Tiny exports signal big shifts in cancer tissue, researchers find, page 14.

Cancer Community @ Illinois
FROM BENCH TO LIFE:
Better prevention, detection, diagnosis, and treatment
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ON THE COVER
The imaging method allowed the researchers to fine-tune five wavelengths of light to study five distinct cancer processes, and combine them in images like this to see how they dynamically relate to one another. Image courtesy of Stephen Boppart and Haohua Tu.

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.

Director: Rohit Bhargava
Project Manager: Margaret Browne Huntt
Managing Editor: Sue Johnson
Contributing Writers: Liz Ahlberg Touchstone, Sarah Banducci, Margret Berg Miller, Margaret Browne Huntt, Sue Johnson, Marcia Pool, Diana Yates, Adle Zhai, Beckman Institute Communications Office
Photography: Amanda Foley, Ashley Lawrence, L. Brian Stauffer, Thompson-McClellan Photography
Design: Jason M. Bentley

BECKMAN INSTITUTE
FOR ADVANCED SCIENCE AND TECHNOLOGY

Department of Bioengineering

ENGINEERING AT ILLINOIS
To the Cancer Community at Illinois - our faculty, staff, undergraduate and graduate students, student groups, external partners, and community members and other supporters, THANK YOU for a wonderful year. We should be very pleased as, together, we have accomplished much this academic year. I look forward to us working together in future community activities to take cancer research and education to an even higher level at Illinois.

The achievements and developments from this year are noteworthy. Each year, we continue to welcome new faculty and staff members to our community. Our annual community meeting that was held in October provided a progress report and outlined plans for the future. Many thanks to the speakers for your continued engagement and support. Our researchers won kudos for exceptional studies, were awarded many prestigious awards and provided exciting advances that can change cancer care and lives in the future. Together, our faculty were awarded national centers and initiated many exciting new studies.

I would like to once again recognize the generous support of Ira and Debra Cohen and collaborations with the University of Chicago and University of Illinois at Chicago for the researcHStart program. Thank you to Carle Foundation Hospital for their support of the C★STAR program which is making excellent progress. The Mayo Clinic & Illinois Alliance continues to be strong and multiple studies with our partners at UIC are ongoing. Finally, the exciting new college of medicine at the University formulated a curriculum and selected a new Dean, Prof. King Li, who is a distinguished cancer researcher.

Exciting times indeed for our community! We are all eagerly looking forward to what lies ahead for us.

Robert Bhargava

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**STEERING COMMITTEE**

- **Stephen A. Boppart**
  Electrical & Computer Engineering; Bioengineering
- **John Erdman**
  Food Science and Human Nutrition
- **Timothy M. Fan**
  Veterinary Clinical Medicine
- **Barbara Fiese**
  Human Development & Family Studies
- **H. Rex Gaskins**
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  Kinesiology & Community Health
- **Zeynep Madak-Erdogan**
  Food Science & Human Nutrition
- **Erik Nelson**
  Molecular and Integrative Physiology
- **William D. O’Brien, Jr.**
  Electrical & Computer Engineering
- **Edward J. Roy**
  Pathology
- **Margaret Browne Huntt**
  Cancer Community (Ex-officio)
The Cancer Community is pleased to welcome three new faculty to our group: Sheeva Abbaszadeh, assistant professor in the Department of Nuclear, Plasma, and Radiological Engineering; King Li, MD, dean of the Carle Illinois College of Medicine; and Michael J. Spinella, professor in the Department of Comparative Biosciences.

SHIVA ABBASZADEH
Assistant Professor, Department of Nuclear, Plasma, and Radiological Engineering

Dr. Abbaszadeh is an assistant professor in the Department of Nuclear, Plasma, and Radiological Engineering. The goal of her research is to develop state-of-the-art technology to provide the necessary tools to visualize and detect cancer at the molecular level, and to further our understanding of disease mechanisms. This research involves radiation detection and instrumentation for molecular imaging, computational problem solving, and quantitative characterization of biological processes. She previously developed a novel high-gain, high-resolution X-ray imaging detector that is currently being pursued for commercial use in low-dose mammography where maintaining excellent image quality at high spatial resolution is crucial. The proposed technology, based on direct conversion amorphous selenium, enables better detection of small tumors and facilitates early cancer diagnosis. Shiva was also instrumental in the development of a high-resolution, high-sensitivity positron emission tomography (PET) system and associated signal processing algorithms. The preclinical system will enable imaging and evaluating novel molecular agents to improve the diagnosis and understanding of diseases. The next generation of high specificity molecular imaging probes have limited uptake, which often makes them difficult to visualize and quantify in PET. Example applications include monitoring cell trafficking for cancer metastasis and monitoring the interaction of the immune system and tumor cells over time. The proposed PET system is based on 3-D position-sensitive cadmium zinc telluride photon detectors, which have excellent spatial and energy resolution properties to address the challenging requirements for these applications.

KING LI
Dean and Chief Academic Officer, Carle Illinois College of Medicine

King Li is the inaugural dean and chief academic officer of the Carle Illinois College of Medicine. He is a renowned researcher, educator, inventor and clinician in molecular imaging and radiology. Holding 16 patents, with another six pending, he has a long track record of developing and commercializing intellectual property as well as setting up and administering large clinical and translational research programs.

MICHAEL J. SPINELLA
Associate Professor, Department of Comparative Biosciences

Dr. Spinella joined the Department of Comparative Biosciences and the University of Illinois at Urbana-Champaign in August 2016. After receiving his PhD in biochemistry in 1992 from Albany Medical College, Dr. Spinella performed training fellowships in cancer biology and molecular therapeutics at the Massey Cancer Center in Richmond, VA and at the Memorial Sloan Kettering Cancer Center in New York. He was a member of the faculty in the Department of Pharmacology at Dartmouth Medical School from 1999-2016. Dr. Spinella's laboratory is focused on the molecular genetics of cancer, especially in the areas of mechanisms of tumorigenesis, cancer therapy and drug resistance. One research focus is on uncovering mechanisms that account for the curability of metastatic testicular germ cell tumors in order to inform novel therapeutic strategies for advanced somatic solid tumors including glioblastoma and breast cancer. Other interests include the concept of differentiation therapy and the identification of mechanistic links between stem cell pluripotency, cancer and response to chemotherapy.
Based in Urbana, Illinois, Carle is a vertically integrated regional health system featuring two hospitals, a physician group, and a medical plan. Carle's mission is to serve people through high quality care, medical research, and education. Carle has 6,595 total employees and 413 physicians. We are pleased to help them welcome four new physicians who specialize in cancer.

**Welcome New Carle Cancer Physicians**

**Daniel Barnett**  
Radiation Oncologist  
Dr. Barnett attended medical school at University of Illinois College of Medicine in Urbana, IL. He completed his residency in Radiation Oncology with the University of Wisconsin, Madison, WI. He holds a PhD in Philosophy and Cell and Developmental Biology. He is an active member of the American Society of Clinical Oncology (ASCO), the American Society of Radiation Oncology (ASTRO) and the Radiological Society of North America (RSNA).

**Pratima Chalasani**  
Medical Oncologist, Hematologist  
Dr. Chalasani attended medical school at Southern Illinois University School of Medicine in Springfield, IL where she served as Chief Resident. She completed her fellowship at Gunderson Health System in La Crosse, WI. She is board certified in Internal Medicine and board eligible in Medical Oncology, as well as Hematology. She is an active member of the American Society of Clinical Oncology (ASCO) and the American Society of Hematology (ASH).

**Suparna Mantha**  
Medical Oncologist, Hematologist  
Dr. Mantha attended medical school at University of Arkansas for Medical Sciences in Little Rock, AR. She completed her fellowship with Scott and White Hospital at Texas A&M Health Science Center in Temple, TX. She is board certified in Internal Medicine and board eligible in Medical Oncology, as well as Hematology. She is an active member of the American Society of Clinical Oncology (ASCO), the American Society of Hematology (ASH) and the Texas Society of Clinical Oncology.

