PATHWAYS
University of Illinois at Urbana-Champaign Fall 2015

FROM BENCH TO LIFE:
Better prevention, detection, diagnosis, and treatment
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ON THE COVER
Angela Lee, pictured above and on the cover, is one of four high school students who participated in researchHStart at the University of Illinois at Urbana-Champaign. Also on the cover are Isabella Lee (left), Callie Miller (center), and Katie Finn (right), who comprised the inaugural researchHStart group on the Urbana-Champaign campus. Read the full story on pages 8 - 9.

PATHWAYS
A publication of the Cancer Community at Illinois, University of Illinois at Urbana-Champaign. Each issue highlights the interdisciplinary and translational work being done within the community by faculty, staff, students, and external partners.

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Greetings! The Cancer Community at Illinois (CC@IL) continues to grow and thrive. The 2014-15 academic year was busy with the implementation of several educational programs and the formation of multi-PI research teams. Our cancer community continues to carve out a unique identity in the national scene with innovative programs and impactful research, especially related to science, technology, and research translation. Please read more about these exceptional achievements in this issue of Pathways.

The researchStart program for high school students launched with four amazing students, highlighted on the cover. I would like to personally thank Professors Harley, Pan, and Dobrucki for their time and commitment to this program. They served as faculty mentors and their laboratories each supported one student. Special thanks to Ira and Debra Cohen for supporting this program and their enthusiastic engagement with students.

The inaugural cohort of undergraduate Cancer Scholars completed their first year, with many impressive achievements and research experiences. The second cohort of students began the program in August. I am grateful to the many individuals and groups that make this program possible (Profs. Pool, Pan, Smith, and Carney, as well as AE3 in the College of Engineering).

We continue to work collaboratively with Carle. In announcing the Cancer Scholars for Translational and Applied Research (C-STAR) program, we hosted Carle Physician Week at Illinois. Through this activity, campus hosted Carle physicians and staff who met with faculty advisors and their students to discuss research project proposals. Consequently, the first cohort of C-STAR scholars was selected, highlighted in this issue. Collaborative training grants at both the graduate and undergraduate level were reviewed at the National Institutes of Health with great enthusiasm.

We also extend special thanks to Ms. Armgard Haken for her service to the cancer community as she moves to a new position at the university. Ms. Amanda Foley has provided invaluable assistance that allows our community to function smoothly. I am also grateful to the IHSI staff for their help with the community and production of this issue.

To each faculty, staff, student, community member, donor, friend, and partner — thank you for your continued support. We had a magnificent year! I expect only more to come as we head into 2016. Best wishes for the New Year!

Yours,

Rohit Bhargava, PhD
CC@IL Faculty Coordinator
Dr. Linda Trinh is an assistant professor in the Department of Kinesiology and Community Health and the director of the Exercise Oncology Laboratory (EOL) at the University of Illinois at Urbana-Champaign. She completed her post-doctoral training at the University of Toronto in sedentary behavior and cancer survivorship and received her PhD from the University of Alberta in exercise oncology. Her research interests are focused in the area of physical activity and cancer control from a health and exercise psychology perspective. She is particularly interested in physical activity promotion and reductions in sedentary behavior across all cancer survivor groups, essential for symptom management, improving quality of life and physical functioning, and cancer prognosis.

Trinh’s current research is focused on establishing the link between physical activity and/or sedentary behavior and health outcomes among obesity-linked (i.e., kidney, breast, colon) and older cancer survivor groups (i.e., prostate). In addition, Prof. Trinh has expertise in developing and implementing theory-driven physical activity interventions for the adoption and maintenance of physical activity throughout the cancer survivorship period. A key feature of these interventions is the inclusion of behavior change techniques through various modes of delivery including print material, face-to-face, and web-based technology. She also evaluates the feasibility and effectiveness of physical activity interventions for larger scale, randomized controlled clinical trials.

Trinh’s research involves an interdisciplinary team of experts in medical oncology, kinesiology, rehabilitation medicine, epidemiology, psychology, health promotion, and knowledge translation.

Illinois researchers continue to make strides to improve cancer detection, prevention, diagnosis, therapy, and quality of life.

The Cancer Community at Illinois (CC@IL) is the focal point for cancer-related activities across campus and helps nucleate new programs and ideas to advance cancer research and healthcare. Bringing together campus research, education, engagement, and economic development resources for collective success, we focus campus attention on cancer to build an environment that enables faculty, staff, and students to achieve goals in this area.

We also catalyze large projects, specifically focused on applying science, engineering, and technology to cancer. Believing that our unique and comprehensive strengths enable us to mount challenges that few other universities are poised to consider, we seek to develop projects and training programs that lead to significant research and translational gains while providing novel opportunities for our students.

The CC@IL is a program of the Interdisciplinary Health Sciences Initiative (IHSI) and is also supported by the Beckman Institute for Advanced Science and Technology and the Department of Bioengineering.

To learn more about our programs, activities, and opportunities and to get involved with the community, please visit our website, cancer.illinois.edu. We welcome your interest and look forward to seeing you at one of our events very soon.
Katzenellenbogens Awarded the Endocrine Society’s Koch Lifetime Achievement Award

The Society's highest honor, this annual award recognizes lifetime achievements and exceptional contributions to the field of endocrinology. It honors practicing physicians and academics worldwide whose research and advancements have contributed to the diagnosis, treatment, and understanding of diseases involving the human endocrine system, including cancers. The award includes a $25,000 honorarium and further recognition at the Endocrine Society's annual meeting in Boston in April 2016.

