Seed Grants for New Ideas in Cancer Research

2014-2015 ANNUAL REPORT

UNC LINEBERGER

For UNC Lineberger physicians and scientists, seed grants not only yield early results, but also help develop the ideas that grow into large, federally funded projects aimed at transformative breakthroughs in care.

Over the past few decades, we have made remarkable progress, but solving a problem as intractable as cancer will require a willingness to take on risks and the kind of big-picture thinking that fuels medical breakthroughs. The Seed Grant Program at UNC Lineberger Comprehensive Cancer Center gives skilled researchers the opportunity to find answers to some of cancer's biggest challenges and develop promising new concepts for basic cancer research, clinical care, prevention, early detection and survivorship. An increasingly competitive funding environment has magnified the need for and impact of investments in this type of innovative research.

Funded by private support and state funds, seed grants have helped UNC become a top 10 institution for research funding.

A Catalyst for Great Ideas

The United States is a global leader in biomedical research, but our leadership depends on federal investment, primarily through the National Institutes of Health (NIH) and the National Cancer Institute (NCI). However, federal funding is in jeopardy. While the number of applicants for NCI grants has increased by 30 percent since 1998, the number of awards has remained the same. Fewer than one in seven researchers who apply for a research grant from the NCI will receive one—a historic low.

In making funding decisions, the NIH and NCI evaluate the significance of the research, approach and level of innovation. These criteria, coupled with the competitive award process, favor applicants who can show experience and preliminary data. Being able to discuss preliminary studies, data or experience pertinent to the application greatly improves the proposed project's likelihood of success, especially for young cancer investigators.

Seed grants give UNC Lineberger scientists an advantage in this competitive landscape. For the past 28 years, the program has maintained a steadfast focus on three guiding priorities:

- Accelerating cancer research by funding promising novel ideas with no other source of funding;
- Providing venture capital to gather vital preliminary data to help secure major external funding for program implementation, human trials and further research; and,
- Ensuring young, bright cancer researchers have the opportunity to establish a history of success, keeping them engaged and building a future in cancer research.

RETURN ON INVESTMENT

Jonathan Serody, MD, had just completed a fellowship in clinical bone marrow transplantation at Fred Hutchinson Cancer Research Center in Seattle, Washington when he was offered a faculty position in the Department of Medicine at UNC. "My wife did her undergraduate work at UNC, and I really liked the area," says Serody. "We agreed that Chapel Hill would be a great place to raise our children, so in 1993, we moved across the country and became Tar Heels. We've been here ever since."

In his early days at UNC, Serody was the recipient of several small research grants that proved to be pivotal in his career. "Oftentimes, if you're just starting out in research or you're new to an area, a small grant can help fund experiments and produce enough data to spur larger investments from other institutions and organizations. There's a real multiplying effect," explains Serody. "Unfortunately, even if a researcher's findings are novel, even groundbreaking, if they don't have enough money to pay for their research, it's difficult for them to validate their work to potential financial suitors."

Serody is now the associate director of translational science at UNC Lineberger and a medical oncologist in the UNC Lineberger Leukemia and Lymphoma Multidisciplinary Care Program. When asked why he's stayed at UNC Lineberger for 26 years, Serody says his family has put down roots here, and he's had the opportunity to work with some amazing people. "But to be a successful researcher, that's not enough," Serody explains. "I've stayed here at UNC because of their commitment to supporting advanced research. It has been critical to my work and the resulting accomplishments."

One of those accomplishments is UNC Lineberger's new T-cell therapy clinical trials. Serody says this experimental form of immunotherapy was once only available in a handful of U.S. cancer centers but will now be located right here in Chapel Hill. Initially, a trial will open for Hodgkin lymphoma, followed by acute lymphoblastic leukemia and additional cancers as the program expands. "We use healthy cells from a patient's own immune system, multiply them in a state-of-the-art 'clean' facility, and then infuse them back into the patient's blood," explains Serody. "These super-cells then seek out the cancer cells and launch a precise immune attack against them. T-cell therapies have shown remarkable results in early clinical trials against some advanced childhood and adult leukemia patients who had run out of therapy options. Thanks to combined external investments of $5 million, we are giving hope to people where, before, there was none."