**Priyank Patel**  
Medical Oncologist, Hematologist  
Dr. Patel attended medical school at Smolensk State Medical Academy in the Russian Federation. He completed his fellowship at Michigan State University in East Lansing, MI and has been practicing at the Roswell Park Cancer Institute in Buffalo, NY. He is board certified in Internal Medicine and board eligible in Medical Oncology as well as Hematology. He is an active member of the American Society of Clinical Oncology (ASCO), the American Society of Hematology (ASH), European Society of Medical Oncology (ESMO), Association of American Physicians of Indian Origin (AAPI), and American Medical Association (AMA).

**About the Carle Cancer Center/Mills Breast Cancer Institute**

The Carle Cancer Center/Mills Breast Cancer Institute serves as the premier cancer treatment and support center in east central Illinois. This facility has been designed to house the comprehensive cancer program, breast center, and translational research facility, offering more resources to help patients in the fight against cancer. With the area’s largest and most specialized team of fellowship trained oncologists, surgeons and staff, patients get in for diagnosis and start treatment for their disease as soon as possible. The Carle Cancer Center provides comprehensive oncology services, including on-site nutrition services, medical genetics, nurse navigation services, social work/support groups, radiology services, palliative care support, survivorship services, and specialty clinics for a variety of disease sites. This multidisciplinary approach to care aids patients and family members in addressing the immediate and long-term effects of cancer within a culture that puts clinical trial participation as the top priority. Amongst the strengths of the Carle Cancer Center is their long-standing history of being designated and funded as a National Cancer Institute (NCI) Community Clinical Oncology Program (CCOP) since 1983 and their continuation as a National Clinical Oncology Research Program (NCORP) since 2014. Currently, there are approximately 90 cancer-based trials actively recruiting patients to advance care at Carle Cancer Center/Mills Breast Cancer Institute, with approximately an additional 110 research studies that continue to follow patients through their cancer journey post-treatment.
The University of Illinois provides state-of-the-art facilities where cancer research is conducted. Located at various sites across campus, Cancer Community members are able to conduct their work.

**Beckman Institute for Advanced Science and Technology**
The Beckman Institute for Advanced Science and Technology is an interdisciplinary research institute involved in basic research in physical sciences and engineering, and in the life and behavioral sciences. It houses the Imaging Technology Facility and the Optical Coherence Tomography Facility.

**Biomedical Research Center (BRC) at the Mills Breast Cancer**
The BRC is located on the third floor of the Mills Breast Cancer Institute at Carle. This facility unites the clinical resources of Carle with the scientific resources of Illinois to create a laboratory setting where cutting edge medical research happens daily. Resources that are available include over 17,000 square feet of Biosafety Level 2 laboratory space, modular benchtops and storage to create customized research space, cell culture, microscopy, and Fluorescence Activated Cell Sorting (FACS).

**Carl R. Woese Institute for Genomic Biology**
The Carl R. Woese Institute for Genomic Biology (IGB) is dedicated to advancing research in human health, agriculture, energy use and production, and the environment. Research at the IGB falls under one of three program areas: systems biology, cellular and metabolic engineering, or genome technology. The IGB houses a microfabrication laboratory, a plant growth facility, and a microscopy suite.

**Coordinated Science Laboratory**
The Coordinated Science Laboratory (CSL) is a premier, multidisciplinary research laboratory that focuses on information technology at the crossroads of computing, control, and communications. Led by a faculty of world-renowned experts and researchers, the CSL uses innovations to explore critical issues in defense, medicine, environmental sciences, robotics, life-enhancement for the disabled, and aeronautics.

**Frederick Seitz Materials Research Laboratory**
The Frederick Seitz Materials Research Laboratory (FSMRL) operates an extensive array of central user facilities and is widely recognized as one of the premier midscale facilities in the nation. These facilities are organized with the guiding philosophy that materials science research is most effectively advanced through a shared instrumentation mode supported by skilled professionals. The FSMRL central facilities occupy about 50,000 square feet of laboratory space. The facilities can be divided into six core areas: electron microscopy, surface analysis, x-ray scattering, laser spectroscopy, micro/nanofabrication, and computation.

**Micro and Nanotechnology Laboratory**
The Micro and Nanotechnology Laboratory (MNTL) is one of the nation’s largest and most sophisticated university-based facilities for semiconductor, nanotechnology, and biotechnology research. It is a user facility, with over 8,000 square feet of class 100 and class 1000 clean room laboratory and state-of-the-art ultra-high-speed optical and electrical device and circuit measurements.
Theoretical and Computational Biophysics Group

The Theoretical and Computational Biophysics Group is a pioneer in the realm of high-performance computing. The group maintains a wide selection of computers divided into four main categories: computing power, visualization equipment, desktop workstations, and infrastructure. The group also relies extensively on the nation’s supercomputers.

National Center for Supercomputing Applications

The National Center for Supercomputing Applications (NCSA) provides powerful computers and expert support that researchers in all disciplines can use for advanced modeling, simulation, and data analysis. The National Petascale Computing Facility (NPCF) is an 88,000-square-foot, state-of-the-art data center that houses the NCSAs Blue Waters supercomputer, as well as several other supercomputers.

Roy J. Carver Biotechnology Center

The Roy J. Carver Biotechnology Center provides state-of-the-art facilities for molecular biology research, including DNA and protein sequencing and oligonucleotide and peptide synthesis. The W. M. Keck Center for Comparative and Functional Genomics conducts research on the comparative genetic organization, evolution, and function of plant, animal, and microbial genomes and provides sequencing and oligonucleotide synthesis, DNA microarray facilities, and bioinformatics specialists. The Protein Sciences Facility aids researchers in protein sequence analysis, peptide synthesis, and 2D gel electrophoresis. Services offered by the Immunological Resource Center include the creation, purification, and immunochemical labeling of antibodies. In addition to a state-of-the art cell sorter, the Flow Cytometry Facility maintains several satellite flow cytometry machines throughout campus.

College of Veterinary Medicine

The College of Veterinary Medicine has modern clinical and basic sciences facilities for research, ranging from basic biomedical studies to applied clinical and field studies under controlled confinement and natural environmental conditions, as well as unique specialty laboratories equipped with state-of-the-art equipment.

The Center for Microscopic Imaging (CMI) provides students, faculty, and research staff with advanced instrumentation in microscopy for teaching and research. The Geographical Information Systems (GIS) Laboratory encompasses a range of technologies, including digital mapping, analysis of remotely sensed imagery, spatial statistics, and the use of global positioning systems (GPS). The Veterinary Diagnostic Laboratory (VDL) is an American Association of Veterinary Laboratory Diagnosticians (AAVLD)-accredited facility that provides fee-for-service diagnostic testing to support biomedical research. The VDL is staffed by faculty experts in the fields of pathology, molecular diagnostics, bacteriology, mycology, virology, and parasitology, who are also available for research collaborations.
Bhargava Named Agilent Thought Leader

In January 2017, Agilent Technologies Inc. presented Rohit Bhargava with an Agilent Thought Leader Award in recognition of his pioneering work in the development of infrared spectroscopic imaging, and its application to life sciences research. Bhargava, professor of bioengineering, is the founder and director of the Cancer Community at Illinois, which is slated to become the Illinois Cancer Center in 2017. The award includes funding and technology from Agilent, which will enable Bhargava to develop new applications and software to facilitate infrared analysis of histological samples, in particular for cancer detection and diagnosis.

Faculty Receive GEBI Endowed Appointments

Cancer Community faculty members were among those named for Grainger Engineering Breakthroughs Initiative (GEBI) endowed appointments. Rashid Bashir, a professor of bioengineering and a member of the 3D Micro- and Nanosystems Group at the Beckman Institute, has been named as the first Grainger Distinguished Chair in Engineering. Rohit Bhargava, a professor of bioengineering and a member of the Bioimaging Science and Technology Group at the Beckman Institute, was named as a Founder Professor of Engineering.

