

University Cancer Research Fund

Annual Report 2012–2013

Dear Members of the General Assembly,

On behalf of the Committee – and on behalf of North Carolina's cancer patients and their loved ones, both current and future – thank you for your ongoing support of the University Cancer Research Fund and the research it fuels. The economic and health benefits of this landmark investment have been significant and will continue to have an impact for years to come.

Although prevention, diagnostic, and treatment tools are improving, cancer remains our state's deadliest disease and the No. 2 cause of death nationwide. It is crucial to continue supporting and conducting research that will rein in and eventually cure this disease. The University Cancer Research Fund has been a critical investment in the fight against cancer, and as a scientist I have been inspired by the difference our students and faculty are making in this fight.

Thanks to the University Cancer Research Fund, UNC has emerged as a leader in research aiming to better understand the genetic underpinnings of this disease, to develop more effective and less toxic treatments, and to improve cancer outcomes for the people of our state. This report highlights several of those research efforts, including some in which UNC has taken a notable leadership role in national or international collaborations.

The report also includes many notable economic benefits of UCRF: For every dollar the state has invested, more than four dollars are generated

in return. UCRF has leveraged record amounts of research funding from outside North Carolina, has increased the number of research patents and discoveries, and has produced results that have helped create new jobs and spinoff companies. More than 140 outstanding cancer researchers have been retained or hired with UCRF support.

As you likely know, my successor, Carol Folt, takes office as Chancellor on July 1, and I am excited about the leadership she will bring to the University. As Chair of the Cancer Research Fund Committee, I have been honored to play a role in overseeing this landmark investment by the General Assembly and the State in the health of North Carolinians. I am proud to share this annual report with each of you.

Sincerely,



Holden Thorp, PhD
Chancellor, University of North Carolina at Chapel Hill
Chair, Cancer Research Fund Committee

Economic Impact of University Cancer Research Fund

The UCRF fuels a significant economic impact on the state, yielding **more than four dollars in return for each dollar invested**. From 2008 to 2012, the UCRF:

- Had an overall economic impact that reached \$293.8 million in FY 2011–2012 and totaled \$968 million over the years since UCRF inception, including \$420.9 million in direct impact and \$547.2 million in indirect and induced effects.
- Brought in \$88 million in extramural funding (FY 2012) directly linked to faculty who were recruited or retained by UCRF funds, results of innovation grants, or UCRF technology and infrastructure investments.

Thanks to UCRF investment UNC-Chapel Hill **ranked 9th in National Institutes of Health (NIH) funding** in FY 2012. Without those UCRF-related grants, UNC Chapel Hill would have ranked 17th.

Despite declining to flat federal funding, the NIH increased awards to UNC Chapel Hill faculty members between 2007 and 2012, while awards to many comparable institutions decreased during that time period.

The UCRF's focus on innovation has led to **an increase in inventions, licenses, and spinoff companies**.

- Since 2007, 10 startup companies whose progress is directly attributable to UCRF-funded research have been launched, creating private-sector jobs.
- In the five years before UCRF was established, UNC Lineberger members reported 46 inventions and made 18 licensing agreements. In FY 2011–12 alone, members and UCRF-assisted faculty were reported 58 inventions and 25 licenses.



Fast Facts

Cancer replaced heart disease as North Carolina's leading cause of death in 2007. That same year, the General Assembly created the University Cancer Research Fund (UCRF) to provide ongoing state support for cancer research. A nation-leading investment to promote innovation in cancer research, improve cancer diagnosis and treatment, and reduce the incidence of cancer in North Carolina, the UCRF receives nearly \$50 million annually from state tobacco taxes, settlement funds and appropriations.

This ongoing research support complements two other critical state investments in cancer facilities: the NC Cancer Hospital, which has been treating patients from all 100 counties since its opening in 2009, and the Imaging Research Building, scheduled to open in winter of 2014. Together, these investments form a synergistic approach to fighting North Carolina's deadliest disease.

UCRF's objectives are to create a nation-leading cancer research effort and to reduce North Carolina's cancer burden 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 three primary research priorities:

- **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.

The University Cancer Research Fund is governed by a seven-member Cancer Research Fund Committee, established by the NC General Assembly in 2007. The committee is chaired by UNC-Chapel Hill Chancellor Dr. Holden Thorp. The four other permanent members are Director, UNC Lineberger Comprehensive Cancer Center (Dr. Shelton Earp); Dean, UNC School of Medicine (Dr. William Roper); Dean, UNC Eshelman School of Pharmacy (Dr. Robert Blouin); and Dean, UNC Gillings School of Public Health (Dr. Barbara Rimer). Two other members, elected by majority vote, are: Dr. Edward Bentz, Jr., president and CEO of Dana-Farber Cancer Institute; and Dr. John Mendelsohn, president of the University of Texas MD Anderson Cancer Center.

Cancer Genetics

UNC has emerged as a national leader in the fast-growing field of cancer genetics, which is the study of the genetic changes that determine how and why cancer develops. This field of study plays an important role in early detection, treatment, prevention and prognosis. It helps doctors identify which types of treatments work best for each individual patient, avoiding ineffective treatments and adverse side effects.

UNC researchers take leadership roles in national cancer genome work

The University Cancer Research Fund enabled a major investment in genomic technology that helped UNC become one of just 12 cancer centers in an unprecedented, large-scale collaboration to categorize the genomic changes that occur in cancer. The Cancer Genome Atlas (TCGA) grant is a five-year award from the National Cancer Institute and the National Human Genome Research Institute that will bring a total of \$20 million in outside funding to UNC. The project is fueling rapid advances in cancer research including categorizing tumors in new ways, identifying new therapeutic targets, and allowing clinical trials to focus on patients who are most likely to respond to specific treatments.

UNC has taken a leadership role in this national collaboration, which also includes Harvard University, Johns Hopkins University, Memorial Sloan-Kettering, and MD Anderson. Led by Chuck Perou, PhD, and Neil Hayes, MD, UNC has performed the RNA sequencing and analysis for all the major TCGA reports, and more RNA sequencing is being done at UNC than anywhere else in the world.