Dr. Serody received four modest seed grants early-on in his career at UNC. These monies morphed into significant investments by external agencies, which led to successful cancer research.

- 1994: A seed grant of $12,000 led to T-cell immunotherapy research to fight leukemia.
- 2000: A seed grant of $30,000 led to two additional grants from the National Institutes of Health (NIH) totaling nearly $1 million. Serody's lab used the funds to develop drugs that help prevent graft-versus-host-disease (GVHD) in cancer patients.
- 2002: A seed grant of $25,000 leveraged $1.6 million in NIH funding, which was used to repurpose two existing drugs that greatly benefitted breast cancer research.
- 2005: A seed grant of $50,000 led to an NIH "R21" Exploratory/Developmental Research Grant, as well as a Susan G. Komen Grant for the development of a vaccine therapy for breast cancer.

Private Support Fuels Progress

We are grateful to the many generous donors who share UNC Lineberger's commitment to investing in early stage research. Since the inception of the Seed Grant Program in 1986, donors have contributed more than $7 million and supported 300 seed grants. UNC Lineberger currently has 41 permanently endowed, named seed grant funds:

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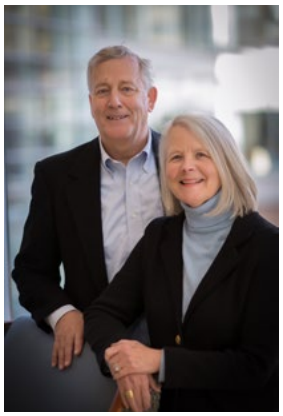


Monty and Nancy White: Putting Down Roots, Planting the Seeds of Discovery

Monty and Nancy White met as undergraduates at UNC-Chapel Hill, and like most Tar Heels, the couple's devotion to the place we call "Blue Heaven" has become stronger through the years. "Even after we graduated from Carolina in 1970, we found ourselves coming back time and time again, attending sporting events and enjoying the company of good friends," says Nancy. "We have roots here. It's always been our home-away-from-home."

The Whites now reside in Raleigh, where they own a farm filled with horses, dogs, burros, a goat and a chicken. "The animals outnumber the humans!" Monty says with a smile. "Our daughters Anna and Sydney grew up and moved away, but we still have lots of critters to keep us company." Monty grew up in Raleigh, working in his grandfather's automotive parts business during summer vacations and in the years following his graduation from UNC. The family eventually sold the automotive parts business to CARQUEST, and then in 1987, he and his brother Bill, also a UNC alum, began a real estate company called White Oak Commercial. "That's when Nancy and I began investing more of our time, energy and resources into the academic and research needs of the university."

For years, Nancy has been active on various UNC boards, including The Institute for the Environment and the College of Arts and Sciences. In 1998, Monty and Nancy were asked to join the UNC Lineberger Board of Visitors, and they happily accepted the invitation. "Cancer has directly affected our lives in very personal ways," says Nancy. "Monty's father died of lung cancer when he was 71, and I lost my mother to the same disease when she was just 69. My father passed away from melanoma at age 93. As you can imagine, UNC Lineberger's cancer research is a cause near and dear to our hearts."

In 2003, Monty and Nancy established the White Seed Grant Fund, which was designed to provide seed grant support for UNC Lineberger faculty research. The couple agrees it is one of the smartest investments they've ever made.

"When Nancy and I attend Lineberger board meetings, we get excited hearing about cutting edge technology, new clinical trials and lives being saved," says Monty. "We realize there is hope. Researchers and physicians are making progress in fighting this horrible disease, and scientific breakthroughs are happening right here in Chapel Hill. We want to be a part of that success. One day our seed grant fund could help spark a discovery that leads to a cure. That is money well-spent."