Boppart Receives the IEEE Award

Stephen Boppart, professor of electrical and computer engineering and bioengineering, received the IEEE Engineering in Medicine and Biology Society Technical Achievement Award.

Kong Named AIMBE Fellow; Receives Distinguished Promotion Award

Hyun Joon Kong, an associate professor of chemical and biomolecular engineering and a member of the Bioimaging Science and Technology Group at the Beckman Institute, will be inducted as a fellow into the American Institute for Medical and Biological Engineering (AIMBE). He was nominated, reviewed, and elected by peers and members of the College of Fellows for outstanding contributions to the fields of biomaterials, bioimaging contrast agents, and tissue engineering.

Cheng, Cunningham Elected AAAS Fellows

Cancer Community members Jianjun Cheng and Brian T. Cunningham are among six Illinois faculty members elected 2016 Fellows of the American Association for the Advancement of Science, chosen for their efforts to advance science applications that are deemed scientifically or socially distinguished. Cheng, the Hans Thurnauer Professor of Materials Science and Engineering was recognized “for the discovery, development and clinical translation of nanomedicines and biomaterials, especially for targeted cancer therapies.” Cunningham, a professor of electrical and computer engineering and bioengineering, and the director of the Micro and Nanotechnology Laboratory, was honored for “exceptional contributions to the advancement of photonic crystal-based biosensing.”

Imoukhuede Receives NSF CAREER Award

Princess U II Imoukhuede, an assistant professor of bioengineering, is the recipient of a National Science Foundation CAREER award for her proposal, “Identifying the role of cross-family signaling in angiogenesis.” The National Science Foundation's Faculty Early Career Development Program's CAREER Awards are prestigious and competitive awards given to junior faculty who exemplify the role of teacher-scholar through outstanding research, excellent education, and the integration of education and research within the context of the mission of their respective organizations. The program will provide five years of support.
Elizabeth Jeffery, professor emerita in the Department of Food Science and Human Nutrition, was named the 2016 recipient of the American Society for Nutrition/Dannon Institute Mentorship Award. This award recognizes nutrition educators who have demonstrated outstanding mentoring qualities by developing successful investigators of nutritional sciences.

Zeynep Madak-Erdogan, professor in the Department of Food Science and Human Nutrition, has received the 2016 Mary Swartz Rose Young Investigator Award from the American Society for Nutrition. This award is given to an investigator within 10 years of postgraduate training for outstanding research on the safety and efficacy of bioactive compounds for human health.

Paul Hergenrother, professor of chemistry, received the 2017 ACS Cope Scholar Award for innovative use and application of organic synthesis to solve critical problems at the frontiers of chemical biology and translational drug discovery.

Jeffrey Reipient of Mentorship Award

Elizabeth Jeffery, professor emerita in the Department of Food Science and Human Nutrition, was named the 2016 recipient of the American Society for Nutrition/Dannon Institute Mentorship Award. This award recognizes nutrition educators who have demonstrated outstanding mentoring qualities by developing successful investigators of nutritional sciences.

Pierce Hadley, member of the 2014 Cancer Scholars Program cohort, was named the recipient of the William R. Schowalter Award, which recognizes outstanding leadership, creativity, encouragement of others, and dedication to the college. At the Beckman Institute, he works in the Chemical Imaging and Structures Laboratory run by Rohit Bhargava, a professor of bioengineering and director of the Cancer Scholars Program. Hadley founded the Urbana campus Stereolithography Printing Organization, the mission of which is to develop 3D printed products for educational research and biomedical applications, as well as the brainstorming organization Think Illinois, which strives to create student projects and discussions across disciplines on campus.

Amy Baek, postdoctoral research assistant in the laboratory of Dr. Erik Nelson was awarded a fellowship from the Susan G. Komen Foundation for her proposal, “Elucidating the mechanisms by which a cholesterol metabolite promotes metastasis.”

Diane Ehlers of Edward McAuley’s lab, received a post-doctoral fellowship from the American Cancer Society for her proposal, “Physical activity and cognitive function does response after breast cancer.”
The Cancer Community at Illinois’ Annual Meeting was held Wednesday, October 19, 2016 at the Beckman Institute for Advanced Science and Technology.

More than 60 people gathered for a productive morning of updates on the Cancer Community at Illinois’ activities and plans. Neal Cohen, director of the Interdisciplinary Health Sciences Initiative (IHSI) and Rohit Bhargava, director of the Cancer Community at Illinois, kicked the day off with opening remarks, with Bhargava also providing an annual update. Next the inaugural Carle Illinois College of Medicine dean, King Li, provided a keynote address and shared his vision for the innovative, engineering-based college of medicine.

The agenda also included two panel discussions. The first was “Collaborative Campus-Based Initiatives and Programs.” This panel included Paul Hergenrother (chemistry), Brian Cunningham (biology), and Ravi Iyer (CCBGM). The second panel was titled, “Working with Clinical Partners.” This panel was moderated by emeritus professor John Erdman (food science and human nutrition) and included Kesh Kesavadas (HCESC), Kendrith Rowland (Carle), and Bryan White (Mayo Clinic and Illinois Alliance).

The Interdisciplinary Health Sciences Initiative (IHSI) has been working hard to make its website a hub/portal for resources that are helpful to researchers in the health sciences. This semester IHSI’s website launched the “Research Resources” section, a compilation of information and links that support and catalyze clinical and translational research. The information is compartmentalized in easy to find sections including Health Science Funding Opportunities, Cancer, Biostatistical Services, and more.

The IHSI Research Resources will continue to expand and will be updated frequently. If you don’t see what you are looking for, or if you have a suggestion for information to include, please email healthinitiative@illinois.edu.
During the spring 2017 semester the Cancer Community at Illinois presented a Faculty Seminar Series. Each session featured a group of faculty giving brief individual talks, followed by a period for Q&A. Rex Gaskins, chair of the Cancer Community steering committee, served as moderator for the sessions. All sessions were held at the Health Care Engineering Systems Center (HCESC). The speakers for the three seminars are as follows:

**Thursday, March 2 | 3 – 4:30 p.m.**
- **Stephen Boppart** (Bioengineering, Electrical and Computer Engineering)
  - Intraoperative Label-Free Optical Imaging of Breast Tumor Margins and the Tumor Microenvironment
- **Timothy Fan** (Veterinary Medicine)
  - Leveraging Comparative Oncology for Expediting Drug Development

**Thursday, April 6 | 3 – 4:30 p.m.**
- **Rohit Bhargava** (Bioengineering)
  - Chemical Imaging for Digital Molecular Pathology
- **Rex Gaskins** (Animal Sciences)
  - Microbial Sulfur Metabolism and Colorectal Cancer Risk
- **Edward Roy** (Pathology)
  - Immunotherapy of Gliomas
- **T. Kesh Keshavadas** (Health Care Engineering Systems Center)
  - Precision Surgery Through Robotics

**Thursday, May 4 | 3 – 4:30 p.m.**
- **John Erdman** (Food Science and Human Nutrition)
  - Impact of Dietary Lycopene or Tomato Consumption on Prostate Cancer Risk
- **Barbara Fiese** (Family Resiliencey Center)
  - Nutritional Challenges for Cancer Survivors: Food Security as a Potential Pathway
- **William Helferich** (Nutritional Sciences)
  - Soy Components and Breast Cancer—A Double-Edged Sword
- **William O’Brien** (Quantitative Ultrasound)
  - Early Detection and Translation

The jointly funded-seed funding program that was developed between Carle and the University of Illinois at Urbana-Champaign has just announced a call for proposals for its second round of funding. The program provides a funding infusion to support and encourage new lines of research and collaboration among Carle physicians and Illinois investigators.