In addition to being active CC@IL members, Benita Katzenellenbogen is currently the Swanlund Chaired Professor of Molecular and Integrative Physiology, and John Katzenellenbogen is the Swanlund Chaired Professor of Chemistry.

Paul J. Hergenrother and Timothy Fan Anti-Cancer Drug in Clinical Trial

PAC-1, a compound discovered and developed by Cancer Community members Profs. Paul Hergenrother and Timothy Fan at the University of Illinois at Urbana-Champaign, is now being taken by cancer patients at the UI Cancer Center in Chicago as part of a Phase 1 clinical trial. Those interested in enrolling in the trial can get more information at the clinicaltrials.gov webpage: clinicaltrials.gov/ct2/show/NCT02355535

Rohit Bhargava Elected a Fellow of the Society for Applied Spectroscopy

Prof. Rohit Bhargava was recently named a fellow of the Society for Applied Spectroscopy, recognizing individual members for their outstanding service to the field of spectroscopy. His lab focuses on theory and simulation, developing new instrumentation and making chemical imaging practical for digital molecular pathology in cancer.

Bhargava has made seminal contributions to the development of infrared spectroscopic imaging and its applications. He was given the William F. Meggers Award in 2014, a national honor for most outstanding paper appearing in Applied Spectroscopy.

Princess Imoukhuede Receives Multiple Honors

Dr. Imoukhuede, assistant professor in Bioengineering and Cancer Community CC@IL member, has been selected a 2015 Cellular and Molecular Bioengineering (CMBE) Young Innovator. In addition, she is a recipient of a Basic Science Research Award from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and was given a travel award from the American Society of Nephrology.
Pet dogs may be humans’ best friends in a new arena of life: cancer treatment, said University of Illinois veterinary clinical medicine professor Timothy Fan. Physiological similarities between dogs and humans, and conserved genetics between some dog and human cancers, can allow pet dogs to serve as useful models for studying new cancer drugs, he said.

In a meeting sponsored by the National Cancer Policy Forum of the National Academies’ Institute of Medicine in Washington, D.C., Fan and 15 other experts in the field described the benefits of using pet dogs with naturally occurring (rather than laboratory-induced) tumors in early cancer drug trials.

“We have a lot of dogs in the United States, approximately 70 million, and it’s believed that about 25 percent of pet dogs will develop some form of cancer in their lifetime,” he said. “We’re using dogs to help guide drug development for people, but at the same time we’re offering new, innovative therapies that would otherwise never be available to dogs, to help them as well.”

Several attributes make pet dogs attractive subjects for such studies, Fan said. “Dogs tend to develop cancer as a geriatric population, just like people,” he said. “Because the tumors develop spontaneously, there is a heterogeneity in that tumor population, as a human being would have. The size of the tumors and the speed of growth of those tumors are comparable in dogs and human beings. So there are many attributes of a dog that develops cancer spontaneously that recapitulate the biology that we see in people.

Some studies have already begun using dogs to test new cancer therapies. Starting in 2007, for example, Fan began testing an anti-cancer drug called PAC-1 (developed by UI chemistry professor Paul Hergenrother) in pet dogs with naturally occurring lymphomas and osteosarcomas. The results in dogs allowed the scientists to advance PAC-1 as a potential therapy against human cancers. The drug is now in phase I human clinical trials at the UI Cancer Center in Chicago. Other investigational therapeutics historically piloted in pet dogs with cancer include muramyl tripeptide, an immune-stimulating agent that could not be tested in immune-deficient mice or rats with induced cancers, Fan said.

“Because you’re taking a human cancer tissue and implanting it in a mouse, that’s a foreign tissue and the mouse’s immune system will reject it,” he said. “So you have to transplant those tissues into an immunocompromised mouse. Dogs are immunocompetent, and so were an ideal study subject for testing immunomodulatory cancer therapies.

“Another example in which dogs have been important in demonstrating drug activity was an anti-cancer compound produced by the pharmaceutical company called Gilead Sciences,” he said. “The company produced a pro-drug, which must be activated by a naturally occurring enzyme in human leukocytes before it can become effective. Mice and rats lack this enzyme, but dogs have it, so the compound was tested in dogs.”

Fan also addressed the strengths and limitations of using mice and rats in preclinical trials of cancer drugs. “We’ve relied almost exclusively on murine preclinical models, and we’ve been able to show that investigational agents are very good at fighting cancer in these models,” he said. “But only about one in 10 of the agents that show great activity in mice will show similar activity in humans. So the question that we begin to ask is: Why is the hit rate so low?” It may be that laboratory-induced cancers in mice fail to mimic the natural process of cancer development in humans, he said. “The formation of cancer in those mice is very artificial, it’s very accelerated, and its’ in the context of an incompetent immune system,” Fan said. “So we can easily understand as scientists why there would be some limitations to that model.”

There also are limitations to the use of pet dogs in cancer drug trials. “There are some tumors that will not be that relevant,” Fan said. “Colon cancer, for example, is heavily driven by diet, and we don’t see much colon cancer in dogs. So pet dogs might not be a suitable model for colon cancer in humans.”

Mice and rats will likely always be used in preclinical trials of cancer drugs and do offer some significant advantages, Fan said. They are cheaper to rear, their lifespans are shorter, and genetic manipulations of these animals can produce specific and uniform traits. That genetic homogeneity allows researchers to identify how a drug agent is working “without having to deal with a lot of confounding factors,” he said. “But are human beings genetically identical? Absolutely not,” Fan said. “There is heterogeneity in the human population and in dogs. So I would argue that if your drug agent produces positive results in dogs, that would give me greater confidence that those findings would be translatable to people.”
NEW SYNTHETIC TUMOR ENVIRONMENTS
MAKE CANCER RESEARCH MORE REALISTIC

by Austin Keating, UI News Bureau

Tumors are notoriously difficult to study in their natural habitat – body tissues – but a new synthetic tissue environment may give cancer researchers the next-best look at tumor growth and behavior.