Seed Grant Award Process

The Seed Grant program is administered by senior cancer center leaders who review and critique applications. At least two peer scientific experts evaluate and score each proposal, a NIH-style study section evaluates the top-scoring proposals, and a scientific advisory board identifies top priorities for funding.

Seed grants are significant—and highly competitive—awards for our faculty researchers. Each year, we receive far more promising proposals than we are able to fund.

In 2015, with input from UNC Lineberger faculty and internal and external advisors, we revised the existing program to add two tiers of award that are larger in scope than those previously offered. The "regular" seed grants became Tier 1 Pilot Grants ($50,000); to these were added Tier 2 Stimulus Grants ($100,000-$200,000) and Tier 3 Multi-Project Grants (up to $400,000). We also added targeted RFAs to the mix, to stimulate proposals in new, high-priority areas.

With award recipients from a wide variety of departments and disciplines, the Seed Grant Program reflects one of UNC Lineberger's greatest strengths—multidisciplinary depth. UNC Lineberger is the largest research entity at the University of North Carolina, with approximately 300 scientists from 25 departments, including all five health affairs schools (medicine, public health, dentistry, nursing and pharmacy) as well as the College of Arts and Sciences. The Seed Grant Program encourages collaboration across campus as our faculty members work to combat cancer from all directions.

2014-2015 Seed Grant Awards

UNC Lineberger awards seed grants in three funding tiers across three research program areas:

- Clinical/Translational, which supports early-stage research that can translate basic science discovery into clinical applications.
- Basic Science, which supports research to identify cancer-driving mechanisms in cells and potential drug targets.
- Population Science, which supports innovative research in cancer prevention, early detection, health promotion, epidemiology and survivorship.

AWARD RECIPIENTS

Carey K. Anders, MD - $100,000
Dissecting the biology of breast cancer brain metastases (Clinical/ Translational - Tier 2)

Janelle C Arthur, PhD - $50,000
High-throughput in vivo approach to identify and quantify tumor-associated resident microbes (Basic Science - Tier 1)

Jeannette T. Bensen, PhD, MS - $50,415
Understanding the relationship between environmental inorganic arsenic and prostate cancer (Population Science - Tier 2)

Leah Frerichs, PhD/ Dan Reuland, MD, MPH - $50,000
Development of a Decision Aid and Patient Navigation Intervention to Address American Indian Colorectal Cancer Screening Disparities (Population Science - Tier 1)

J. Victor Garcia-Martinez, PhD - $300,000
Non-canonical approaches to cancer vaccine development (Basic Science - Tier 3)

Yanzhe Gao, PhD - $50,000
Validating Hormad1 as a Novel Therapeutic Target in Radio-resistant Cancer Cells (Basic Science - Tier 1)

William Kim, MD - $200,000
Combinatorial mTOR / SRC inhibition overcomes acquired everolimus resistance (Clinical/ Translational - Tier 2)

David S. Lawrence, PhD - $200,000
Photochemotherapy (Basic Science - Tier 2)

Chad Pecot, MD - $200,000
Fate-Mapping Cancer Cells from Lymph Nodes to Uncover Novel Metastatic Biology (Basic Science - Tier 2)

Barbara Savoldo, MD, PhD - $197,466
Exploiting the iC9 safety switch to pharmacologically modulate CD19.CAR-T cell function (Clinical/ Translational - Tier 2)

Marcey L. Waters, PhD/ David C. Williams, Jr., PhD - $100,000
Development of Stapled Peptide Inhibitors of the MBD2-NuRD Interaction to Target DNA Methylation Dependent Gene Silencing (Basic Science - Tier 2)

Claire Yang, PhD - $50,000
Social Relationships and Cancer Mortality: The Role of Inflammation (Population Science - Tier 2)