The Carle Illinois Collaborative Research Seed Funding Program welcomes research proposals from a broad array of disciplines and clinical areas. This round of funding will focus on four priority areas: population health, imaging, data analytics, and rural health. In these areas the aim is to: foster collaboration between Carle clinicians and Illinois researchers; support innovative approaches to the challenges facing clinical care; promote opportunities to improve positive health outcomes; enable collaborators to acquire preliminary data for a subsequent external collaborative grant applications; and stimulate significant external research or clinical trial funding from either government or corporate sources. Applicants can apply for up to $50,000. The program anticipates making up to five awards, but the number and size of the awards will be determined by the size of the projects and the available budget. Proposals can be submitted beginning March 15, 2017 and will be accepted through April 28, 2017. Award notifications will be made by June 30, 2017.
By Diana Yates, University of Illinois News Bureau

A new study reveals that African-Americans have measurable differences in the number and type of bacteria that live in the colon—and those differences are related to their higher-than-average colon cancer risk. The study, reported in the journal Gut, looked at colonic tissue biopsies from 197 African-Americans and 132 non-Hispanic whites collected over a two-year period ending in 2012.

The study found that African-Americans have more sulfide-producing bacteria in their colon than non-Hispanic whites in the U.S. These microbes are a normal part of the gut ecosystem, however an overabundance of sulfide in the colon can lead to inflammation and DNA damage, said University of Illinois animal sciences professor Rex Gaskins, who led the new research with Nathan Ellis, who was at the University of Illinois at Chicago at the time of the study. Ellis is the scientific director of the Cancer Biology Research Program at the University of Arizona, Tucson.

“We found that African-Americans have an increased abundance of bacteria that make hydrogen sulfide, which we demonstrated more than a decade ago to be a potent genotoxin,” Gaskins said. The study also revealed that Bilophila wadsworthia, a bacterium that produces hydrogen sulfide from the amino acid taurine, was significantly more abundant in African-Americans with colon cancer than in their healthy counterparts. “These bacteria are using nutrients associated with an animal-based diet,” Gaskins said.

African-Americans have significantly higher incidence of colon cancer than other Americans. In 2013, there were 33.5 colon cancer cases per 100,000 African-Americans, compared with 26.8 per 100,000 whites. “We are beginning to connect the dots between these dietary factors and one’s risk of developing colon cancer risk,” he said. “Our research adds to the evidence that the microbes that inhabit the colon are part of the equation and should not be overlooked.” The National Cancer Institute and the American Cancer Society supported this research.

By Liz Ahlberg Touchstone, University of Illinois News Bureau

“By hijacking a cancer cell’s own metabolism, researchers have found a way to tag and target elusive cancers with small-molecule sugars. This opens treatment pathways for cancers that are not responsive to conventional targeted antibodies, such as triple-negative breast cancer.”

Researchers found a way to mark the cells using a class of small-molecule sugars called azides. Once metabolized in the cell, they are expressed on the surface, and can be targeted by a molecule called DBCO. The researchers tested the azide-based targeting system in mice with tumors from colon cancer, triple-negative breast cancer and metastatic breast cancer. “We found the tumors had very strong signals compared with other tissues,” Cheng said. “For the first time, we labeled and targeted tumors with small molecule sugars in vivo, and we used the cancer cell’s own internal mechanisms to do it.”
Researchers at the University of Illinois report they can alter blood cell development through the use of biomaterials designed to mimic characteristics of the bone marrow. The findings, reported in the journal Science Advances, are a first step toward developing more effective bone marrow treatments for diseases like leukemia and lymphoma.

Blood cells flow throughout the body delivering life-supporting oxygen and nutrients. As these cells are used and recycled they are regenerated by bone marrow, the soft tissue inside the body’s long and hollow bones.

Certain regions of bone marrow contain hematopoietic stem cells, the precursors of all blood and immune cells, said University of Illinois chemical and biomolecular engineering professor Brendan Harley, who led the research with postdoctoral researcher Ji Sun Choi.

One of the major tools that oncologists use to treat leukemia and lymphoma involves transplanting HSCs. The donor stem cells must locate marrow cavities and start producing blood and immune cells. However, there is a limited quantity of available donor HSCs and the success rate of transplantation is low.

“The goal is to create better tools to both expand the number of donor HSCs and improve their capacity to repopulate the bone marrow after transplantation,” Harley said.

Harley and Choi gathered samples of HSCs from mice and then grew them in the lab using biomaterials engineered to mimic some of the extracellular matrix properties of the native bone marrow.

Their goal was to examine how these engineered systems could alter the HSCs’ capacity to proliferate and differentiate to become blood cells.

The researchers examined two main elements of the matrix that regularly interact with HSCs: collagen and fibronectin. They found that the HSCs that were exposed to collagen proliferated more rapidly but that they had differentiated, meaning they were no longer stem cells. When exposed to fibronectin, the stem cells proliferated less rapidly, but were able to maintain their stem cell-like nature.

“With the right combination of stiffness in the matrix and the presence of fibronectin, we identified a class of biomaterials that show promise for being able to maintain and eventually expand these stem cells outside of the body,” Harley said. “An engineered bone marrow will be of enormous value for treating hematopoietic cancers such as leukemia, but also for understanding the process of bone marrow failure and other hematopoietic diseases.”

This project is only the first step in controlling the signals from the matrix that influence HSCs, Harley said. He and other researchers in his lab are currently investigating other features of the matrix that can be manipulated to increase the number of stem cells and make them more effective in transplantation.

The National Science Foundation, National Institutes of Health and the American Cancer Society of Illinois supported this research.
Microscopic shifts in metabolism and increases in tiny transport vesicles out of tumor cells preface larger changes to the tumor environment and could prepare the way for cancerous cells to spread and metastasize, University of Illinois researchers report. They saw cancer-causing biological events at both the molecular and tissue scales as they happened, imaging the cells with precise wavelengths of light – no chemicals, dyes or genetic manipulation needed.

Performed with rat and human cancer tissue, the study looked at five changes seen in a tumor's environment as it develops, grows and spreads. There are techniques to study each of these separately, but all involve disturbing the cellular environment with chemical dyes, fluorescent probes or genetic manipulation, for example. The Illinois group used finely tuned wavelengths of light to see the structural and molecular makeup of tissue in its natural state. The researchers isolate the signals from specific cancer processes by focusing on distinct wavelengths and combine the images to see how the processes interact.

“We're starting to connect the dots here. This is the first time all of these pieces have been looked at together. No one's been able to visualize the tissue this way and see the changes dynamically,” said Dr. Stephen Boppart, the leader of the study, published in the journal Science Advances. Boppart is an Illinois professor of electrical and computer engineering and of bioengineering, and also is a medical doctor.

The researchers were particularly interested in vesicles, the tiny packages that cells use to transport things in and out of the cell. Cancer cells pump out vesicles at an increased rate. Many cancer researchers believe this to be a response to the stress from molecular changes in the tissue.
Because the Illinois imaging technique doesn’t disturb the cells and thus can watch them over time, the researchers saw that a wave of vesicles came before the larger tissue-scale changes like new blood vessels or recruitment of neighboring cells. Together with changes in metabolism, increased vesicle production could be a cause of the larger-scale changes in cancer tissue rather than an effect, the researchers say.

“This paper is important because it connects the microscopic scale – the molecular and vesicle scale – with the larger-scale events in the tissue,” said Haohua Tu, a research scientist at the Beckman Institute for Advanced Science and Technology at Illinois and the first author of the paper. “Also, this is the first time we’ve compared changes in metabolism and vesicle production, and we found that they are linked. Both are microscopic events, but their concurrence leads to a lot of large-scale changes associated with tumor progression. The conclusion is that the combination of these two signals early cancer development and should be a focus of cancer therapy, rather than only focusing on larger-scale events later.”

The study also provides evidence that vesicles from cancer cells may play a role in spreading the cancer to other tissues in addition to changing a tumor’s local environment, the researchers said.

“Often, when there is a tumor in one tissue, cells elsewhere have undergone changes because of that tumor,” Boppart said. “Are all these changes happening because there was some sort of environmental carcinogen that caused tumors at different points? Or did the tumor give off vesicles that changed the microenvironment to prepare it for those later cells that metastasize?”