Neil Hayes, MD, is working on categorizing head and neck tumors

Perou was the primary author of the TCGA breast cancer report, which defined in a genetic sense the different types of breast cancer and the presumed new targets in each. Researchers found dozens of key differences in the genes among the four major types of breast cancer: triple-negative, luminal A, luminal B, and HER2-enriched. Each of these differences could be a potential target for new drugs that could be designed to treat different cancer tumors. Follow-up research done in Perou's lab suggests that triple-negative breast cancers are more biologically diverse than previously thought, with at least four disease

CANCER FACTS

- In 2011, more than 18,000 North Carolinians died of cancer. It was the leading cause of death for both men and women, and for all races other than Native Indian.
- More than 40 percent of North Carolinians will be affected by cancer during their lifetime.
- In addition to costing lives, the yearly 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.
- With the increase in population and aging, North Carolina's cancer burden is expected to double over the next two decades.
- The NC Cancer Hospital treats patients from all 100 counties in North Carolina.



Chuck Perou, PhD, led the effort to define different types of breast cancer

spread throughout tissues. This should, but in cancer is not, under tight control by the body's defenses" Hayes said. "Most common tumors have relatively little information in the public record as to how these different abnormalities are created. Subtypes, such as those we describe, provide attractive models to understand cancer prognosis and design better treatment."

Hayes also was a major author on the TCGA lung cancer report, which discovered potential therapeutic targets in a common type of lung cancer (lung squamous cell carcinoma) after comprehensively characterizing the squamous cell's genome. The researchers found a large number and variety of DNA mutations that appear to have important effects on the initiation and progression of lung cancer. Three families of enzymes, along with several signaling pathways, were identified as potential therapeutic targets. These findings should stimulate new clinical trials for patients with this type of lung cancer.

In another TCGA study, researchers discovered that colon and rectal cancers are, genetically speaking, nearly indistinguishable. Researchers also found that colorectal tumors with high levels of genetic errors were more aggressive. This research is helping doctors identify new signaling pathways, which control gene activity during cell development, to improve the development of therapies that target colorectal cancer, the fourth most common type of cancer in both men and women.

UNC's work on TCGA helped spark a spinoff company in 2011. GeneCentric Diagnostics, Inc., a company co-founded by Perou and Hayes with partners from Hatteras Ventures, has two new license agreements with UNC-Chapel Hill for promising technologies that target a tumor's molecular details to improve the way doctors diagnose different types of cancer and allow oncologists and patients to make better informed treatment decisions.

The company holds the license to the Lung Subtype Platform (LSP) technology, which can distinguish multiple subtypes of lung cancer based on a genetic "fingerprint" from a tumor sample. Perou and Hayes also hold exclusive commercial rights to a 13-gene biomarker called "Hypoxia Signature" that is associated with cancer spreading to other organs and lymph nodes as well as poor outcomes for patients. Certain molecules promote angiogenesis, or the formation of new blood vessels, which plays a key role in cancer as tumors need blood vessels to grow and spread, and it's believed that Hypoxia Signature could help doctors identify likely responders to drugs that would inhibit the growth of new blood vessels, thereby reducing a tumor's ability to grow and spread.

Genetically customized cancer care is a goal for UNCseq

UNCseq (pronounced U-N-seek) is a new genetic sequencing protocol (LCCC 1108) designed to create a cancer treatment plan for an individual patient based on that patient's specific tumor. This "genetic profiling" protocol will be especially important for situations where standard therapeutic options are not effective or applicable.

For scientists, the UNCseq protocol will help provide the genetic data needed to pursue new treatments and to test the effects of clinical therapies currently being investigated. UNCseq will use next-generation sequencing of tumor DNA to define optimal chemotherapy in patients with advanced cancer in clinical real-time. Researchers will analyze tumor samples obtained from a biopsy or surgery, and use sequencing to identify the molecular changes that may influence outcomes or choice of therapy. A person's normal gene sequence must also be obtained to properly compare and analyze the aberrations in the tumor.

If researchers find and validate a molecular alteration that can be treated with a drug targeted to that change, the UNC system will provide this information to the

subtypes. Further research should identify the distinct biomarkers within these four subtypes and develop drugs that target their individual biology.

Working with a different research group, Hayes also validated four distinct cancer subtypes of head and neck squamous cell carcinoma. Head and neck squamous cell carcinoma is the seventh most common form of cancer in the United States, but is relatively understudied compared to other types of cancers. Analyzing almost 140 samples of head and neck cancer, the research team found four gene expression subtypes and suggested a link between these subtypes and observed genomic events that affect cancer genes.

"A cancer results when broken molecules initiate a cascade of abnormal signals that ultimately results in abnormal growth and

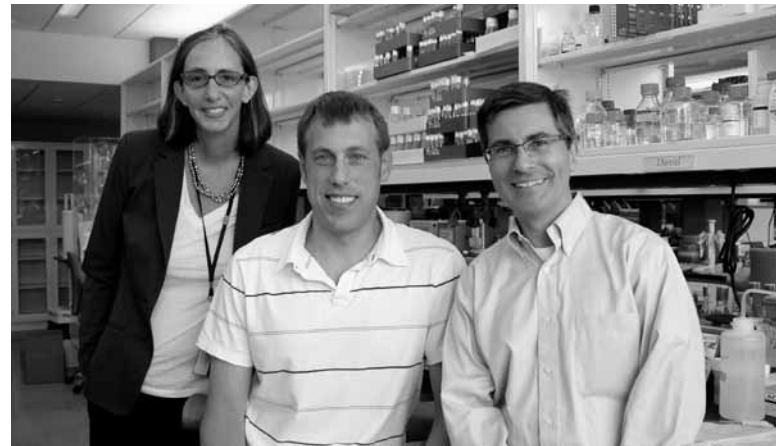
patient and their doctor so that they can discuss this treatment option. Findings may also provide patients with information leading to their enrollment in a clinical trial of a targeted therapy directed toward that molecular change.