Award Abstracts

Clinical/Translational Recipients

Carey K. Anders, MD
Dissecting the biology of breast cancer brain metastases

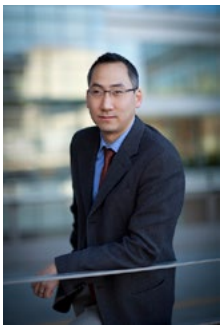
Breast cancer is the most commonly diagnosed cancer in the United States. Among women with breast cancer, about 30 percent will develop breast cancer brain metastasis. This burgeoning clinical problem is associated with poor prognosis and no approved systemic therapy. The current standard of care to treat breast cancer brain metastasis is neurosurgery and/or radiation therapy, but right now, recurrence of the cancer in the skull is inevitable, often in the face of progressive extracranial disease. And patients with certain subtypes of breast cancer - including triple negative breast cancer and HER2-positive breast cancer - commonly experience recurrence of the disease in the brain.

Treatments that can treat the cancer in the whole body to control both intracranial and extracranial disease are urgently needed. Identifying the underlying biological mechanism driving metastasis, and in particular, the mechanism driving breast cancer brain metastasis, is critical to the development of effective anti-cancer agents to both prevent and treat metastases. But such a study has yet to be performed in human tissues with matched primary breast cancers and brain metastases.

UNC Lineberger researchers have proposed using a genome-wide approach to study a range of genetic changes that occur within breast cancers that have spread to the brain. Their approach will harness high-throughput DNA whole exome sequencing to study point mutations and copy number variations in matched primary tumors, brain metastases, and non-brain metastases using surgically-resected human tumor tissues. They plan to make the following comparisons: (1) primary breast cancer or non-brain metastases to matched brain metastasis from the same patient to define brain metastasis-specific alterations; (2) primary breast cancers that metastasize versus those that do not metastasize to the brain, identifying markers for increased risk of brain metastases.

This proposal provides a novel direction for this laboratory, and expected results will undoubtedly lead to new hypotheses to foster future extramural funding. Ultimately, the researchers hope to identify novel therapeutic targets to exploit in the prevention and treatment of breast cancer brain metastases.

William Kim, MD
Combinatorial mTOR / SRC inhibition overcomes acquired everolimus resistance



About 65,000 new cases of the most common kidney cancer type, renal cell carcinoma, occur each year in the United States, and the incidence of the disease is rising. Of the types of renal cell carcinoma, clear cell renal cell carcinoma is the most common histologic subtype.

While clear cell renal cell carcinoma is notoriously resistant to cytotoxic chemotherapy, a better understanding of the molecular biology underlying renal cell carcinoma has led to the development of targeted therapies for these tumors. Those targeted therapies can be broadly grouped into the categories of VEGFR and mTOR inhibitors. While mTOR inhibition

prolongs survival, the actual tumor response rate is only 5 percent -- suggesting robust resistance mechanisms within the cell to these drugs.

UNC Lineberger researchers believe they have found a potential mechanism that underlies the resistance to these drugs. Specifically, they found that mTOR inhibition results in upregulation of cytokines, which they have termed “cytokine reprogramming” and upregulates the TYK2/SRC pathway to promote acquired resistance to mTOR inhibitors.

The award will fund research to comprehensively characterize mTOR inhibitor-induced cytokine reprogramming as well as the therapeutic value of combinatorial targeting of mTOR and SRC, using a novel genetically engineered mouse model clear cell renal cell carcinoma. In aggregate, the research will explore the innovative concept of cytokine reprogramming, and define a mechanism of resistance to mTOR inhibition, both of which have immediate clinical applicability.

Barbara Savoldo MD, PhD
Exploiting the iC9 safety switch to pharmacologically modulate CD19.CAR-T cell function

Breakthroughs have been made in a type of cancer treatment known as immunotherapy, which harnesses the power of the body’s own disease-fighting immune system to fight cancer. A specific type of immunotherapy called CAR T-cell therapy, or chimeric antigen receptor T-cell therapy, involves genetically engineering immune cells called T-cells to be able to recognize and destroy cancerous cells. UNC Lineberger researchers want to take this research a step further by making this treatment safer.