Boppart hopes that the findings on vesicles and the role they play in signaling cancer progression will open new avenues of exploration for cancer detection, progression and treatment. The researchers have developed a portable version of the imaging device for use in operating rooms and biopsy suites, and are now testing whether it can identify increased vesicle production in cancer patients and assess how aggressive a tumor is. They also are conducting further studies into the vesicles to see what they contain.

“We also know from other studies that these vesicles carry a lot of information about where they came from and where they’re going,” Boppart said. “Imaging is great, but you have to know where to look. There’s no way we can look at the whole body on the cellular level. But if we can take a drop of blood, scan it for cancer-related vesicles and know where they came from, then we know where to look for the tumor.”

The National Institutes of Health supported this work.
A diverse group of women came together at the University of Illinois Women's Resources Center for a Breast Cancer Forum on Friday, October 14, 2016. The forum featured talks by Dr. Zeynep Madak-Erdogan, assistant professor in the Department of Food Sciences and Human Nutrition speaking about “Breast and Cervical Cancer, Screening and Prevention” and Dr. Erik R. Nelson, assistant professor in the School of Molecular and Integrative Physiology speaking on “Recent Advances in Cancer Research.”

Following their presentations, both speakers engaged in discussion and encouraged the audience to “think before you pink” in regard to pink ribbon-related products and promotions, making sure companies they support are being transparent about proceeds that actually fund breast cancer research. Both Madak-Erdogan and Nelson are members of the Cancer Community at Illinois.

The event was sponsored by the Women's Resources Center, the Cancer Community at Illinois, and Sigma Gamma Rho Sorority, Inc.

The Central Illinois Cancer Symposium was held on Friday, September 30, 2016 at The Forum at Carle Foundation Hospital.

The Central Illinois Cancer Symposium is an annual event for health care professionals to receive the latest updates in cancer screening, diagnosis, and treatment. This year’s symposium focused on the Continuum of Cancer Care.

The morning session included opening remarks from Carle physician, Magesh Sundaram and talks from other Carle physicians about cancer screenings, the genomics of colon cancer, new surgical approaches to colon cancer, GI cancer immunology, and GI survivorship.

The afternoon session began with a talk on new anticoagulants and anticoagulant regulation in cancer patients. University of Illinois researchers followed with a presentation on current concepts in cancer research. Hong Chen, PhD, and Zeynep Madak-Ergodan, PhD, were the speakers representing the Cancer Community at Illinois.

The day concluded with talks on sexual survivorship conditions and the OSTRICH Rectal Cancer Center of Excellence Program.

Dr. Nelson spoke to a packed room at the Beckman Institute for Advanced Science and Technology, drawing an audience ranging from undergraduate and graduate student to Carle physicians. Her talk, titled “Emerging Technologies, Trends, and the Future of Surgery,” took a historical but also first-hand perspective. Dr. Nelson’s research and practice at Mayo Clinic is in the field of colon and rectal cancer. Her research efforts have helped reduce the impact of surgery on patients with early-stage disease through the safe introduction of laparoscopic and minimally invasive surgical approaches. Her work has helped reduce the cancer burden in patients with locally advanced and recurrent rectal cancer through studies examining the role of complex surgeries and intraoperative radiation therapy.

Dr. Nelson has made use of both comprehensive clinical research databases and clinical trials to achieve her research goals. She regards innovations like 3D printing used to model human systems and anatomy, as well as sequencing the human genome as key advances for the future of medicine and surgery.

She quoted NIH Director Francis Collins’ perspective on the future of medical research, that “the promise of a revolution in human health remains quite real; ... we invariably overestimate the short-term impacts of new technologies and underestimate their long-term effects.”

The Health Innovations Lecture Series features talks held monthly at Carle or the University of Illinois campus that focus on a wide variety of innovative topics including medical research, public health, ethics, epidemiology, genomics, and many others. The series is designed for faculty, researchers, physicians, nurses, and other health professionals. For select lectures, health professionals may have the option to receive continuing medical education credits (CMEs) and a certificate of completion. Members of the public are welcome to attend.

Building Relationships

The Cancer Community builds strong relationships that translate into real outcomes for the patients. Working with partners at Carle and the University of Illinois at Chicago Cancer Center, these partnerships enhance opportunities for clinical and translational research, external research funding and medical and health science education. Pictured: Rohit Bhargava, Jennifer Eardley, Jennifer Woodard, and Robert Winn.

AACR 2017

Emily Chen and Phuong Le presented research at the annual American Association for Cancer Research (AACR) meeting in Washington, D.C. in April 2017.
University of Illinois researchers are leading the charge in the area of the tissue microenvironment with expertise in biology and bioengineering, computational methods and imaging. The National Institutes of Health (NIH) also recognized Illinois’s excellence by awarding a National Research Service Award Institutional Training Grant to the Urbana campus. This funding will help develop the next generation of scientific leaders. Illinois faculty member Rohit Bhargava is the PI of this award and more than 35 Illinois faculty from across campus will contribute to this new interdisciplinary training program for graduate students. Rex Gaskins, faculty member in the Department of Animal Sciences, will serve as deputy director for the training program.

The inaugural group of TiMe Training students and their programs are: Jee-wei (Emily) Chen (chemical and biomolecular engineering), Kyung Hwa (Iris) Choi (mechanical science and engineering), Jamila Hedhl (bioengineering), Seth Kenkel (mechanical science and engineering), Eunkyung (Clare) Ko (bioengineering), Phuong Le (bioengineering), Joanne Li (bioengineering), Jan Lumibao (nutritional sciences), and Ruibo Wang (materials science and engineering).

For more information visit www.time.illinois.edu.

Bioengineering student and Cancer Scholar, Madelyn O’Gorman, has been active in lab-based research since she arrived at the University of Illinois. Her desire to experience research in a clinical setting with an emphasis on translational medicine led her to take advantage of an exciting opportunity to spend the summer doing research at the Mayo Clinic as part of the Summer Undergraduate Research Fellowship (SURF) program. The SURF program is a 10-week immersive research experience that gives students a taste of what a career in biomedical research is really like. This experience is an excellent complement to the Cancer Scholars Program at Illinois because the students are tackling real-world clinical problems head-on.

While at the Mayo Clinic, Madelyn worked in Dr. Stephen Ekker’s lab, which aims to identify novel key genetic players critical for clinically relevant processes such as blood vessel, sensory organ and kidney development. Dr. Ekker also has ties to Illinois. He is a University of Illinois alum, whose advisor was the late Carl R. Woese.

In Dr. Ekker’s lab, Madelyn engineered and tested new skin therapeutic platforms using gold nanoparticle bioconjugation and small molecule inhibitors applied topically, in the form of a cream. These therapies were used to treat sunburn and prevent long term effects of radiation damage, such as metastatic melanoma and skin aging. Once optimized, the platform has the potential to be extended to other more severe skin disorders that do not currently have a cure, such as psoriasis or rosacea.

At Illinois, Madelyn works in Professor Andrew Smith’s lab in the bioengineering department. Her project involves creation of a live-cell imaging platform for better understanding of cancer metastasis. She would like to incorporate some of the therapeutic techniques she acquired at Mayo Clinic into her research at Illinois. She hopes to find a project where she can study the mechanism of angiogenesis and applications of nanomedicine—the main foci of her SURF project. She said, “Having more knowledge about the process of blood vessel infiltration in response to disease states can be applied to a large spectrum of medical disorders from something as acute as sunburn to later-stage cancers. The opportunities for the advancement of therapies with engineered nano-carriers are
becoming more and more prevalent as well, taking a major place in the future of medicine.”

Between her research at Illinois and her SURF experience at Mayo Clinic, Madelyn seems to have homed in on a direction for her future research career remarking, “With the movement toward more complex therapeutic delivery vehicles and recent advancements in nanomedicine, I hope to find a niche where I may incorporate my background in therapeutics and biomaterials into the development of innovative drug delivery mechanisms.”