The V Foundation awards translational grant to UNC team

The V Foundation for Cancer Research, one of the nation's leading cancer research foundations, has awarded a \$600,000 grant to a team of UNC researchers.

W. Kimryn Rathmell, MD, PhD; Jason Lieb, PhD; and Ian Davis, MD, PhD, were awarded a 2012 Translational Grant to focus on finding new treatments for kidney cancer, or renal cell carcinoma.

Dr. Lieb is a scientist who has made important fundamental discoveries about how genes are regulated; Dr. Rathmell is a disease focused physician-scientist who studies the genetics of kidney cancer; and Dr. Davis, also a physician-scientist, bridges those two with a lab focused on understanding broadly how DNA packaging impacts cancer. The research program of each investigator has been



Kim Rathmell, MD, PhD; Jason Lieb, PhD; and Ian Davis, MD, PhD, are working together to find new treatments for kidney cancer, or renal cell carcinoma.

expanded by the UCRF.

Each one of the scientists was awarded a V Scholar grant earlier in their careers. The team hopes that the grant will help them find new approaches to renal cancer treatment by applying the entire spectrum of medical science. They want to start with fundamental questions about gene packaging and how gene regulation plays a role in the development of cancer, and to understand what goes wrong with genes that can lead to cancer.

The V Foundation's translational grant program, created in 2000, aims to bring the benefits of new laboratory findings to patients more quickly and efficiently. The UNC grant was one of 10 awarded nationwide.

Developing New Cancer Treatments

About one third of cancer patients in the United States will die with an advanced disease that is resistant to treatment. Scientists are working to identify the unique vulnerabilities in cancer cells in order to develop new drugs and delivery methods that would effectively kill the tumor while sparing normal tissues. But the process of discovery to drug development to total completion of drug testing takes more than 10 years, with only one in 20 drugs receiving FDA approval. Investments from UCRF have supported UNC's work to find a shorter, more effective path from discovery to commercialization.

UNC, GSK partner on clinical trial

Pharmaceutical company GSK has partnered with a team of UNC researchers to test how protein kinases — proteins expressed in human tissues that play a key role in cell growth — respond to an experimental breast cancer drug.

Last year, a UNC research group led by Gary Johnson, PhD, announced the development of the first broad-based simultaneous test of large numbers of protein kinases. This powerful test can measure both the presence and activity of up to 70 percent of all human kinases at the same time — giving researchers a more comprehensive view of how breast cancers resist treatment with kinase inhibitors.

The UNC-GSK collaboration is using this simultaneous testing method to study the activity of kinases both before and after the experimental drug GSK1120212 is administered. This drug blocks a kinase called MEK but is not yet approved by the FDA for use in breast cancer patients.

Of the 518 known human kinases, about 400 are expressed in cancers, but which ones and how many are actually active in tumors has been difficult to measure.

Despite the effectiveness of kinase inhibitors such as Herceptin®, Gleevec® and lapatinib, most cancers eventually become resistant.

Previous tests have only been able to measure less than 10 percent of the kinases, limiting researchers' ability to form effective combinations of drugs that block multiple kinases. Johnson and colleagues' testing method will enable doctors to design the best combinations of kinase blocking drugs for aggressive breast cancer. This work could especially benefit patients with triple negative breast cancer (TNBC) because there are fewer drugs available to block molecules that affect tumor growth, and kinase-blocking drugs have the potential to be a more effective treatment method.

Frye epigenetics/chemical brain tumor probe

Successful cancer research relies on collaborative, cross-disciplinary teamwork. UCRF was key in leveraging private support to establish the Center for Integrative Chemical Biology and Drug Discovery in the Eshelman School of Pharmacy. Center director and Fred Eshelman Distinguished Professor Stephen Frye, PhD, is committed to sharing his research tools with other academic scientists in order to accelerate progress and discovery.



A research assistant professor in Frye's lab, Lindsey James, PhD, has discovered a chemical probe that can be used to investigate the role of malignant brain tumor domain proteins in biology and disease. The new probe, named UNC1215, was the cover story of the March 2013 issue of *Nature Chemical Biology*. It can be used to investigate the L3MBTL3 methyl-lysine reader domain.

"Before this there were no known chemical probes for the more than 200 domains in the human genome that recognize methyl lysine. In that regard, it is a first in class compound," James said. "The goal is to use the chemical probe to

understand the biology of the proteins that it targets."

In the past five years, chemical probe development has allowed researchers to observe the role of signaling pathways in cancer development and point to potential targets for new therapies. Almost 40 percent of the genes that drive cancer can be mapped to dysfunction within signaling pathways.

James' research was supported by grants from UCRF and the National Institutes of Health.

UNC leads effort to better understand how Hepatitis C leads to liver cancer

Two scientists at UNC have received \$2.35 million to better determine how the Hepatitis C virus causes the development of liver cancer as part of a five-year grant from the National Cancer Institute. Hepatitis C-induced liver cancer is one of the fastest growing causes of cancer death in the U.S.

Teams led by Lishan Su, PhD, professor of microbiology and immunology, and Stanley Lemon, MD, professor of medicine and microbiology and immunology, will work together using technologies developed in each of their laboratories to collaborate on the research project.

Lemon's lab will use its recombinant DNA virus technology to help determine how genetic changes in Hepatitis C may affect the progression of disease, including liver cancer. Su's lab has developed a mouse model of Hepatitis C that replicates the course of the virus in humans, including factors such as inflammation and immune response. This extraordinary model allows study of a virus that heretofore could not be studied in the mouse.

Together, these technologies will study whether inflammation associated with Hepatitis C causes liver cancer, or whether the virus facilitates the development of cancer by affecting host cells in other ways. Chronic Hepatitis C infection is the leading cause of liver cancer in the United States.

Lemon and Su's work centers on a newly developed mouse model that, when infected with the Hepatitis C virus, develops a human immune response to the virus and to human liver diseases.

Affecting about 3.2 million Americans, Hepatitis C is the most common chronic blood-borne infection in the country, according to the Centers for Disease Control. Liver cancer is the third leading cause of death worldwide and the ninth leading cause of cancer deaths in the United States. Chronic hepatitis virus infections account for more than two thirds of these cases.