They are working on developing genetically engineered CAR T-cells that can recognize a particular cellular marker on cancer cells called the CD19 antigen. This type of CAR T-cell has shown remarkable antitumor effects in phase I clinical trials in patients with B-cell lymphoid malignancies. However, in its current form, major caveats remain to be addressed to make this approach safely and reproducibly applicable. The treatment can be accompanied by a life-threatening systemic inflammatory response syndrome in patients who are given these cancer-fighting cells, long-term and likely unnecessary B cell failure, and graft versus host disease.

UNC Lineberger researchers believe they can develop a “safety switch” that would help control some of the negative side effects resulting from the infusion of the CAR T-cells. They believe this switch would either eliminate CAR T-cells on-demand, or control their side effects without entirely shutting down the CAR T-cells.

They are planning to test this hypothesis by pre-clinically validating the approach in a humanized leukemia mouse model. They plan to translate the proposed strategy in a phase I clinical trial of T-cells transduced with the CD19.CAR retroviral vectors infused into patients with B-cell malignancies.

Basic Science Recipients

Janelle Arthur, PhD

High-throughput in vivo approach to identify and quantify tumor-associated resident microbes

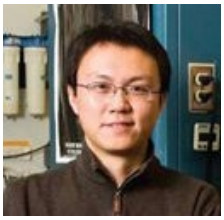
Inflammatory bowel disease patients have a high risk of colorectal cancer. Patients with these diseases harbor an altered community of micro-organisms in their intestines, including increased amounts of mucosally-adherent bacteria. However, the characteristics of microbes that allow tumors to colonize and that augment tumor growth during an inflammatory reaction are not completely understood.

UNC Lineberger researchers have a hypothesis to explain the relationship between tumor colonization, tumor growth and inflammation: that inflammation promotes colorectal cancer by augmenting colonization of the mucosa lining of the intestines with resident pro-carcinogenic bacteria. A specific subset of E. coli bacteria called "adherent-invasive E. coli," are abundant in patients with both inflammatory bowel disease and colorectal cancer, are linked to inflammation and cancer in mouse models, and often produce virulence factors that impact tumor development.

However, it has been impossible to distinguish this type of E. coli in experiments in the body without labor-intensive ex vivo culturing, however, because functional attributes of the strain that were determined through in vitro, or laboratory experments in the test tube, have been used to identify it. Therefore, it is unknown if this particular E. coli strain as identified in these in vitro laboratory experiments does actually colonize tumors better than other strains in the body. To address this, researchers have developed a novel high-throughput in vivo approach coupling genomics and gnotobiotics.

They hypothesize that human irritable bowel syndrome-associated strains of this type of E. coli are better able to colonize tumors of the colon than other strains. Their aim is to determine the extent to which in vitro-characterized clinical intestinal bowel disease-associated bacteria of this type differ from other strains in colonizing inflamed, non-inflamed, tumor and non-tumor mucosa in mice. This project will lead to independent funding to validate the tumor-promoting ability of robust colonizers in gnotobiotic models and comparative genomics to molecularly define the phenotype of this strain of E. coli. This will inform novel microbiota-based diagnostic and therapeutic approaches for intestinal bowel disease patients at risk for colorectal cancer.

Yanzhe Gao, PhD



Validating Hormad1 as a Novel Therapeutic Target in Radio-resistant Cancer Cells

Resistance to combined chemotherapy and radiation treatment is a major cause of mortality in many cancer patients. Therefore, there is an urgent need to devise novel strategies to treat radio-chemotherapy resistant cancers.

Radiotherapy and many chemotherapies kill cancer cells and normal cells by causing irreparable DNA double stranded breaks, but cancer cells often acquire resistance to these double-stranded breaks. The gaps in our knowledge of DNA damage tolerance limit our understanding of tumorigenesis and preclude effective prevention and treatment of cancer.