She is currently looking into graduate schools for bioengineering, specifically those with a strong clinical connection that will provide opportunities for her to be more involved in translational medicine.

In Madelyn’s opinion, the SURF program is an experience that anyone interested in biomedical research should have. She cites the techniques learned and connections made in Rochester as extremely valuable. The SURF program has opened her eyes to exciting possibilities for advancement in the medical field.

The Cancer Scholars Program (CSP) is an undergraduate educational model that provides a unique student learning experience through exposing students to research early in their career, focused training on a grand challenge, and working across disciplines. In 2014, the CSP was established through a Strategic Instructional Initiatives Program (SIIP) grant administered by the College of Engineering’s Academy for Excellence in Engineering Education (AE3). This initial funding and subsequent funding in 2015 allowed the CSP faculty team to establish the framework for the model and support students in summer experiences.

Seeking to connect student learning to engineering practice, the CSP interweaves a grand challenge problem throughout multiple courses and experiences in the curriculum thereby treating this learning experience as a multiple input process instead of a single event. Traditionally, students learn engineering skills in isolated coursework without a connection to real-world problems, facilitating loss of interest, and are rarely exposed to co-curricular educational development opportunities (e.g. research experiences) in the first year. However, the CSP model (Figure 1) seeks to engage students from the beginning through coursework, experiences, and cohort support.

Each year the CSP enrolls a cohort of approximately twelve students who develop knowledge through a series of CSP courses, individual research experiences, and cohort interactions. With the exception of capstone design (senior year) in which students enroll in their home department’s capstone course, CSP students enroll in one CSP course each year: Frontiers in Cancer Research (freshman year), Healthcare Innovations (sophomore year), and Innovation and Engineering Design (junior year). The CSP structure is organized so each cohort of CSP students enrolls in a CSP course (or senior design) in fall semester; spring semester consists of research, mentoring, and skills training (as a cohort group). Summer is available for research continuation, immersion experiences, or electives to further develop the student’s portfolio. Currently, the CSP is in its third year of operation with thirty-five students (total). The inaugural cohort is composed of all Bioengineering students; the second and third cohorts are composed of Bioengineering, Electrical and Computer Engineering, and Computer Science students. All CSP students have strong academic records, even prior to college, with the average incoming ACT being 34.4 across all three cohorts. Many of the CSP students have authored conference papers earlier in their career than other Bioengineering students, and some have won regional conference and campus awards. Additionally, the CSP is appreciated by females as each cohort is composed of approximately 50% females and no females have left the program.

The best evaluation of the program is seeing how the CSP program affects the students participating in it. Here’s what the CSP students had to say about the program.

“The Cancer Scholar’s Program has been amongst the top highlights of my 2 years at college. It is the perfect program to coalesce one’s passion and skills (even not related to BioEngineering) to battle Cancer. Some unconventional, yet effective classroom strategies allow, even non Bio related majors, such as mine, to be an active participant in class discussions and a benefactor of this program. The staff and faculty heading the CSP have acted as my teachers, friends and guides all at once. Reliving my moment of joy when I learned that I was accepted to be a part of CSP, I feel proud to be a part of this noble initiative and super happy for all the future Cancer Scholars.”—Arvind Kamal

“The Cancer Scholars Program provided resources for me to begin engaging in undergraduate research as a freshman. The skills and experience I gained from undergraduate research enhanced my skills as a candidate for an international research position and an internship in industry.”—Lily Barghi

“The CSP has helped me be able to see the potential I hold. I did not believe it possible for me to be a part of a research group till later on latter freshman year. But by the end of my freshman year, I have already been a part of two labs. I see my peers also succeeding in the research groups they have joined, which helps me see that we, the students, can also make an impact, even from day one.”—Anonymous

http://cancer.illinois.edu/education/undergraduate/csp/
In 2015, the Carle Foundation Hospital, through its Cancer Center, and the University of Illinois at Urbana-Champaign jointly established the Cancer Scholars for Translational and Applied Research (C★STAR) graduate education program. The program fosters translational research and near-term benefits to the patients served in the community.

The long-term collaborative goals of the program are to foster connections and innovative research projects between Carle physician-scientists and Illinois faculty. The aim is for the projects to develop a foundation for tangible translational outcomes. A broad range of fields are represented including engineering, bioinformatics, social work, public health, medical programs, counseling, etiology, and a number of clinical areas of study.

On April 19 the C★STAR program held a reception where the collaborative research teams each had the opportunity to give a short presentation on their work. The research teams and presentations are listed below.

### Relationships among Physical Activity, Quality of Life, and Cognitive Function in Breast Cancer Survivors

**UI Faculty Mentor:** Edward McAuley, Kinesiology & Community Health  
**Student Researcher:** Elizabeth Awick  
**Carle Physician Mentor:** Kendrith Rowland  

**Project Description:** Research has suggested that many cancer survivors experience a loss of mental acuity following their diagnosis and treatment; this phenomenon is colloquially referred to as “chemo brain.” Past work has also suggested that acute bouts, or single sessions, of physical activity may help preserve cognitive function. We conducted two studies supported by C★STAR: a pilot study and a larger trial replicating and extending the pilot project.

The first study, Activity & Cognition after Treatment (ACT) for Breast Cancer, examined the effects of 30 minutes of exercise compared with 30 minutes of seated rest on cognitive function. Our larger study, Making Activity Time for Cognitive Health (MATCH), was designed to examine if the effects of exercise and rest on cognitive function over time differed as a result of the time spent exercising. Women completed an exercise and a resting session, similar to ACT, and they were also randomized to one of three time groups (i.e., 10, 20, or 30 minutes) signifying the time spent exercising and resting. This allowed us to explore differences between varying durations of exercise for ultimately determining how long women need to walk for obtaining the greatest cognitive benefits.

### Health-related Quality of Life (HR-QOL): Relationships Among Dietary Patterns, Eating Behaviors, Nutritional Status, and Patient-centered Survivorship Outcomes

**UI Faculty Mentor:** Anna Arthur, Food Science & Human Nutrition  
**Student Researcher:** Sylvia Crowder  
**Carle Physician Mentor:** Kalika Sarma

**Project Description:** The team plans to conduct population-based research to study the complex relationships among dietary patterns, eating behaviors, nutritional status, and patient-centered survivorship outcomes such as health-related quality of life (HR-QOL) and chronic symptoms of head and neck cancer (HNC) survivors. 100% of HNC patients develop severe side effects as a result of their tumor location, treatment with chemoradiation and/or surgical resection of the tumor. Common symptoms include difficulty swallowing, dry mouth, taste alterations and dental problems, leading to compromised food intake, malnutrition, increased susceptibility to infection and decreased HR-QOL and survival. To date the majority of research has focused on the short-term impact of these side effects despite the fact that over 50% of HNC survivors report chronic presence of these symptoms. The dissertation research will directly address this knowledge gap by identifying patients at high-risk for nutritional decline secondary to chronic, severe symptoms that
compromise eating in the long-term. This research will also lead to the development of dietary interventions aimed at improving HR-QOL and reduction of symptoms in this patient population. To reach these goals, the team will use a mixed-methods approach. First, they will quantitatively examine longitudinal associations between dietary patterns and symptom burden in a large, observational cohort study of newly diagnosed HNC patients. These quantitative study results will be supplemented with qualitative data collected at the Carle Cancer Center to determine the long-term impact of symptom burden on eating behaviors and nutritional status in HNC survivors. The results will have a high potential to be translated to the clinic by providing a strong foundational framework for advancements in the nutritional management of HNC patients.