University of Illinois researchers have developed a new technique to create a cell habitat of squishy fluids, called hydrogels, which can realistically and quickly recreate microenvironments found across biology.

To illustrate the potential of their technique, the Illinois team mixed breast cancer cells and cells called macrophages that signal cancer cells to spread and grow into a tumor. They were able to observe how differently cells act in the three-dimensional, gel-like environment, which is much more like body tissues than the current research standard: a flat, hard plastic plate.

Led by materials science and engineering professor Kristopher Kilian, chemistry professor Jeffrey Moore and graduate student Joshua Grolman, the team published its results in the journal Advanced Materials.

Kilian said his team’s synthetic microenvironment lies somewhere in the middle of two extremes in the field of modeling biology: the hard plastic plate, and expensive mouse avatars that are created by injecting human tumor cells into mice.

"This is really the first time that it’s been demonstrated that you can use a rapid methodology like this to spatially define cancer cells and macrophages," Kilian said. "That’s important, because once you have that architecture, then you can ask fundamental biological questions."

University of Illinois researchers have developed a new technique to create a cell habitat of squishy fluids, called hydrogels.

Kilian said these questions range from the basic – how macrophages signal to the breast cells – to the more long-term: Can therapeutics be used to disrupt that communication?

What sets the team’s model apart from mouse avatars and hard plastic plates is that it can replicate much more accurately the sizes and shapes of the microenvironment within the patient’s problem area. The materials that pharmaceutical companies use to test drugs’ effects on cells don’t allow for three-dimensional vascularization, a network of capillaries that carry drugs and other materials throughout the body. The team’s model does, creating networks that go from straight, to snakelike, to any shape.

“Now, researchers can ask more sophisticated biological questions than they could,” Kilian said.

And they can do it quickly. The process the team came up with to produce the synthetic environments takes an estimated 15 minutes, discounting the time it takes to grow the cells and a few other steps, Grolman said.

Grolman described it as a tool that could not only help inform science, but also aid in drug screening.

“The microenvironment actually has a significant effect on how the cells respond to a drug,” Grolman said. “These companies might have the next big drug, but they might not know it.”

“The long-term vision would be: A patient goes in and finds out they’ve been diagnosed with some sort of solid tumor,” Kilian said. “You take a biopsy of those cells, you put it into this device, grow them and see how they respond to different treatments.”

The National Science Foundation and the American Cancer Society Illinois Division supported this work. Kilian and Moore are affiliated with the Carl R. Woese Institute for Genomic Biology at Illinois. Moore also is affiliated with the university’s Beckman Institute for Advanced Science and Technology and the Frederick Seitz Material Research Lab.
Four research groups at the University of Illinois at Urbana-Champaign graciously welcomed a set of ambitious, inquisitive, and forward-thinking high school students this past summer. The students’ summer mission: experiencing the every day reality of cancer research. The Cancer Community @ Illinois coordinated the researchStart program, an 8-week research and career development experience for high school students, in its first year at the Urbana campus. “We were very lucky that we actually got to expand the program from Chicago. The ACS [American Cancer Society] donors, Ira and Debra Cohen, have been big supporters of the U of I and they really wanted this to happen here in Urbana-Champaign,” said Cancer Community at Illinois faculty coordinator Rohit Bhargava.

researchStart provided hands-on, full-time work in a cancer research environment under the supervision of an established, funded investigator. The researchStart students were each mentored and trained in technical skills by graduate students, fellows, and technical staff in the investigator’s laboratory. Projects were designed by the investigator for the students to be independent, limited, and achievable in eight weeks. As active members of the research group, students were expected to participate in lab meetings, seminars and journal clubs as required by the investigator. They participated in various workshops to gain a broader understanding of cancer-related careers and develop problem-solving and presentation skills.

Without further ado, meet the impressive 2015 class of Urbana-Champaign researchStart students and learn about their summer experience:

**ANGELA LEE**

**Personal Info:** Angie is from Springfield, Illinois, and is a senior at the Illinois Math and Science Academy in Aurora, Illinois. She likes reading fiction, writing, peer tutoring, and figure skating.

**Research Lab and Project:** Angie was mentored by graduate student Shachi Mittal in Professor Rohit Bhargava’s Chemical Imaging and Structures Laboratory. Her project focused on using the chemical information provided by infrared spectroscopy to create digital hematoxylin and eosin (H&E) stains. Angie’s presentation title was “Stainless Staining.”

**How has your view of cancer and cancer research changed as a result of researchStart?**

Before this program, I used to think of cancer as a terrible disease that required painful treatments like chemotherapy, and I thought that cancer research was all about searching for a cure. But my research project falls under the category of detecting cancer, not treating it, so I’m viewing cancer from a completely new (but very interesting) perspective. As a result of the program, I’ve learned how to do things like recognize the morphological differences between normal and cancerous tissue, so I now understand cancer and cancer research from a deeper and more scientific point of view.

**How will this research opportunity prepare you for a career in research and/or medicine?**

Because of this research opportunity, I know that I want to continue doing research as an undergraduate student, with the further goal of obtaining an MD/PhD degree. Conducting research is very fulfilling, but being able to contribute to the scientific community and apply the results of my research to current medical practices is even more rewarding, which is why I want to be a physician-scientist. This research opportunity was incredible because I was working towards developing something that has clinical applications, which is similar to the type of research that I would be doing as a physician-scientist.