UNC Lineberger researchers have a broad, long-term goal to solve the problem of how cancer cells acquire resistance to double-stranded break-inducing therapies. Based on preliminary work, they have hypothesized that a certain protein called Hormad1, a “cancer/testes antigen” that is normally restricted to only sex cells in the body, is aberrantly up-regulated in many cancers. It promotes double-stranded break repair via homologous recombination. Homologous recombination allows proliferation of cells harboring spontaneously-occurring or therapy-induced DNA double-stranded breaks.

The specific aims of this research are to: (1) to define the mechanism of Hormad1-mediated homologous recombination, and (2) to determine the effects of Hormad1 expression on tolerance of therapeutic DNA damage. The proposed research is innovative because there is no paradigm for how the cancer/testes antigen affect genome maintenance, tumorigenesis or cancer therapy. The work is significant because our results will lead to novel strategies that target DNA repair and combating chemo/radio-resistant cancers but are innocuous to normal cells.

J. Victor Garcia-Martinez, PhD
Non-canonical approaches to cancer vaccine development

The body’s immune system has cells that can recognize and destroy cancer cells that have specific cancer-related markers called antigens. But cancer cells can disrupt the process that puts those markers on the cell surface – allowing them to escape detection. But now, scientist are working on using disease-causing viruses to spark an immune system response to cancer.

Scientists are looking at using viruses to fight cancer by using them as carriers. They use the natural ability of viruses to insert viral genetic material into the host cell to insert DNA into the host immune system cell. The inserted DNA causes the host cell to create cancer cell markers so the immune system can recognize and target the cancer. Recently, scientists have found that they can use cytomegaloviruses vaccine carriers to create a response by immune cells called CD8 T-cells. The immune respose is capable of preventing or clear infection of pathogens in primate models. Scientists believe that the potent, durable and therapeutic CD8 T-cell response generated by cytomegalovirus-based vaccines holds remarkable promise for the development of new vaccine strategies. However, it is currently unknown if CMV-based vectors are similarly effective at generating a human CD8 T cell response. In addition, the ability of CMV-based vaccines to control and eliminate cancer cells has not been tested.

UNC Lineberger researchers want to adapt CMV-based vaccines for use in humans, and establish the efficacy of CMV vaccines in the treatment or prevention of human cancers. Their goal is generate CMV-based cancer vaccines that provide strong and lasting immunity to cancer. They propose an innovative multi-disciplinary approach that focuses the expertise of three UNC investigators on the problem. In their first project, they plan to define the mechanism by which CMV stimulates CD8 T-cell responses to provide acute and persistent antigen recognition. Their second project aims to generate human CMV (HCMV) strains that precisely recapitulate the functional genotype of successful primate CMV-based vaccine strains, and adapts recombinant HCMV vaccine strains to express B cell lymphoma-specific antigens. And in a third project, they plan to use a novel HCMV-susceptible, fully autologous, humanized mouse model to test the efficacy of HCMV vaccine vectors against B cell lymphoma in vivo.

Together, these projects seek to translate promising results from primate models to a human model for CMV-based vaccines, and apply recent advances in CMV-based vaccine design to the treatment and prevention of cancer. The combined efforts of the projects will determine if HCMV vaccine strains induce an expanded, non-canonical CD8 T cell response capable of preventing, controlling or eradicating B cell lymphomas in the context of a fully functional human immune response.

David Lawrence, PhD
Photochemotherapy

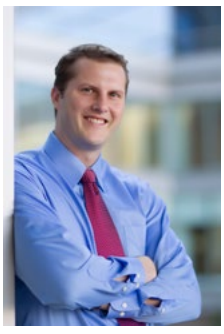
Researchers want to reduce the negative side effects of cancer treatments to other parts of the body using an innovative solution: by using light as an "on and off switch" for drugs. They believe that this strategy -- of using light-activated treatments -- would give them control over where and when drugs are activated, reducing side effects to other parts of the body.

The lab of David Lawrence, PhD, a UNC Lineberger member and Fred Eshelman Distinguished Professor of Pharmacy, developed a technology that can transform virtually any drug into a phototherapeutic while providing the means to assign specific wavelengths for the release of specific drugs from a carrier.