The Impact of Cholesterol on the Ovarian Tumor Microenvironment and Cancer Progression

UI Faculty Mentor: Erik Nelson, Molecular & Integrative Physiology  
Student Researcher: Sisi He  
Carle Physician Mentors: Ronald Kimball & Marta Spain

Project Description:
Ovarian cancer remains a highly lethal disease with a relapse rate of 50%-75% within 18 months of standard-of-care treatment. Hence, there is an urgent need for new therapeutic or lifestyle strategies to prolong progression-free survival (PFS). Importantly, epidemiological studies have implicated elevated cholesterol as a negative prognostic factor. Conversely, ovarian cancer patients taking cholesterol lowering drugs (HMGCoA-R inhibitors; statins) exhibit significantly increased PFS. These observations strongly suggest that cholesterol impacts ovarian cancer progression. Therefore, the team hypothesizes that the effects of cholesterol/27HC were being mediated via the tumor microenvironment. Specifically, treatment with exogenous 27HC significantly enhances the infiltration of M-MDSCs, a myeloid-immune cell type known to be pro-tumorigenic, at least in part through their suppression of cytotoxic CD8+ T cells. On the other hand, significantly less MMDSCs are found in tumors from CYP27A1-/- mice. Collectively, our preliminary data strongly indicate that cholesterol, via its metabolite 27HC, acts as a modulator of the microenvironment to promote tumor progression. Our long-term goal is to understand the molecular mechanisms responsible for the link between high cholesterol and increased ovarian cancer recurrence. Our specific goal for this proposal is to explore the effect of elevated cholesterol and 27HC on tumor progression and the tumor microenvironment (specifically MMDSCs). This project will (1) establish the mechanisms by which cholesterol promotes ovarian cancer progression, and (2) confirm the associations between elevated cholesterol, 27HC, M-MDSCs and tumor grade and outcome in patient samples. Thus, by exploring the links between cholesterol, 27HC and ovarian cancer progression, this research will serve as the foundation for the development of much needed novel strategies for the treatment of ovarian cancer.

Fluorometric Microculture Cytotoxicity Assay for Personalized Medicine

UI Faculty Mentor: Paul Hergenrother, Chemistry  
Student Researcher: Evijola Llabani  
Carle Physician Mentor: Maria Grosse Perdekamp

Project Description:
Metastatic breast cancer (MBC) is responsible for 90% of breast cancer deaths and has an overall 5-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.

We examine an ex vivo cytotoxic screen of patient-derived tumor samples with each of the drugs approved for MBC, in combination with novel experimental drugs (PAC-1), and emerging compounds (267). PAC-1 was discovered in the Hergenrother lab and is now undergoing a Phase 1 clinical trial in cancer patients, while 267 is a promising. Our central hypothesis is that single agents and drug combinations identified via a semi-automated fluorometric microculture cytotoxicity assay (FMCA) will provide information on the optimal drug regimen for each MBC patient in the clinic and extend their overall survival. In addition, we envision acquiring molecular profiling of the tumor samples to assess key biomarkers, and organize the information in a bioinformatics database. This database will correlate molecular profile patterns with drug combinations and help predict treatment for other patients in the future. We believe that FMCA can also be extended to tumor samples from other metastatic diseases, including ovarian cancer (OC), which ranks fifth in cancer deaths among women.

Development of a microRNA Panel to Facilitate Prognosis Stratification and Personalized Nutritional Intervention in Colorectal Cancer

UI Faculty Mentor: Yuan-Xiang Pan, Division of Nutritional Sciences  
Student Researcher: Laura Moody  
Carle Physician Mentor: Suparna Mantha

Project Description:
Prognosis and treatment of colorectal cancer (CRC) are currently based on the tumor-node metastasis (TNM) staging system, which...
considers the extent of tumor invasion into the bowel wall and the presence of lymph node and distant metastases. Depending on TNM stage, patients will receive treatment ranging from surgical tumor removal in stage I to a combination of bowel resection surgery, radiation therapy, and chemotherapy in stage IV. Recent advances in molecular genomic and epigenomic research have identified many alternative markers that will facilitate the molecular stratification of CRC. TNM staging is limited because it requires invasive endoscopic screening and does not provide biochemical analysis of the tumor or the patient's systemic state. Blood-based tools are necessary for efficient and effective prognosis stratification; however, biomarkers such as carcinoembyronic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) detect CRC with low sensitivity and specificity, especially in early stage CRC [Duffy, et al 2003, 2007]. We and others have suggested microRNA (miRNA) as an alternative to traditional CRC stratification measures. miRNA are epigenetic regulators that are implicated in the development of CRC and are modifiable by diet and lifestyle [Olivo-Marston, 2014]. In a preliminary study using a CRC mouse model, we found that high-fat diet (HF) suppresses exercise (EX) promotes expression of miR-378, a known prognostic marker that is repressed in CRC. Although promising, miRNA assays have not been have not been standardized to give actionable, relevant information and thus have not been implemented in a clinical setting. The goal of the proposed work is twofold: (1) to identify and validate a miRNA panel that is capable of differentiating between pathological stages of CRC and (2) to determine how nutritional status shifts miRNA expression and ultimately affects metabolic pathways.

**Intraoperative Determination of Tumor Aggressiveness by Real-Time Label-Free Nonlinear Imaging and Characterization of Tumor-Associated Microvesicles**

**UI Faculty Mentor:** Stephen Boppart, Electrical & Computer Engineering & Bioengineering  
**Student Researcher:** Yi (Edwin) Sun  
**Carle Physician Mentor:** Zheng (George) Liu  

**Project Description:**  
Tumor-associated microvesicles (TMVs), as a special kind of cellular communication carriers, have been found in recent studies to play vital roles in directing the invasion and metastasis of tumor cells. Furthermore, TMVs have also been found in ex-vivo images of rat tumor tissue. However, the intraoperative label-free imaging of TMVs in fresh human tumor tissue has not been realized yet. Here we propose to use a portable nonlinear imaging system to intraoperatively study the presence and dynamic of TMVs in the tumor microenvironment, which is promising to rapidly determine tumor aggressiveness and further unravel mechanisms of cancer cell invasion. With the help of different nonlinear modalities, we can not only visualize cellular metabolic activity and collagen fibers, but also observe the signal generated by TMVs, mainly from third harmonic generation (THG) and three-photon fluorescence (3PF). With label-free imaging, it is also possible to determine the spatial extent of TMVs in tumor tissue using the information of tissue structures like collagen fibers and adipose from second harmonic generation (SHG) and two-photon fluorescence (2PF). The research team hopes to gain more insight and understanding of TMVs will be unraveled to indicate their relationship to tumor aggressiveness, and the mechanisms of tumor cell invasion and metastasis.

**Improving and expanding Active Tissue Targeting via Anchored ClicK (ATTACK) Chemistry**

**UI Faculty Mentor:** Jianjun Cheng, Department of Materials Science and Engineering  
**Student Researcher:** Rubio Wang  
**Carle Physician Mentor:** Yujie Zhao  

**Project Description:**  
Cancer targeted therapy has long been pursued to improve the accumulation of drugs in tumor and minimize undesired exposure to other parts of the body. A key challenge lies in the identification of receptors in cancer tissues and development of corresponding targeting ligands. The discovery of unnatural sugars, such as Ac4ManAz (Nature 2004, 430, 873-877), that can be metabolized and expressed on cell surface provides a pathway to introduce chemical receptors, such as azido (N3) group, onto cell surface. In combination with click chemistry, the cell surface chemical receptor can be used as anchors for covalent attachment of imaging or therapeutic agents conjugated to corresponding click chemistry counterparts. The binding affinity and receptor density of chemical receptors are superior to native receptors on cell surface that are commonly used in antibody based targeting techniques. The small molecule based bioorthogonal targeting ligands are also suitable for recapitulate the tissue microenvironment (TIME) by modifying cell surface. On key drawback of Ac4ManAz, however, is its lack of capability to differentiating cancer vs normal healthy cells.