"A number of studies have documented that inflammation plays a role in liver cancer," Lemon says. "But there is evidence that there is more to the story of virus-cell interaction in the development of cancer. We believe that the virus is interacting specifically with host cell tumor suppressor pathways to promote cancer and we

want to understand what drives this progression from infection to cancer in order to figure out how to stop it."

Lemon and Su are both members of the Lineberger Cancer Center and the Center for Infectious Disease. Lemon is also a member of the Center for Translational Immunology. Lemon was recruited with UCRF funds from Texas and Su's model development was funded by a UCRF innovation award.

Scientists use imaging to measure treatment efficacy, early detection

Just as digital technologies and the use of visuals continue to evolve in everyday use, digital imaging in clinical and translational research is also advancing. Two UCRF-funded research teams are exploring ways to use digital imaging to improve treatment and detection of cancer.

The lab of Otto Zhou, PhD, is working to develop a new X-ray imaging system that will help improve the early detection of breast cancer. Mammography is now the most effective screening and diagnostic tool for early detection of breast cancer, but the current two-view mammography method lacks sensitivity and has a very high false alarm rate. X-ray digital breast tomosynthesis (DBT) is an emerging technique for producing multi-slice images to provide depth resolution and improved contrast. It has the potential to allow radiologists to see tumors at an early stage even in very dense breasts using a similar dose as the common two-view mammography. It is generally expected that DBT scanners will replace a large fraction of conventional mammography systems in the coming years, but current models require long scanning time which can lead to patient discomfort, blurry images and other problems.

Zhou's lab is working to develop the next generation DBT scanner with significantly improved system performance at potentially reduced dose and cost. This proposed device is based on new carbon nanotube (CNT) multi-pixel field emission X-ray (MBFEX) technology. The pixilated and spatially distributed MBFEX source can generate x-ray radiation from multiple views without any mechanical motion of the source, detector, or object. Dr. Zhou's innovative feature can increase the imaging speed, reduce the size and cost of the equipment, and enable experiments on new imaging configurations that could give better imaging quality and potentially reduce imaging dose. These are not feasible with conventional DBT models.



Otto Zhou, PhD, is developing new technology to detect breast cancer

Imaging technologies are also being tested to measure responses to cancer therapy in order to enhance doctors' ability to adjust a patient's treatment. Paul Dayton, PhD, has conducted preclinical experiments using ultrasonic molecular imaging (USMI) and Dynamic Contrast Enhanced-Perfusion Imaging (DCE-PI) to measure responses to therapy for pancreatic cancer.

Dayton, associate professor of biomedical engineering, worked with Jen Jen Yeh, MD, associate professor of surgery and pharmacology, to evaluate these non-invasive imaging technologies. USMI can characterize the biologic processes at the cellular and molecular levels using biological markers that bind to specific proteins on cancer cells, allowing a regular ultrasound to detect signals from cancer cells that would otherwise be undetectable. DCE-PI is used to monitor blood flow, which increases abnormally as tumors grow. It can provide important information about tumor malignancy based on changes in blood vessel structure or density.

"What we found is that using two non-invasive technologies, we can detect response to therapy earlier than by relying on tumor volume changes," Dayton said. "Having new non-invasive, inexpensive technologies available to measure response to therapy earlier during the course of treatment would be a significant advance in the ability to tailor a person's treatment to improve outcomes."

UNC researcher leads test of whether diabetes drug can help treat cancer

UNC Lineberger member Victoria Bae-Jump, MD, PhD, used her preliminary data funded by UCRF to design a national clinical trial exploring whether a commonly used diabetes drug could help treat patients with endometrial cancer. Her work led to her leading this trial across the U.S.

Obesity and diabetes have been linked to poorer survival and increased recurrence rates in endometrial cancer, suggesting that the effects of obesity may play a role in the development of endometrial cancer. This means obesity could lead to biologically different tumors than those that arise in leaner women, and could



Vicki Bae-Jump, MD, PhD, is working on better treatment for endometrial cancer

trials to identify the best science in clinical research.

possibly require different treatment approaches.

Metformin is an anti-diabetic medication that has been shown in preliminary studies to have anti-tumorigenic effects. Bae-Jump's national trial will try to determine whether metformin is broadly useful as a chemotherapeutic agent for all women with endometrial cancer and whether it is more effective in obese cancer patients.

Bae-Jump was recently appointed to a two-year term as a junior investigator on the Gynecologic Cancer Steering Committee of the National Cancer Institute, a member institute of the National Institutes of Health. The committee addresses, designs and prioritizes gynecologic cancer clinical

medicine, Basch also serves as Director of Cancer Outcomes Research at UNC.

Basch's clinical expertise is prostate cancer, and his research expertise includes patient-reported outcomes, clinical informatics, and drug regulatory policy. His work focuses on developing ways to better evaluate patient symptoms and adverse events, with a goal toward improving patient safety and outcomes through more availability of information during drug development, stronger doctor-patient communication, and better practice of cancer care.

Shelley Earp, MD, director of UNC Lineberger, said, "We are thrilled to have Dr. Basch bring his national leadership in outcomes research to UNC, joining a team that spans multiple schools, colleges, and disciplines with the goal of discovering what really works in cancer care through comparative effectiveness research. His expertise in the effort to inform health care decisions, and particularly in integrating the patient perspective, brings additional depth to an already strong team."

Basch is a federally appointed member of the Methodology Committee of the Patient-Centered Outcomes Research Institute (PCORI), a member of the Board of Directors of the International Society for Quality of Life Research (ISOQOL), Co-Chair of the Health Outcomes Committee of the Alliance for Clinical Trials in Oncology, and a member of the Board of Scientific Advisors of the National Cancer Institute. He leads an ongoing NCI initiative to develop a patient-reported adverse event monitoring system for use in clinical research and is study chair for multiple trials employing patient-reported endpoints.

