the Cabarrus Health Alliance (Cabarrus county), the Cape Fear Valley Health System (Cumberland county), First Health of the Carolinas (Moore county) and the YWCA of the Greater Triangle (Wake county).

D — Improving Breast Cancer Screening Using Evidence-Based Strategies UNC and the Susan G. Komen NC Triangle Affiliate are collaborating to promote the use of evidence-based breast cancer screening programs. UNC offers group training and individual consultation on finding, selecting and adapting evidence-based intervention strategies, program planning and evaluation to community organizations in a 20-county, and expanding, service area of the Triangle Affiliate. UNC is collecting individual and organization-level data to assess the effects and cost of the training and technical assistance intervention. Data will be used to determine the intervention's potential for broader dissemination and development of future research.

E — Social Marketing and the HPV Vaccine 'Protect Him' is a social marketing campaign to promote the HPV vaccine for boys in a 13-county region in south-central NC. Using brochures, posters, and radio ads to raise parents' awareness of HPV and HPV vaccination for preteen boys, the campaign will run from June 15-September 15, 2012. Funding for this effort comes from an R21 award from the National Institutes for Health and is led by Noel Brewer, PhD, who is supported by UCRF.

F — Adolescent AFIX Study CDC's AFIX (Assessment, Feedback, Incentives, and eXchange) program is a model for training healthcare providers to improve their immunization practices. Research shows that AFIX trainings increase the uptake

of childhood vaccines, but can the program do the same for adolescent vaccines such as HPV vaccine? In collaboration with the North Carolina Division of Public Health, researchers at the UNC Gillings School of Public Health are investigating this question.

G — Jeanne Hopkins Lucas Carolina Breast Cancer Study African American women in North Carolina die more often from breast cancer — and there is no simple answer as to why. Building on ground-breaking work done at UNC, the Jeanne Hopkins Lucas Study is conducting a comprehensive, population-based study that includes epidemiologic, biologic and clinical data to help understand the factors that contribute to this disparity. The study is ongoing in 44 counties across the state and is named for General Assembly member Jeanne Hopkins Lucas, the first African American woman to serve in the state senate, who died of breast cancer in 2007.

H — NC SPEED Outreach Network How can we better prevent cancer across North Carolina? How do we work with our communities to increase screening rates and early diagnosis? Will a program that works in Wilmington work in Asheville? To find out the answers to these questions, we have established a statewide network to facilitate and improve the quality of cancer prevention and control research across the state of North Carolina. Research associates in Asheville and Wilmington work with UNC Lineberger faculty as they establish linkages and serve as facilitators for research undertaken by UNC and other researchers in North Carolina communities and health systems.

I — Patient Navigator Education The health care system can be confusing and intimidating — even more so when you're facing a cancer diagnosis for yourself or a loved one. Ensuring that records are transferred, specialist appointments are made in the right order and a coherent,

individualized treatment plan is the goal of all cancer care. To help make this a reality for patients across the state, we are working with hospital systems in Buncombe, Dare and Pitt counties to evaluate the impact of patient navigators on the receipt of timely, appropriate care for cancer patients.

J — Reducing Disparities in Breast Cancer Screening Why do some racial, ethnic and socioeconomic groups face disparities in the incidence of cancer and cancer outcomes? Why are some groups less likely to be screened than others? As partners in the Southeastern U.S. Collaborative Center of Excellence for the Elimination of Disparities, UCRF is helping UNC researchers and public health professionals to assist with to eliminate racial disparities in breast cancer screening rates.

K — UNC Cancer Network — Clinical Outreach The UNC Lineberger and the NC Cancer Hospital are bringing the expertise of UNC's academic medical center to doctors and patients across the state through a clinical outreach network across that includes telemedicine, physician collaboration and clinical trials access. Partnering with local doctors can help patients receive the best care possible in their home communities — where they have social support and established relationships with their health care providers.

L — UNC Lineberger LiveSTRONG Center of Excellence in Cancer Survivorship As cancer survivorship rates increase across the United States, survivors face new challenges. How do they transition to life after cancer treatment? Do they have the tools and resources available to help move beyond the illness and positively impact the quality of their lives? How can primary care physicians and oncologist work together to improve the care of cancer survivors? UNC Lineberger is one of seven LiveSTRONG Cancer Survivorship Centers of Excellence nationwide working to answer these questions.

M — Research Partnerships UNC partners with NC Central University, NC State University, and East Carolina University. Projects include the study of mechanisms behind and treatment for human and canine lymphoma and pancreatic cancer and research into the causes of racial disparities in Barrett's Esophagus (a precursor to esophageal cancer) and triple-negative breast cancer.