We recently developed a technology called ATTACK (Active Tissue Targeting via Anchored ClicK Chemistry) that can control metabolic activity of Ac4ManAz and cell membrane N3 labeling specifically in cancer cells. The cancer-specific labelling is achieved by developing and using an unnatural sugar with its metabolic activity inhibited by a moiety (“P” in Scheme 1) that can be cleaved by cancer specific enzymes. We demonstrated that C-1 modification on Ac4ManAz to Ac3ManOP using ether linkage could fully block the metabolic activity of this unnatural sugar. By incorporating a trigger cleavable moiety onto C-1 position of Ac4ManAz, we achieved trigger specific labeling of cell surface. Specifically, we demonstrated cancer-specific sugar activation by histone deacetylase and cathepsin L, two enzymes that are substantially overexpressed in cancer cells, and the subsequent cancer specific labeling with the N3 biomarker on cancer cell membrane. We used this technology for targeted delivery of chemotherapeutics and observed significant improvement in targeting and anti-cancer efficacy in mouse tumor models, demonstrating the viability of using ATTACK as an unprecedented cancer targeting technology.
The researchStart program allows high school students to explore exciting careers in cancer research. Participants work full time in the laboratories of established cancer researchers, gaining hands-on experience in areas at the forefront of the field. Through the generous support of Ira and Debra Cohen, students are able to participate in several activities ranging from an introductory cancer research boot camp ranging from safety training to fun-filled events such as baseball games and Escape rooms. The students share their thoughts about the program in their own words.

**SAMUEL (SAM) HOTCHKISS**
Faculty Mentor: Dipanjan Pan, Bioengineering

The summer experience with researchStart has solidified my preexisting interest in later lab work and ultimately a career at least partially involving research. A large portion of my daily summer work involved running several tests on a collection of samples relevant to my project. The experience I gained measuring size, UV absorbance, and fluorescence of these nanoparticles required me to develop proficiency with various machines in the lab.

**CAITLIN O’CALLAGHAN**
Faculty Mentor: Zeynep Madak-Erdogan, Food Science & Human Nutrition

Although I have worked on research projects before, this was my first time working with cancer and drug development. In the lab I gained valuable firsthand experience in cell culture by working alongside the other lab members. I learned how to run a western blot, BCA assay, feed cancer cells, and so much more! From a young age I always knew that I wanted to join the medical field and as I grew older I narrowed my interest to bioengineering. My summer experience has exposed me to bioengineering with a chemical focus which was great for helping me focus my interests.

**HAILAN SHANBHAG**
Faculty Mentor: Rohit Bhargava, Bioengineering

I learned a lot about what aspects of bioengineering I enjoyed and what I didn’t enjoy as much. I realized I enjoyed doing data analysis. This made me realize that I was more drawn to the engineering side of bioengineering, and really look forward to learning about electrical and computer engineering to help with data analysis. A lot of work I did really needed a strong background in programming and electrical engineering, and it’s made me realize how exciting and also important these areas of study are.

**Thank You**

The researchStart program would like to thank the hosting faculty and their departments and colleges for their continued support in providing this summer research experience.

University of Illinois at Urbana-Champaign
2016 researchStart Site Team

Rohit Bhargava, PhD
Professor of Bioengineering

Margaret Browne Huntt, PhD
Associate Director, Cancer Community, Interdisciplinary Health Sciences Initiative

Amanda Foley, BA
Program Coordinator, Beckman Institute for Advanced Science & Technology

Cathy Tingley
Administrative Aide, Interdisciplinary Health Sciences Initiative

Maria Pool, PhD
Director of Undergraduate Programs, Bioengineering

Karin Jensen, PhD
Teaching Assistant Professor, Department of Bioengineering
JONATHAN WANG
Faculty Mentor: Andrew Smith, Bioengineering

In joining researchHStart, I expected to gain hands-on experience in state-of-the-art labs at a leading research university. In my mind, this experience would act as an introduction to the research aspect of a career in medicine. During my time in the lab, I have been introduced to quantum dots and their use in imaging at the cellular level. I have developed skills in image analysis of stained samples through programs such as MatLab, Cell Profiler, ImageJ, and Microsoft Excel. … My experience has opened my eyes up to the research that drives the advancement of medicine, encouraging me to pursue a balance of clinical evolvement and research in the future.

YADAVALLI BHARGAV
Faculty Mentor: Princess U Il Imoukhuede, Bioengineering

My experience during the researchHStart program has greatly influenced my professional choices and career path. I came into the program not really knowing much about how to conduct scientific research and what it entails on a daily basis. After my 8 weeks in the lab, I have a strong understanding of my project as well as a grip on how to contribute during lab meetings. Also, I originally thought I was going to major in computer science, but this program has showed me that I can intersect both computer science and biology. This has affected my career path as I now want to do something in the field of computational biology or bioinformatics. More importantly, the researchHStart program has connected me with professors, undergraduates, graduates, faculty from other universities, and other likeminded high schoolers. These are resources even first year undergraduates would not have access to.

KAVIAMUTHAN (AMU) KANAKARAJU
Faculty Mentor: H. Rex Gaskins, Animal Sciences

This summer experience showed me many different fields in science. It helps me gear myself towards the sciences and research as I move toward college. This program showed me all the different types of research that I can explore in college. The lectures and presentations allowed me chance to learn about other research and connect with other professionals. This program helped me make my decision to pursue education and career in scientific research and the medicine field. Personally, my skills in observation, work ethics, and attention to details have improved. Overall, this was a fun learning experience that also positively affects my future steps and goals.

ResearchHStart students took part in an escape room activity.
Be The Match (BTM), which is operated by the non-profit National Marrow Donor Program, manages the largest bone marrow donation registry in the world.

With over 600 chapters around the world, BTM has been behind countless life-saving marrow transplants. The Illinois chapter, Be The Match On Campus (BTMOC), was founded by a group of ambitious students in 2014. Starting with only six members, BTMOC has grown to include more than 30 people. The group focuses on recruiting people to register for the international bone marrow donation pool, which includes voluntary donors from all over the world, and raising money for bone marrow registry testing.

“BTMOC is an organization that gives back to the community, helps a lot of people, and makes a difference in peoples' lives,” says Devi Patel, president of BTMOC at the University of Illinois at Urbana-Champaign.

The main goal for the Illinois chapter of BTMOC is to keep raising awareness of bone marrow donation. The group wants to let more students and campus community members realize they can be the donor that patients are waiting for, “because everyone has the power to help cure blood cancer and potentially be someone's lifesaver,” says Devi. BTMOC also seeks to get rid of the stigma of bone marrow donation and educate people that donating is not a scary process.

BTMOC has held at least one or two bone marrow drives each month since its founding at Illinois. Through collaborations with different organizations on campus, including Greek communities and ethnic student organizations, BTMOC is typically able to get eight volunteers to help coordinate a bone marrow drive and 30 to 50 sign-ups for the donor registry. Currently, the group has a 50 percent retention rate of sign-ups, which means only half of the people that register at the bone marrow drives will finish all the testing and become official donors. BTMOC is working to increase the percentage of loyal participants. Aiming to reach out to more students, BTMOC also looks to hold “Swab Parties” during other organizations’ chapter meetings. Representatives give a short presentation to educate people, and have a quick donor drive to let people sign up. BTMOC hosts multiple tribute nights and fundraising events each semester to cover the $100 cost of swab testing.

Right now, many minority patients cannot find a match in the national marrow registry because the majority of the donors in the pool are Caucasian. BTMOC is aware of this situation, and is adapting its activities, agenda, and specific goals based on the urgent needs of patients. BTMOC is reaching out to a diverse population and engaging people from minority groups to increase the database and the chances of patients finding a match.

To get more information about Be The Match On Campus and their activities, visit their Facebook page at facebook.com/UIUCBeTheMatch/.
GRANTS

Rohit Bhargava
National Institutes of Health (NCI), “Translational Molecular and Cellular Imaging Technologies for Prostate Tumor Pathology” (08/2016 – 07/2019)

Stephen Boppart

Barbara Fiese

Paul Hergenrother

Edward McAuley

PUBLICATIONS


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
Senior Research Development Manager, Associate Director, Cancer Community
mbrowne@illinois.edu
217-244-1354

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.

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