**What is the best part of being in this program?**

Getting to be a part of an amazing and knowledgeable lab group and doing interesting research without the stress of being an actual PhD student.
What do you think makes the University of Illinois at Urbana-Champaign special?
This summer I worked at the Beckman Institute, which was a phenomenal place to do research since it’s interdisciplinary, and many times in research, complex projects require collaboration from many people with different areas of expertise. U of I is special because the researchers are always willing to help each other and nearly everyone contributes to other peoples’ projects, not just their own. The campus has a supportive environment and cutting-edge technology for people to work on a variety of projects that they’re interested in, and as a result, the people here are developing amazing tools and greatly contributing to the scientific community.

Research Lab and Project: Mentored by Bioengineering PhD student Enrique Daza in Professor Dipanjan Pan’s MatMed Laboratory for Materials in Medicine, Callie had the opportunity to do research on pH therapy and nanoparticle drug delivery methods. Her presentation title was “Cesium Chloride pH Therapy and Micelle Drug Delivery Techniques.”

You’ve done the “academic research experience” once before. How was researchHStart different?
Working alongside some of the leading scientists, bioengineers, and researchers in the field of cancer research at Illinois has been an amazing experience. Not only did I learn valuable lab techniques, research methods and how to use many different types of lab equipment, but I also discovered my passion for searching endlessly for answers. This summer has prepared me for a lifetime of learning and my career in the sciences and medicine.

Research Lab and Project: During the researchHStart program, she worked under the direction of MD/PhD student Christian Konopka in Professor Wawrzyncie Dobrucki’s Molecular Imaging Laboratory. Bella participated in research about novel multimodal multifunctional targeted tracers and prostate cancer. Her presentation title was “A RAGE Targeted Multimodal Probe for Assessing Prostate Cancer Progression.”

What is your favorite part of being in researchHStart?
I love how this program is so much more than just a research project to complete. Along the way, you also meet amazing people, learn how it’s like to be a part of the research community, and gain skills that you can use forever.

How has your view of cancer and cancer research changed as a result of the program?
Before this program, I had never really thought about all the detailed steps that must be taken before any type of analysis is performed. For example, if you want to perform autoradiography on some tumor tissue slices, you must prepare the slices yourself, which means maintaining a mouse with a tumor growing on it, injecting the radioactive isotope, sacrificing the mouse, dissecting the tumor, and operating a cryostat to finally get the slides prepared.

How will this research opportunity prepare you for a career in research and/or medicine?
This research opportunity has not only provided me with technical research skills, but it has also prepared me mentally for what to expect in my future years. Without this opportunity, I would have gone into college still uncertain about pursuing a career in medical research, having not experienced the day-to-day life of a cancer researcher.

What do you think makes the University of Illinois at Urbana-Champaign special?
U of I has a very positive atmosphere. All the students, faculty, and staff that I’ve met have been very friendly, open, and eager to help.
C★STAR PROVIDES STELLAR OPPORTUNITIES FOR GRADUATE STUDENTS

New Program Fosters Cancer-Related, Clinically-Relevant Research
by Ashley Lawrence and Margaret Browne Huntt

The University of Illinois, through the Interdisciplinary Health Sciences Initiative (IHSI), and Carle Health System, through its Cancer Center, have debuted the Cancer Scholars for Translational and Applied Research (C★STAR) Program, thanks to cross-campus funding and matching support from Carle. IHSI, the uniting initiative for health sciences and technology on the Illinois campus, supports faculty-driven research around health challenges, by catalyzing interdisciplinary research teams in a variety of ways. C★STAR is a graduate education program that supports translational research. It is a complement to the Cancer Scholars Program (cancer.illinois.edu/undergraduate), which began during fall 2014. Together with the Beckman-Carle Postdoctoral Fellows program, the University and Carle are now providing opportunities to Illinois students at all levels.

“Illinois researchers and Carle physicians have been engaged in projects together for some time now. What was missing is student engagement. The C★STAR program provides the student access to physicians and resources to conduct innovative studies that eventually benefit patients,” explained Rohit Bhargava, professor in bioengineering and Cancer Community @ Illinois Coordinator.

This campus-wide, interdisciplinary program was developed to encourage near-term benefits to patients served by Carle and in the greater Champaign-Urbana community, and it specifically:

• Funds three to six University of Illinois at Urbana-Champaign graduate students per year;
• Provides up to three years of funding per student, subject to an annual review of progress;
• Focuses research on clinically-relevant projects related to cancers of the breast, prostate, lung, gastrointestinal, and gynecology;
• Matches students with a UI faculty mentor and a Carle physician mentor for the duration of the research project;
• Allows students and faculty to participate in grand rounds at Carle, site-alternating workshops, and joint seminars.

“The C★STAR Program represents our desire to communicate and share ideas. It allows projects to grow across both institutions. As I consider C★STAR, and the potential of the new medical school, the impact that is possible over the next few decades is extraordinary,” said James C. Leonard, MD, president and chief executive officer, The Carle Foundation.

Magesh Sundaram, MD, division head of oncology services at the Carle Cancer Center, believes even with Carle’s status as a National Cancer Institute (NCI) Community Clinical Oncology Research Program, the local cancer research enterprise can go to the next level.

“All of these graduate research projects will be a piece of the puzzle that builds the foundation toward an NIH T32 training grant. We want to grow minds here, and build both organizations so these great minds choose to stay to live here and continue their work in Champaign-Urbana,” Sundaram says.