One of the major projects Basch will oversee is the Integrated Cancer Information and Surveillance System (ICISS), a system built from North Carolina data that will provide a model for the nation. UCRF funding has helped build and support this database, which provides a rich informatics resource for scientists. ICISS links multiple population, clinical and other data sources, containing all of North Carolina's cancer cases and linkage to health claims data for 5.5 million people insured by Medicare, Medicaid, State Employees' Health Insurance, and Blue Cross/Blue Shield of North Carolina.

ICISS is being used to measure outcomes of cancer control activities, especially among vulnerable subgroups and communities that have been traditionally under-represented. Projects will eventually include other



Ethan Basch, MD, MSc, focused on comparative effectiveness research to improve cancer care

academic centers in North Carolina, and there are already two projects formed in collaboration with Duke University outcomes researchers. ICISS claims data are expected to include about 80 percent of the North Carolina population with cancer. This rich datasource will enable researchers to take an unprecedented look at the cost and quality of care. Scientists will be able to examine what treatments are most effective, what parts of the state need more access to cutting-edge cancer care, what environmental or economic factors affect prognosis, and other important issues that will better our understanding of cancer – providing a pathway to enhance our efforts to improve cancer outcomes for patients in North Carolina.

Self-screening for cervical cancer could improve early detection

UNC Lineberger member Jennifer Smith, PhD, and North Carolina Central University faculty member Walter Charles, are co-leading a pilot study aimed at improving cervical cancer detection among rural North Carolina women.

A lack of access to Pap testing and follow-up treatment could contribute to the higher risk of invasive cervical cancer for poor, rural, African-American, Hispanic and Native American women. Smith, associate professor of epidemiology in the UNC Gillings School of Public Health, believes a mailed, at-home, self-screening test could help reduce that risk.

Smith and Charles' pilot study explores the efficacy of mailing self-administered screening tests for human papillomavirus (HPV) and cervical cancer to a consenting sample of 200 women in rural communities. The self-screening test is mailed back for analysis, and HPV results will be provided by phone. Follow-up screenings and treatment would be conducted by the NC Breast and Cervical Cancer Control clinic when appropriate.

"If successful, a mailed at-home self-screening test can immediately impact the delivery of preventive screening for many at-risk women," Smith said.

Smith has also received a UCRF Innovation Award to extend this project to Latino women in North Carolina.

Optimizing Cancer Outcomes

The UCRF's third research priority is to work to improve cancer outcomes in North Carolina. Through outreach initiatives and population-based studies, UNC is working with communities all across the state to understand how best to implement effective cancer prevention and control strategies. A new effort on comparative effectiveness will provide results-based research that is more applicable to North Carolina's diverse population.

UCRF, community college system join forces to improve health

UNC Lineberger member Laura Linnan, ScD, and her public health colleagues are working with North Carolina's community colleges to help inform community college employees, students and nearby residents about the latest in evidence-based cancer and wellness information in an effort to encourage good health and prevent disease.

North Carolina's community college system has students and employees in nearly every county. With more than 850,000 students, it is estimated that 1 in 8 North Carolinians has a connection to the state's community colleges.

"They are a really important part of their community, a hub of activity that includes students, faculty, staff and residents of the county," Linnan said. "It was clear that here was an opportunity to do some really exciting work with promoting health and reducing cancer risks, as well as for other diseases."

Physical activity, reducing tobacco use/exposure and diet can play an important role in preventing disease, including cancer. By promoting evidence-based interventions aimed at education and improving behaviors, Linnan and her community college partners hope to improve the quality of life and reduce the incidence of cancer among the staff, students and community residents that North Carolina's community colleges serve.

"A major part of our mission statement is about improving the quality of life in our communities. If you don't have good health, you can't enjoy a good quality of life," said Dr. Scott Ralls, N.C. Community College System President. "We value our partnership with UNC Lineberger Comprehensive Cancer Center and look forward to continuing to incorporate healthy lifestyle options into the everyday activities on our campuses."

Since 2007, UCRF has helped recruit more than a dozen new faculty members who work in the area of public health interventions. Their work has helped establish a community-based partnership called Health-e-NC (Health for Everyone in North Carolina), a statewide effort to improve cancer outcomes for the diseases that hit North Carolina's citizens the hardest. Health-e-NC aims to find out what really works in the areas of cancer prevention, detection, diagnosis, treatment and survivorship, and to develop the most effective ways 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 uptake and maintenance of proven prevention, treatment and survivorship programs and strategies.

UNC lands national expert to lead outcomes research

A medical oncologist and health services researcher who is recognized as a national expert in cancer outcomes has joined UNC Lineberger to lead its cancer outcomes research. UCRF funding helped to successfully recruit Ethan Basch, MD, MSc, from Memorial Sloan-Kettering Cancer Center. An associate professor of

Statewide Projects:

Partnering with NC Community Colleges to Prevent Cancer -- UNC researchers and the North Carolina Community College System formed a collaborative research partnership with the goal of understanding community college motivations, preferences, resources and needs related to adopting and implementing cancer prevention-related evidence-based activities for their students, employees and community residents.

CHART: Carolina Health Assessment & Resource Tool is an online resource tool that UNC researchers can use to assess and modify behavioral risk factors for cancer. Study participants answer module-based questions on such health behaviors as physical activity, nutrition and tobacco use, and then immediately receive personalized, evidence-based and theory-guided feedback. CHART is available online and via mobile devices and can be used in a wide variety of interventions & research to improve cancer outcomes.

Counter Tobacco is an online source for information and campaign materials to counteract point of sale (POS) marketing. Materials on the Counter Tobacco website have been audience-tested and are ready to use in campaigns that engage policy makers, tobacco control advocates, teachers, school administrators, parents, and other community groups. Counter Tobacco is also supported by the Centers for Disease Control and Prevention, Office of Smoking and Health, and the National Cancer Institute.