The researchers plan to partner with the lab of Paul Dayton, PhD, a UNC Lineberger member and a professor at the UNC-Chapel Hill and North Carolina State University Joint Department of Biomedical Engineering, to use new imaging technology. Dayton's lab has developed a new technology, called acoustic angiograp, for imaging blood flow, microvasculature, and molecular markers using ultrasound and microbubble contrast agents.

The researchers have proposed a research program that seeks to combine these state-of-the-art drug delivery and imaging technologies in a preclinical study to reengineer and subsequently image the tumor vasculature as it is remodeled for therapeutic purposes.

Red blood cells will be used as the carrier for delivering vascular modulating agents since red blood cells are biocompatible and enjoy a long circulation lifetime. The collaborative arrangement is new and could potentially prove to be transformative in cancer chemotherapy and photo-surgery. The proposed animal studies are critical for acquiring future financial support for this unfunded research program as well as for generating pre-clinical data for potential commercialization.



Chad Pecot, MD
Fate-Mapping Cancer Cells from Lymph Nodes to Uncover Novel Metastatic Biology

Distant metastases account for 90 percent of cancer-related deaths, yet the fundamental mechanisms behind cancer's spread remain poorly understood. As a result, very few drugs exist that can directly inhibit metastatic biology. Additionally, although nearly all cancers can spread to the lymph nodes, the direct role lymph node metastases have in leading to distant metastases remains a mystery. UNC Lineberger researchers want to shine a light on the role that the lymph nodes play

in the spread of cancer to more distant regions.

Current models of how cancer spreads in the body suggest the most efficient route of progression is spread through the blood, and that the lymphatic system is a dead-end. However, several studies strongly suggest that spread of cancers to the lymphatic system is by no means a dead-end. Furthermore, mechanisms that promote distant metastases from existing lymph node metastases is largely unexplored. UNC Lineberger researchers believe that the spread of cancer to the lymph nodes is important to the spread of cancer to distant regions.

This award will support research to further develop novel models of lymph node metastasis and to elucidate the key molecular pathways responsible for the spread of cancer to the lymph nodes and to more distant regions of the body. Findings from this proposal may shed light on long-standing unanswered questions in metastatic biology, and may open the door to development of new therapeutic targets that effectively block this lethal process.

Marcey L. Waters, PhD, and David C. Williams, Jr., PhD
Development of Stapled Peptide Inhibitors of the MBD2-NuRD Interaction to Target DNA Methylation Dependent Gene Silencing

Researchers want to harness the power of tumor suppressor genes to stop cells from going down the path of uncontrolled, cancerous growth. Because these genes can be silenced in cells, UNC Lineberger researchers are working to discover new strategies to keep them working.

In a new study, they are looking to disrupt a protein complex called MBD2-NuRD, which has been associated with the genetic silencing of certain cancer tumor suppressor genes. Disruption of this complex would provide a novel and promising approach to cancer treatment.

Through an analysis of the molecular details of the MBD2-NuRD complex, they found that a particular peptide, which is a small piece of one of the proteins in the complex, can block the entire complex's function. They believe they have discovered a potential therapeutic strategy for treating both β-hemoglobinopathies and cancer.

They have developed a novel strategy to screen related compounds to rapidly identify more effective inhibitors. Such an inhibitor will provide a powerful new tool to investigate the effects of this interaction on complex formation and gene silencing in the chromatin environment of cells, and how the MBD2-p66α sub-complex interacts with other components of the intact NuRD, thus providing new insights to target this pathway for cancer treatment.

Population Science Recipients

Jeannette Bensen, MS, PhD
Understanding the relationship between environmental inorganic arsenic and prostate cancer

Prostate cancer is the the second leading cause of cancer death among men in the United States. There is clear racial disparity in cancer and incidence for this disease, with African Americans seeing a substantially higher incidence and mortality than whites. UNC Lineberger researchers have hypothesized that environmental exposures to arsenic are linked to prostate cancer, and that this is an understudied and likely significant relationship that may underlie racial disparity.