To bolster C★STAR participation, all student applicants were encouraged to attend Carle Physician Week at Illinois, June 15-19. During this time, students had the opportunity to present their research proposals and connect with Carle Cancer Center clinicians. Physicians and staff at Carle were granted release time to meet and interact with Illinois students and faculty advisors, providing clinically-relevant feedback on proposals. Ultimately, levels of engagement were further strengthened.

“Cancer has led the way in the Carle-UI partnership, with Illinois researchers and Carle physicians collaborating on cancer-based projects for many years now. Ultimately, we’d like to see 100 percent occupancy rates of the Biomedical Research Center lab facilities on the third floor of the Cancer Center. Partnered programs like C★STAR will help achieve this,” says Neal Cohen, Director of IHSI at Illinois, the unit that manages the lab space.
In early August, the IHSI, Cancer Community @ IL, and Carle Health System announced the inaugural group of C★STAR awardees: Elizabeth Awick, Mahdieh Jadaliha, and Evijola Llabani.

Abstracts of the selected students’ proposed research are below:

**Relationships among physical activity, quality of life, and cognitive function in breast cancer survivors**
Elizabeth Awick | Faculty Advisor: Edward McAuley

This project focuses on the relationships among physical activity, quality of life, and cognitive function in breast cancer survivors. Cancer and its treatment are associated with a host of negative consequences, therefore maintaining health status in survivors is an important public health goal.

While standard treatment care may help with adverse effects of chemotherapy, such methods can be costly. Furthermore, it is unclear whether these methods can assist in attenuating cognitive impairment, an important determinant of long-term survival after a cancer diagnosis. Past research has highlighted physical activity as a low cost, lifestyle behavior that provides numerous benefits to women after a breast cancer diagnosis. However, the extant literature examining the relationship between physical activity and cognition in this cancer cohort is equivocal and fraught with methodological problems. This project is a study to determine whether any effects of acute bouts of physical activity on cognitive function (i.e., speed of processing, spatial working memory, and attention) in breast cancer survivors are maintained beyond the exercise session.

**Characterization of lncRNA to identify markers and drug targets**
Mahdieh Jadaliha | Faculty Advisor: Kannanganattu Prasanth

Human genome encodes more than 15,000 long non-coding RNAs (lncRNAs) that underscore the role of lncRNAs in biological processes. Unlike protein-coding genes, the role of lncRNAs in breast cancer (BC) is largely unknown. Therefore, functional characterization of lncRNAs may enable us to identify novel prognostic markers and drug targets. Several studies suggest that lncRNAs function by interacting with RNA-binding proteins (RBPs). The study aims to provide further insights into BC progression and cancer stem cells and may enable us to identify novel molecular targets to develop new and improved strategies for therapy and to identify novel markers for an early prognosis. Traditional cancer therapies such as chemotherapy mostly target proliferating cells. But many epithelial tumors include a very small population of quiescent, slow cycling cancer stem cells. These quiescent cells potentially contribute to chemo-resistance by surviving therapy and re-initiating tumor growth and metastasis. A further understanding of cellular quiescence and cancer stem cells is required to develop new strategies for therapy. The objectives of this project are to investigate the role of lncRNAs and RBPs in BC progression and the molecular mechanism governing cellular quiescence.

**Fluorometric microculture cytotoxicity assay for personalized medicine**
Evijola Llabani | Faculty Advisor: Paul Hergenrother

Metastatic breast cancer (MBC) is responsible for 90% of breast cancer deaths and has an overall five-year survival rate of 25%. It is extremely challenging to treat due to tumor heterogeneity and number/location of metastases. Regardless of hormone receptor status, MBC patients are treated with cytotoxic chemotherapeutics. Several single-agent drugs have been approved for MBC, but no clear consensus has emerged about which agent is superior or what drug to use for specific subtypes. Combination regimens have been extensively investigated, but due to overlapping toxicity profiles of candidate therapeutics, single-agent cytotoxic therapy remains the treatment of choice for MBC patients. Because there exists no standard-of care chemotherapeutic treatment for MBC, there is a critical need to determine the best drug for each patient and to develop novel effective combination therapies. Considering the poor prognosis and varying efficacies of single-agent therapeutics, the overall objective of this project is to inform clinician decisions about single–agent selection for treatment of each MBC patient, and to discover effective combination regimens.

These are one-year awards, however they are eligible for competitive renewal for up to three years, pending demonstrated success.

**C★STAR Long-Term Goals**

The program has these long-term, collaborative goals:

- Foster connections between Carle physician-scientists and Illinois faculty that lead to innovative research projects.
- Develop the foundation for tangible translational outcomes.
- Develop a graduate education program that is supported by federally funded training programs.
- More effectively include Carle physicians, resources, and facilities into multi-PI efforts.
- Employ the program to attract high-quality clinician-scientists to Carle and translation-focused faculty to the university.
IHSI AND CARLE: PARTNERING IN PRE-CLINICAL AND CLINICAL RESEARCH

by Sue Johnson

The Interdisciplinary Health Sciences Initiative (IHSI) and Carle Hospital have built a partnership that is fostering and supporting pre-clinical and clinical research via the Biomedical Research Center (BRC). The BRC, located on the third floor of the Mills Breast Cancer Institute at Carle, unites the clinical resources of Carle with the scientific resources of the University of Illinois to create a laboratory setting where cutting-edge medical research is conducted.

The BRC includes over 9,000 square feet of Biosafety Level 2 laboratory space with modular benchtops that can be customized to the unique specifications of a particular research group. Tor Jensen, director of the BRC, said the space provides researchers and clinicians the ability to work in close proximity with one another to solve real-world challenges.