Evaluation of the North Carolina Adolescent AFIX Program randomly assigned 91 high-volume primary care clinics in North Carolina serving 107,443 adolescents ages 11-18 to receive no visit or an in-person or webinar AFIX visit focused on immunizing adolescents. The state's immunization registry provided baseline and 5-month post-intervention coverage data. Webinar visits were as effective as in-person visits. Both strategies modestly increased coverage of vaccines recommended for adolescents ages 11-12. Web visits for adolescents need improvement to have greater impact on HPV vaccine initiation and to increase catch-up vaccination.

Regional Evidence Academies are regional and statewide meetings that promote evidence-based interventions in response to community-identified health and health care priorities that have been conducted in different regions of North Carolina. Evidence Academies are designed to disseminate evidence-based guidelines and findings from new research, as well as stimulate partnerships between academic and community settings. The first was held in Waynesville, NC in 2010 on the topic of colorectal cancer. The second was held in Tarboro, NC in 2011 on the topic of breast cancer. The third and fourth were held in Asheville and Wilmington in 2012 on the topic of tobacco and lung cancer.

Cancer Transitions Series is a free 2 ½ hour, six-week educational series to help cancer survivors and their caregivers make the transition from active treatment to post-treatment care. Expert panelist including physicians, nutritionists, nurses and fitness experts will discuss topics such as: Get Back to Wellness, Healthy Eating Post-treatment, Medical Care and Surveillance, Physical Activity and Emotional Health and Wellbeing.

In addition, UCRF has supported the Jeanne Hopkins Lucas Breast Cancer Study which investigates the

complex reasons for poor breast cancer outcomes in African-American women; the UNC Health Registry which aims to enroll 10,000 participants from throughout the state to better understand the causes of diseases like cancer; the Integrated Cancer Information and Surveillance System (ICISS) which uses insurance claims data to investigate cancer incidence, mortality, and burden in NC and individual and aggregate data to evaluate health care, economic, social, behavioral and environmental patterns; and UNCseq, a new genetic sequencing protocol that allows for the creation of a cancer treatment plan based on an individual patient's tumor.

Regionally-focused projects:

A — Healthy Stores, Healthy Communities aims to design an integrated community assessment approach to address major behavioral cancer risk factors of tobacco use, diet, and physical activity.

B — Circles of Care: Supporting African Americans with Cancer was a controlled study of the impact of Circles of Care volunteer support teams. The objective was to test the effect of volunteer support teams on cancer communication, quality of life and quality of supportive and palliative care for African Americans living with Stage III or IV lung, colorectal or breast cancer.

C — Meeting the Needs of Cancer Survivors in North Carolina: Assessing and Improving the Medicaid Medical Home Model — This study used North Carolina Central Cancer Registry data linked with Medicaid claims data to assess whether patterns of cancer survivorship care among Medicaid beneficiaries with a history of breast cancer were consistent with evidence-based guidelines and whether surveillance and follow-up practices differ by extent of patient engagement in the medical home program.

D — Improving Colorectal Cancer Screening in NC Medicaid Beneficiaries — This pilot study surveyed and worked with six of the Cape Fear region's medical practices from the Community Care of North Carolina (CCNC) program, which seeks to improve quality of care for Medicaid beneficiaries. The intervention combined mailing patient decision aids to help patients decide about colon cancer screening and telephone-based assistance from a regional patient navigator to help overcome barriers to screening.

E — Addressing Cancer Disparities by Studying Issues of Coverage, Convergence & Cost in Multiple Settings — This research study used a community-based participatory research approach in Cumberland County to identify the combinations of community-based settings that maximize coverage and convergence for interventions with African Americans and Latinos; and identify opportunities to address cancer disparities.

F — A Home-based Motivational Exercise Program for African American Breast Cancer Survivors — The primary aim was to evaluate the feasibility of a motivational 16-week home-based exercise intervention among African-American breast cancer survivors. Secondary aims included the examination of changes in physical activity levels and how these changes affect body composition and quality of life, in addition to other physiologic measures including cardiovascular fitness, muscle strength and fatigue.

G — Reducing HPV-Attributable Cancers through HPV Vaccination — an Interactive Technology Based Approach for Adolescents in School Based Health

Centers — The purpose of this pilot study was to determine sexual risk behaviors and knowledge of HPV disease in males and vaccine availability for males among youth in two rural middle schools in Western North Carolina county, and to develop messages for a School-Based Health Center telemedicine program using texting for increasing knowledge of HPV disease and vaccination among this population. Among adolescent vaccines, HPV4 is licensed for the prevention of cervical, vulvar, vaginal, and anal cancer.