N — School Health Center Project evaluates a sustainable intervention that can eventually be provided to organizations working in N.C. schools to increase rates of vaccination among adolescents, including HPV. Other vaccines include Tdap, meningococcal conjugate and influenza.

More than 100 top faculty have been recruited to or retained at UNC with the help of UCRF. During the last year, the following have joined the UNC-Chapel Hill and UNC Lineberger Faculty:

CANCER GENETICS

Vladimir Jojic, PhD

Department of Computer Science
Previously at Stanford University
Computer science,
computational biology

Joel Parker, PhD

Department of Genetics
Previously at Expression
Analysis, Inc.
Bioinformatics, genomics,
expression analysis

Praveen Sethupathy, PhD

Department of Genetics
Previously at the National Human
Genome Research Institute
Computational genetics,
stem cell biology

DEVELOPING NEW TREATMENTS

Qi Zhang, PhD

Department of Biochemistry &
Biophysics
Previously at UCLA
RNA structure and function

Alexander Kabanov, PhD, DrSc

UNC Eshelman School of Pharmacy
Previously at the University of
Nebraska
Nanotechnology and therapeutics

Matthew Parrott, PhD

Department of Radiology
Previously at UNC
Nanotechnology and Imaging

OPPORTUNITY FUND

Shawn Hingtgen, PhD

UNC Eshelman School of Pharmacy &
Biomedical Research Imaging
Center
Previously at Harvard
Stem cell mediated therapy for
brain tumors

Greg Wang, PhD

Department of Biochemistry &
Biophysics
Previously at Rockefeller University
Epigenetics

CRITICAL INFRASTRUCTURE

Tamara Branca, PhD

Department of Physics &
Astronomy & Biomedical Research
Imaging Center
Previously at Duke University
Imaging

Cheryl Carlson, MD

Department of Medicine
Previously at University of
Washington
Hematologic malignancies

Shannon Carson, MD

Department of Medicine,
Chief of Pulmonary Medicine
Pulmonary medicine, lung cancers

Jay Coghill, MD

Department of Medicine
Bone marrow transplant

Trevor Hackman, MD

Department of Otolaryngology
Previously at Washington University
in St. Louis
Head & Neck surgery

Carrie Lee, MD, MPH

Department of Medicine
Previously at Quintiles
Lung cancers, Phase I clinical trials

Yueh Lee, MD

Department of Radiology
Translational radiology

Matthew Milowsky, MD

Department of Medicine
Previously at Memorial
Sloan-Kettering Cancer Center
Urologic cancers

Autumn McRee, MD

Department of Medicine
Gastrointestinal cancers

Stergios Moschos, MD

Department of Medicine
Previously at University of Pittsburgh
Melanoma, clinical trials

Michael Woods, MD

Department of Urology
Previously at Loyola University of
Chicago
Urologic cancers

Timothy Zagar, MD

Department of Radiation Oncology
Previously at Duke University
Breast cancers

Greg Wang awarded top V Scholar ranking



Greg Wang, PhD

histones — proteins enabling yards of DNA to be crammed into a single cell — depend on chemical tags adorning their exterior. This sophisticated chemical syntax for packaging DNA into tight coils or unraveling it again — proposed as

Greg Wang, PhD, has been awarded the Martin D. Abeloff, MD, V Scholar Award from the V Foundation for Cancer Research for the research project that receives the highest rating from the V Foundation's Scientific Advisory Board. Wang is the 10th V Scholar from UNC Lineberger.

The award of \$200,000 over two years funds Dr. Wang's research into cancer epigenetics, begun during his postdoctoral fellowship in Dr. David Allis' laboratory at Rockefeller University. Allis discovered that

the "histone code" by Dr. Allis and Dr. Brian Strahl, UNC professor of biochemistry and biophysics — is the latest frontier for researchers bent on understanding how genetics encodes life. Cancers use "code" changes to alter the expression of tumor suppressor or oncogenes.

Dr. Wang's research examines how this mechanism works in bone marrow cancers, such as leukemia and lymphoma. His goal is to find out how changes to the "histone code" interfere with the normal modification of these proteins — leading to cancer. The proteins involved in establishing and/or changing the chemical syntax in histones are considered a promising target for drug therapies, so understanding their actions in detail is the next step in developing new treatments for these diseases.

Past V Scholars at UNC Lineberger have gone on to highly productive scientific careers, including Angela Whitehurst, PhD; Ian Davis, MD, PhD; Pilar Blancafort, PhD; James Bear, PhD; W. Kimryn Rathmell, MD, PhD; Jason Lieb, PhD; Blossom Damania, PhD; and Yi Zhang, PhD.



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