“It is exciting to see the range of work that is being done in the BRC,” Jensen said. “From clinical diagnostics and targeted cancer treatments to microfluidic assays for measuring biomarkers in sepsis, the research being conducted at the BRC is yielding new discoveries that are only possible with the clinical and academic partnerships that are the cornerstone of the BRC.”

In addition to state-of-the-art lab space, the BRC provides cell culture, microscopy, and Fluorescence Activated Cell Sorting (FACS) in the facility. The BRC’s tissue procurement services provide clinical samples for advanced research and can provide prep-to-research support for clinical samples. The knowledgeable BRC staff is also available to assist with biosafety and project registration paperwork, protocol, and IRB concerns.

For more information about the BRC, contact the Interdisciplinary Health Sciences Initiative at healthinitiative@illinois.edu.

ILLINOIS FACULTY PRESENT AT CENTRAL ILLINOIS CANCER SYMPOSIUM

The third annual Central Illinois Cancer Symposium was held on Friday, August 14, at Carle Foundation Hospital’s Pollard Auditorium. This symposium is an annual event for physicians, nurses, and other health care professionals to receive the latest updates in cancer screening, diagnosis, and treatment. The program was kicked off by Magesh Sundaram, MD, and featured talks from a wide range of Carle physicians.

The program also featured talks from University of Illinois faculty members Rohit Bhargava, PhD, and Stephen Notaro, PhD. Bhargava, a professor in the Department of Bioengineering, presented “Cancer: Technology to the Rescue.” Dr. Notaro, a lecturer in the Department of Community Health, presented “Delivering End of Life Discussions.”
A world of natural beauty and tranquility aptly describe Allerton Park and Retreat Center in Monticello, Illinois. That beauty and tranquility greeted a group of guests who visited the center on May 9, to discuss cancer survivorship and what it means for individuals, families, and caregivers. Jointly sponsored by Carle Foundation Hospital and the University of Illinois, the event brought together cancer survivors from throughout Illinois for a day filled with workshops and activities. Kimberly Harden, a social worker at the Carle Cancer Center and the event organizer said, “This is the first of what we hope will become an annual event. We hope to empower the survivors’ community that we serve by offering them an opportunity to interact with each other and learn information that could impact their lives positively.” Survivorship programming is an important part of treatment at Carle Cancer Center, where patients receive comprehensive care and additional support beginning from diagnosis to well after a patient has completed treatments. Providers and staff connect patients to education, support groups, financial advising, nutritional services and other resources intended to help patients feel stronger during care and thrive afterward.

Elizabeth Jeffery, Professor Emerita of Nutrition and Professor Emerita of Pharmacology at the University of Illinois at Urbana-Champaign, took to the podium after breakfast, introductions, and welcome remarks. Dr. Jeffery’s keynote, “Broccoli and Other Foods that Help the Body Return to Health” informed the audience about the benefits of various foods such as broccoli and tomatoes. Her address was followed by a series of breakout sessions on financial planning and art therapy. Another session on Nordic Walking took participants on a tour of Allerton’s grounds.

Dr. Sandra Ettema, a faculty member in the Southern Illinois University School of Medicine’s Division of Otolaryngology-Head and Neck Surgery, who specializes in voice, swallowing, and pediatric disorders, followed a vegetable-filled lunch with the afternoon’s keynote address, “Cancer Survivorship: Is It in Your Genes?” Her talk looked at the role of genetics in a patient’s road to recovery. Attendees then moved to the afternoon breakout sessions on mindfulness meditation, cooking, and sex and cancer. Event attendees said the day was informative and that they “had a great time.” Participants also commented that “all the breakout sessions sounded wonderful; it was hard to make a choice.” Overall, the event had just the desired outcome, as shown by numerous positive comments from audience members about the day, including, “great topics, great socialization.”

Elizabeth Jeffery, PhD

Sandra L. Ettema, MD, PhD, CCC-SLP

Dr. Sandra Ettema earned her medical degree and doctoral degrees through the Medical Scholars Program at the University of Illinois (2002, 1999). She also earned her bachelor’s and master’s degrees at the University of Illinois (1993, 1991). In 2010, Ettema was diagnosed with breast cancer found to be BRCA2+. She has an extensive family tree with numerous other family members that have also been affected by the BRCA2+ gene mutation. Ettema is an avid educator and feels obligated to tell her story to as many people as she can, as she inherited the BRCA2+ gene mutation from her father. Family history on both sides is very important to be aware of when obtaining a health history from someone at risk for or diagnosed with breast cancer. Ettema has completed her cancer treatment including surgery, reconstruction, chemotherapy, and radiation, and is five years cancer-free as of April 2015. Dr. Ettema rejoined the faculty of Southern Illinois University in 2014 as an assistant professor in the Division of Otolaryngology-Head and Neck Surgery, specializing in voice, swallowing, and pediatric disorders, after being in private practice for a few years. She is also a member of SIU HealthCare, the medical school’s practice group, as well as a visiting professor at the University of Illinois’ College of Medicine.
The track inside the Armory building at the University of Illinois at Urbana-Champaign welcomed footsteps of determination for the 2015 Colleges Against Cancer (CAC) Relay For Life. More than 1,100 volunteers, many of them students, arrived with pillows and blankets to set up camp for the 12-hour event.

The incoming president of Illinois’ CAC chapter, Kayla McCraren, said it can be difficult to keep a college crowd through the entire relay, but the funds raised prove the staying power of this year’s participants. “While numbers may change, we definitely have raised over $125,000,” McCraren said. “Raising this kind of money in one night is incredibly moving, especially since it is something that my peers accomplished.”