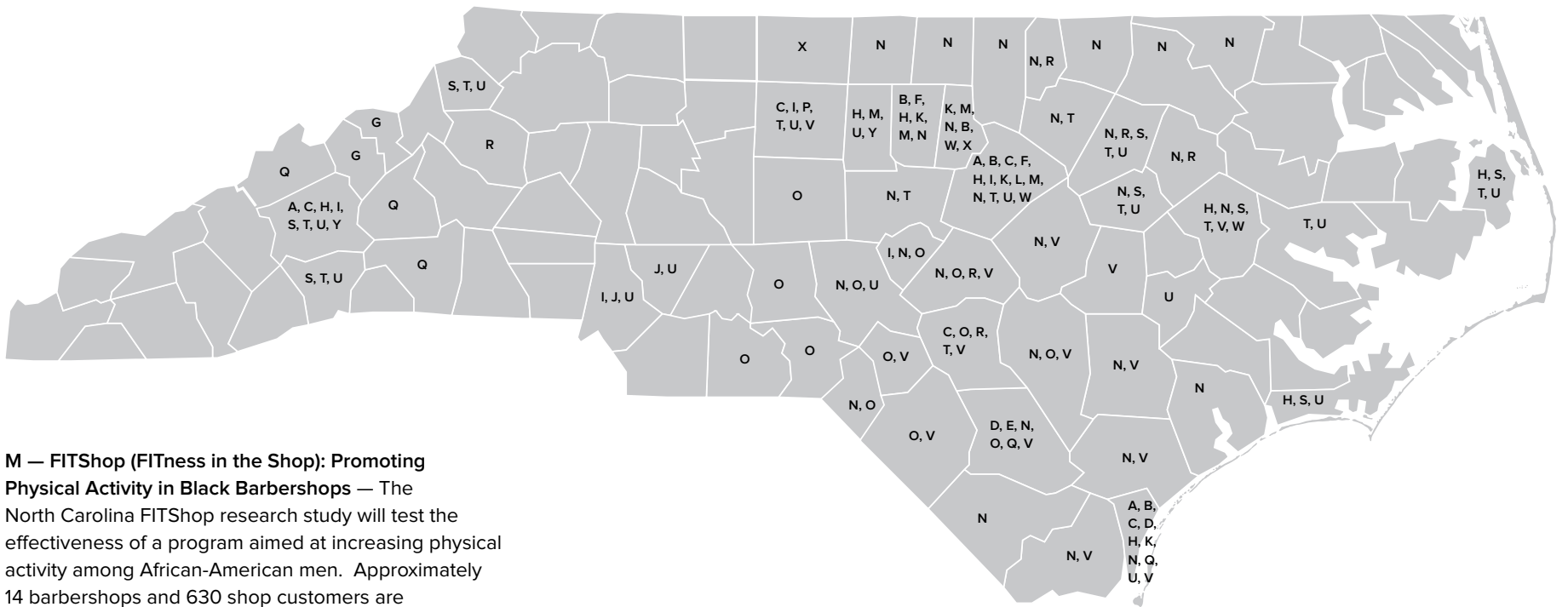
H — Telemedicine Delivery of a Cancer Support Training Intervention: Partnership with Community-Based Survivorship Centers — Pre-intervention training sessions and weekly supervision throughout the Cancer Transitions: Moving Beyond Treatment (CT) program will be delivered via videoconferencing technology. Outcome measures will include: group leader retention, satisfaction with training, and competency with the CT program, as well as participant retention, satisfaction, and health-related quality of life.

I — Improving Care Quality with Virtual Tumor Boards (VTB) Using Videoconferencing Technology — Lineberger Comprehensive Cancer Center Telemedicine Program recently instituted VTBs in several cancer groups -- including hematologic, breast, gastrointestinal, gynecologic, and head and neck -- to engage community-based clinicians across North Carolina. Community Clinicians access the VTBs from their facility via an interactive video network. This study analyzed the VTB program's participant satisfaction as well as impacts of the program on clinician behavior (e.g., treatment decisions and peer consultations).

J — Lose-Now-NC: Feasibility of a large group format community weight loss program coupled with Internet support — This study gathered formative data on the planned large group plus Internet approach through a series of focus groups with constituents typically underserved by weight loss programs; planned for and adapted session materials and protocols; and determined the feasibility by delivering the Lose-Now-NC weight loss program for four months in Kannapolis, N.C. to residents from surrounding communities.

K — Improving Survivorship Care Through Enhanced Communication and Coordination — The pilot study seeks to develop and evaluate a parallel patient and provider version of a personalized Survivorship Care Plan (SCP) for breast, colon, prostate and lung cancer survivors who have completed cancer treatment and are either with or without evidence of disease; and enhance coordinated care between oncology and primary care providers using the SCP and other identified communication strategies. The study will use focus groups and interviews with oncologists and PCPs to evaluate the streamlined provider version of the tailored SCPs and identify other communication strategies that may enhance survivor care coordination; and will assess feasibility of wide-scale implementation into primary care practices.

L — Preventing Lung Cancer through Tobacco Cessation Quality Improvement — The goal of this study is to enhance the care of tobacco users in clinical practice by developing a quality improvement program that encourages providers and practice staff to engage more purposefully in treatments that have the best chance of helping their patients who smoke or use other tobacco products to quit. Study findings will be used to help other clinics provide proven tobacco cessation services to patients.



M — FITShop (FITness in the Shop): Promoting Physical Activity in Black Barbershops — The North Carolina FITShop research study will test the effectiveness of a program aimed at increasing physical activity among African-American men. Approximately 14 barbershops and 630 shop customers are enrolled in this research study. Results will be shared throughout North Carolina and nationally. The study is guided and supported by the North Carolina BEAUTY and Barbershop Advisory Board whose members include shop owners, barbers, chairs of cosmetology schools, hair care product distributors, and other community members. A team of researchers from the UNC Gillings School of Global Public Health, LCCC, and NCCU has received funds from the NCI to support this work.

N — Intervening to increase adoption of Community Guide recommendations: Susan G. Komen NC Triangle to the Coast (Komen NCTC) / Improving Breast Cancer Screening Using Evidence-based Strategies — The Guide to Community Preventive Services (Community Guide) recommends a range of evidence-based strategies to increase mammography screening. The 4CNC and Komen NCTC work together to increase adoption of Community Guide recommendations for breast cancer screening. The project has developed and is evaluating a dissemination intervention that includes grant funding, group training and individual technical assistance sessions for health departments, clinics and other community-based organizations in 29 North Carolina counties.

O — HPV Vaccination Project — A social marketing intervention to motivate parents of preteen boys and health care providers to pursue HPV vaccination. The motivating messages and materials design for the intervention were developed through formative qualitative research.

P — Increasing colon cancer screening in Guilford County — UNC investigators are working with four primary care practices in Guilford County to collect data on patient risk for colorectal cancer and to implement evidence-based approaches to decrease disparities in colorectal cancer screening rates among average risk patients. Project data will be used to model best practices for increasing the reach of evidence-based colorectal cancer screening among African-American and/or uninsured individuals in Guilford County.

Q — Colorectal Cancer Screening in Disadvantaged Communities: A Behavioral Economics Perspective — This CDC-funded study used data from Medicaid and Medicare claims linked to the N.C. Central Cancer Registry to identify specific areas in North Carolina that have low colorectal cancer screening

rates, high colorectal cancer mortality rates, and predictors of low screening rates. Researchers will analyze ways health care consumers make decisions about colorectal cancer screening through conjoint analysis of data collected through focus groups and surveys. Researchers will also develop a simulation model to understand, rank and prioritize potential policy decisions aimed at improving colorectal cancer screening in low-income communities.