Toxic metals such as arsenic are typically consumed through drinking water, and are known carcinogens linked to prostate cancer. Yet, little is known about the role of arsenic in the aggressiveness of this disease, especially among understudied groups such as African Americans. To address this question, researchers will study urine samples from men participating in the North Carolina-Louisiana Prostate Cancer Project, 50 percent of whom are African American.

The researchers believe they will be the first to describe arsenic exposure in men with prostate cancer, and to quantitatively assess the association of arsenic and influence of race in men well-characterized for the aggressiveness of the disease. This research also brings together a strong interdisciplinary team to inform identification of high-risk exposure groups and improve understanding of arsenic dosage and influence on cancer.

Leah Frerichs, PhD, and Dan Reuland, MD, MPH
Development of a Decision Aid and Patient Navigation Intervention to Address American Indian Colorectal Cancer Screening Disparities

Colorectal cancer is a leading cause of death among American Indians, and screening rates for this disease for American Indians remain lower than for other races/ethnicities. Barriers to screening include low knowledge of screening, low perceived susceptibility, and poor provider communication, among other issues.

Combining decision aids and patient navigation interventions have been effective in increasing colorectal cancer-related knowledge, intent, and test completion among underserved populations. However, a culturally-adapted colorectal cancer decision aid and navigation intervention has not been rigorously developed for American Indian people.

This award will support research to help with the development of a culturally-appropriate colorectal cancer screening decision aid and patient navigation intervention for American Indians by adapting general population versions to address relevant barriers.

Researchers plan to conduct focus groups and semi-structured interviews with American Indian patients and health care providers to examine barriers and facilitators, and to elicit specific input regarding an American Indian-focused colorectal cancer screening decision aid and patient navigation intervention. Based on these findings, the researchers will create a decision aid prototype, which they will pilot test for feasibility, usability, and impact on colorectal cancer screening knowledge, self-efficacy, and intent for American Indians.

This study will provide insights into overcoming colorectal cancer screening barriers for American Indians, and it will yield a practical tool and feasibility and efficacy data. This will provide a foundation and preliminary data for a multi-site randomized control trial testing the effectiveness of this decision aid and navigation intervention in increasing colorectal cancer screening in American Indian populations.

Claire Yang, PhD
Social Relationships and Cancer Mortality: The Role of Inflammation

Recent research in the social epidemiology of chronic disease has increasingly linked social stressors, such as social relationship deficits, to cancer outcomes. However, critical gaps exist in our understanding of the nature and strength of such links or underlying biological mechanisms.

UNC Lineberger researchers are launching an interdisciplinary biosocial study to assess the process by which social relationship stressors increase the risk of cancer mortality through inflammatory mechanisms. Drawing on both questionnaire and biospecimen data from the ongoing UNC Health Registry/Cancer Survivorship Cohort study, they aim to examine the effects of social relationship quality (social support and satisfaction with support) on risk of mortality from overall cancer as well as breast, colorectal, and other cancers; to obtain five biomarkers of inflammation using blood serum samples from enrolled patients; to estimate associations between social relationship quality and inflammation; and to test for the mediating role of inflammation in the social relationship-cancer mortality links.

The results of their work may provide new mechanistic knowledge about how specific social conditions “get under the skin” to affect cancer survival.

If you would like to learn more about the Seed Grant Program, please contact the UNC Lineberger Office of Development and Communications at lcccgiving@unc.edu or (919) 966-5905.

UNC Lineberger Comprehensive Cancer Center brings together some of the most exceptional physicians and scientists in the country to investigate and improve the prevention, early detection and treatment of cancer. One of only 45 NCI-designated comprehensive cancer centers in the nation, UNC Lineberger works to understand the causes of cancer at the genetic and environmental levels, conduct groundbreaking laboratory research and translate findings into pioneering and innovative clinical trials.

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