During the opening ceremonies, CAC presented fellow fundraising organizations Illini 4000 and The Portraits Project with a plaque in recognition of their contributions to this year’s relay. In addition to local and regional American Cancer Society speakers, CC@IL faculty coordinator Rohit Bhargava shared information about the new cancer educational programs the University has developed. The event then concluded with a tribute to those directly impacted by cancer.

“All 12 hours are unique in their own right, but one of the most powerful experiences is walking the Luminaria ceremony,” McCraren said in referring to the illuminated bags that line the track. “The lights in the venue are turned off, and we ask that everyone walks the track quietly to remember those we have lost, and to honor those who have survived. It is very touching and powerful to see our community here on campus come together and walk these dedicated laps.”
Phi Gamma Nu hosted its annual Compete for a Cure on May 3, at the First Street and Stadium Drive athletic fields on the U of I campus. Hundreds took part in friendly basketball and volleyball contests.

Dustin Stern, a member of Phi Gamma Nu, launched Compete for a Cure on May 1, 2010, after the death of his mother, Pam Stern, from lung cancer. His two younger brothers, Alec and Ryan, and their father, Larry, were also at this year’s event. “It’s humbling, it’s fabulous, it’s the most amazing thing ever,” Larry Stern remarked. “That we’re six years into this and have raised over $100,000 and all in memory of my wife is unbelievable.”

Each year, members of Illini 4000 bike across the country to raise money for cancer research and patient care. As part of its mission to spread awareness of cancer issues, the organization created The Portraits Project, which documents people dealing with cancer throughout the country. “We’re actually interacting with the people, the survivors, the caretakers, the nurses, the doctors, the daughters, anyone who’s ever been affected,” said Casey Fee, director of The Portraits Project. “It’s kind of this other side that really doesn’t have a lot of exposure.”

Fee also learned that for some participants, the act of telling their stories was liberating, even cathartic. “After the portrait the people will say, ‘This is really therapeutic. I don’t have the space to talk about this, or share my knowledge or give my advice about how I went through it.’” Fee added. “It was kind of a new way for people to spread hope and awareness.”

The Portraits Project held a reception April 12 at the Channing Murray Foundation on the University of Illinois at Urbana-Champaign campus.
Freshman Cancer Scholar Christian Pressnall, left, and graduate student Matthew Kole manage the CC@IL table at the Beckman Institute Open House on March 13. The Cancer Community unveiled both the new high school cancer research program, researchHStart, and the spring edition of Pathways.

The biennial two-day event featured more than 30 exhibits highlighting the pioneering interdisciplinary research done at the University of Illinois. Open to the general public, the event brought in several school groups in addition to students and staff associated with the university.

Steven Gonzalez Jr., founder of The Survivor Games, was first diagnosed with cancer after a camping trip in sixth grade. Now in his early 20s, Gonzalez is drawing on his personal experience to develop a virtual arcade designed to help kids with cancer build friendships, find confidence, and gain strength in a safe, supportive network of peers facing the same health issues. Gonzalez said he was inspired to develop this project because during his treatment he “felt isolation, but video games helped create a sense of normalcy” in his world.

Gonzalez, Jr. talked about his journey with cancer and his project during a seminar sponsored by Cancer Community at Illinois, the Interdisciplinary Health Sciences Initiative, and the Beckman Institute for Advanced Science and Technology. He was joined by Eddie Gonzalez-Novoa, a colleague working with Gonzalez to bring The Survivor Games vision to a much larger community. After the seminar, a roundtable discussion brought together Illinois faculty, staff, and students to explore possible areas of collaboration.

On an April day, volunteers sat on a stage in green capes as crowds cheered, music blared, and clumps of hair fell to the ground at the Student Dining and Residential Programs Building on the Urbana campus. These volunteers were participating in St. Baldrick's Shave for the Brave, an international foundation launched in 2004 to raise money for fighting childhood cancer.

John Wiencek started the Illinois chapter of St. Baldrick’s seven years ago when a sophomore, and since then it has continued to grow. Now headed by his younger brother Matt, a graduating senior, this year’s event raised over $14,000.

First-year Illinois student Sheel Vasavada began planning to participate in Shave for the Brave more than two years ago. She said she was drawn to the fundraiser out of frustration with how underfunded childhood cancer research is and asked her uncle, Anand Buch, to join her. The majority of the 28 head-shaving volunteers were men, but Vasavada wasn’t frightened by the idea of donating her long brown hair. “I don’t have a right to be scared, because my hair is going to grow back, but there are kids whose hair [might] not grow back.” Buch, a 1993 Illinois alumnus, looked at his newly-shaven niece proudly. “She’s always been my game changer, ever since she was little,” he said.
Researchers have found an easy way to produce carbon nanoparticles that are small enough to evade the body’s immune system, reflect light in the near-infrared range for easy detection, and carry payloads of pharmaceutical drugs to targeted tissues. Unlike other methods of making carbon nanoparticles—which require expensive equipment and purification processes that can take days—the new approach generates the particles in a few hours and uses only a handful of ingredients, including store-bought molasses. The researchers, led by University of Illinois bioengineering professors Dipanjan Pan and Rohit Bhargava, report their findings in the journal *Small*.