R — Improving Rates of Colorectal Cancer Screening in Community Health Centers — A study based on the premise that CHCs want to increase colorectal cancer screening rates, but need evidence-based tools that—with training and technical assistance—they can implement and maintain more efficiently and effectively. The purpose of the project is to test the feasibility of an evidence-informed implementation strategy that combines an office-systems toolkit and outreach education.

S — Patient Navigator Education to help patients with cancer overcome obstacles, systems barriers and facilitate timely access to quality medical and psychosocial care — Patient navigation refers to the individualized assistance offered at no cost to patients, families, and caregivers to help to overcome barriers in accessing quality care and treatment. UNC Lineberger partners with health care organizations across the state on how best to implement and conduct patient navigation programs.

T — UNC Cancer Network - Clinical Outreach — 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.

U — UNC Cancer Network - Clinical Trial Network — The UNC Lineberger and the NC Cancer Hospital are working with providers outside of Chapel Hill to make cancer clinical trials available to the community.

V — 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.

W — 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 and triple-negative breast cancer.

X — School Health Center Project — 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.

Y — Evaluation of a Self-Screening Cervical Cancer Test by Mail — As described on page 5, this pilot study is aimed at validating a mailed, at-home self-screening test for cervical cancer. Among a sample of 200 women, it will explore psychological acceptance of the mailed self-administered screening test for cervical cancer. Consenting rural women older than 30 years and lacking the proper screening schedule will recruited, asked to mail self-sampling kits, return mail cervico-vaginal specimens, and obtain HPV test results by telephone. HPV DNA positive, negative, and indeterminate women will be referred to the North Carolina Breast and Cervical Cancer Control Program to conduct a second self-sampling at the clinic, a physician-collected sample for HPV and cytological screening, and, if indicated, follow-up treatment.

More than 140 top experts 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

Jeremy Purvis, PhD
Department of Genetics
Previously at Harvard University
Stem cell biology, systems biology

Matt Wilkerson, PhD
Department of Genetics
Previously at UNC
Computational biology

DEVELOPING NEW TREATMENTS

Elena Batrakova, PhD
UNC Eshelman School of Pharmacy
Previously at University of Nebraska
Nanotechnology, therapeutics

Albert Bowers, PhD
UNC Eshelman School of Pharmacy
Previously at Purdue University
Medicinal Chemistry

Michael Emanuele, PhD
Department of Pharmacology
Previously at Harvard University
Protein stability and ubiquitylation

Jian Jin, PhD
UNC Eshelman School of Pharmacy
Previously at UNC
Medicinal chemistry

Nate Hathaway, PhD
UNC Eshelman School of Pharmacy
Previously at Stanford University
Chemical biology

OPTIMIZING NC OUTCOMES

Ethan Basch, MD, MSc
Department of Medicine
Previously at Memorial Sloan Kettering
Outcomes, health services research, GU cancer

Stacie Dusetzina, PhD
Department of Medicine
Previously at Harvard University
Pharmacoepidemiology and outcomes

Antonia Bennett, PhD
Gillings School of Global Public Health
Health Policy and Management
Previously at Memorial Sloan Kettering
Patient-reported outcomes

Ashley Leake, PhD, RN
UNC School of Nursing
Previously at UNC
Cancer care and quality

OPPORTUNITY FUND

Frances Ligler, PhD
Department of Biomedical Engineering, NC State
Previously at the Naval Research Laboratory
Biosensors, microfluidics, detection

Jennifer Sun, PhD
Department of Biomedical Engineering, NC State
Previously at UCLA

CRITICAL INFRASTRUCTURE

Katarzyna Jamieson, MD
Department of Medicine
Previously at University of Iowa
BMT, hematologic malignancies/ leukemia

Hanna Sanoff, MD
Department of Medicine
Previously at University of Virginia
GI cancers, outcomes

Anna Snavelly, MD
Department of Medicine
Previously at Harvard University
Clinical trial biostatistics

Michelle Roughton, MD
Department of Surgery
Previously at University of Chicago
Breast reconstruction microsurgery

David Williams, Md, PhD
Department of Pathology and Laboratory Medicine
Previously at Virginia Commonwealth University
Hematopathology

Scott Williams, PhD
Department of Pathology and Laboratory Medicine
Previously at Rockefeller University
Stem cell biology

Qing Zhang, PhD
Department of Pathology and Laboratory Medicine
Previously at Harvard University
Hypoxia signaling and cancer progression

Gershon Focuses on New Treatment For Pediatric Brain Tumors

Dr. Timothy Gershon, MD, PhD, assistant professor of neurology and member of UNC Neuroscience Center and Lineberger Comprehensive Cancer Center, was recruited to UNC in part due to UCRF support. Gershon, a pediatric neurologist who specializes in neuro-oncology, conducts research on medulloblastoma, the most common malignant brain tumor in children. His work on the link between brain tumors and glycolysis was recently published in *The Scientist Magazine* and *Cancer & Metabolism*.

He has received a prestigious four-year grant from the National Institute of Health. With this grant, Gershon will focus on the pathogenesis of medulloblastoma and the development of a biologically based antitumor therapy. He hopes to identify developmental mechanisms that normally regulate the growth of the cerebellum and to harness these mechanisms for anti-cancer therapy. His new research builds on research funded by a St. Baldrick's Foundation grant in 2011.

"My interest in basic tumor biology is motivated by the shortcomings of our present technology for treatment of medulloblastoma," Gershon said. Current therapy for medulloblastoma effectively treats the tumor but has substantial morbidity because it relies on brain and spinal radiation, followed by a year of intensive chemotherapy. Children who are long-term survivors are at risk for treatment related complications including cognitive impairment, cerebrovascular disease, short stature, endocrine deficiencies and psychiatric disorders. Some patients also develop recurrent disease, for which there is no effective cure.

Gershon's recently published study focused on how neural progenitors rely on aerobic glycolysis, a metabolic pattern that is co-opted in the aggressive brain cancer medulloblastoma. He found that blocking aerobic glycolysis in medulloblastoma-prone mice reduced tumor growth and extended survival.



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