“If you have a microwave and honey or molasses, you can pretty much make these particles at home,” Pan said. “You just mix them together and cook it for a few minutes, and you get something that looks like char, but that is nanoparticles with high luminescence. This is one of the simplest systems that we can think of. It is safe and highly scalable for eventual clinical use.” These “next-generation” carbon spheres have several attractive properties, the researchers found. They naturally scatter light in a manner that makes them easy to differentiate from human tissues, eliminating the need for added dyes or fluorescing molecules to help detect them in the body. The nanoparticles are coated with polymers that fine-tune their optical properties and their rate of degradation in the body. The polymers can be loaded with drugs that are gradually released. The nanoparticles also can be made quite small, less than eight nanometers in diameter (a human hair is 80,000 to 100,000 nanometers thick).

“Our immune system fails to recognize anything under 10 nanometers,” Pan said. “So, these tiny particles are kind of camouflaged, I would say; they are hiding from the human immune system.” The team tested the therapeutic potential of the nanoparticles by loading them with an anti-melanoma drug and mixing them in a topical solution that was applied to pig skin. Bhargava’s laboratory used vibrational spectroscopic techniques to identify the molecular structure of the nanoparticles and their cargo. “Raman and infrared spectroscopy are the two tools that one uses to see molecular structure,” Bhargava said. “We think we coated this particle with a specific polymer and with specific drug-loading – but did we really? We use spectroscopy to confirm the formulation as well as visualize the delivery of the particles and drug molecules.”

The team found that the nanoparticles did not release the drug payload at room temperature, but at body temperature began to release the anti-cancer drug. The researchers also determined which topical applications penetrated the skin to a desired depth. In further experiments, the researchers found they could alter the infusion of the particles into melanoma cells by adjusting the polymer coatings. Imaging confirmed that the infused cells began to swell, a sign of impending cell death.

“This is a versatile platform to carry a multitude of drugs – for melanoma, for other kinds of cancers and for other diseases,” Bhargava said. “You can coat it with different polymers to give it a different optical response. You can load it with two drugs, or three, or four, so you can do multidrug therapy with the same particles.”

“By using defined surface chemistry, we can change the properties of these particles,” Pan said. “We can make them glow at a certain wavelength and also we can tune them to release the drugs in the presence of the cellular environment. That is, I think, the beauty of the work.” The research team included faculty members in bioengineering, chemical and biomolecular engineering, chemistry, electrical and computer engineering and mechanical science and engineering; and researchers in the Illinois Sustainable Technology Center and the Materials Research Laboratory at Illinois. Pan and Bhargava are faculty members in the Beckman Institute for Advanced Science and Technology at Illinois, and are affiliated with Carle Foundation Hospital.


Among women, breast cancer is the most commonly diagnosed cancer and the second highest cause of cancer related mortality. Therefore, there is a strong impetus to identify chemopreventative and lifestyle modification strategies that reduce the incidence and progression of this disease. This paper reviews our current understanding of how cholesterol might impact breast cancer pathophysiology. Elevated circulating cholesterol has been shown to be a risk factor for breast cancer relapse, while cholesterol lowering drugs such as statins are protective. Since intracellular cholesterol homeostasis is tightly regulated, it was unclear how cholesterol impacted breast cancer. However, we and others have recently shown that a primary cholesterol metabolite, 27-hydroxycholesterol (27HC) has the capacity to signal through the estrogen receptor and liver X receptor to induce breast cancer proliferation and aggressiveness respectively. A series of experiments reviewed in this paper demonstrate strong evidence that 27HC is the mechanistic link between obesity, elevated cholesterol and breast cancer. This work highlights the therapeutic potential for cholesterol or 27HC lowering drugs.

Ruopeng An: Assistant Professor, Department of Kinesiology and Community Health

One in three patients with cancer experiences some type of mental disorder, such as depression. Antidepressants have been found to be effective in treating depressive symptoms in cancer survivors. However, little is known about the prevalence and trends of antidepressant use among cancer survivors. The present study tracked the trend of antidepressant use from 1999 to 2012 among cancer survivors 20 years of age and over using data from the National Health and Nutrition Examination Survey. During 1999-2012, the average rate of antidepressant use among cancer survivors was 18.25%, compared to 12.31% among adults without a history of cancer. The prevalence of antidepressant use among cancer survivors increased rapidly and nearly doubled from 10.64% in 1999-2000 to 20.8% in 2011-2012. In comparison, a smaller increase (7.2 percentage points) was observed among adults without a history of cancer. The trend in antidepressant use demonstrates some nonlinearity. Among cancer survivors, the rate temporarily declined from 21.21% in 2003-2004 to 18.63% in 2005-2006, but resumed its increasing trend thereafter. In sum, antidepressant use among cancer survivors has increased noticeably over the past decade. Future studies are warranted to examine the benefits and risk of side effects of antidepressants in treating depression among cancer survivors.
The Interdisciplinary Health Sciences Initiative (IHSI) at Illinois exists to catalyze, connect, support, and engage health sciences research across the University of Illinois at Urbana-Champaign campus. To that end, we unite researchers around health program areas, one of which is the Cancer Community at Illinois.

IHSI research development specialist Margaret Browne Huntt works to grow the Cancer Community and its collaborations and partnerships. She works directly with Steering Committee members and manages the day-to-day activities of the CC@IL.

If you would like more information about the research, education, or engagement opportunities the Cancer Community at Illinois offers, contact Margaret today.

Margaret Browne Huntt
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Research Study Guide: Building Strong Projects

To help protocols run smoothly and make partnerships as beneficial as possible, IHSI has created this guide for investigators to use as they begin down the path of collaborative research projects. Please contact Margaret with any questions about this process and how your specific research may benefit from IHSI support.

For the latest health sciences news, lecture, and event information, visit the IHSI website: healthinitiative.illinois.edu

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