WINTER 2021

INNOVATION INSIDER

CANCER CENTER AT ILLINOIS

HOW WILL AI TRANSFORM CANCER RESEARCH?

Machine Learning, Image Reconstruction, DNA sequencing. CCIL scientists are wielding technology in the fight against cancer.

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Innovation Insider is a Cancer Center at Illinois publication that highlights the interdisciplinary and translational work of CCIL members, staff, students, and external partners.

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DIRECTOR'S NOTE

It's difficult to imagine life today without internet browsers, magnetic resonance imaging, or the light emitting diode. The inventors of each of these practical and widespread technologies called the University of Illinois Urbana-Champaign home. Now, after more than a century of technological advances that have changed society, my home institution has turned its research focus to cancer, with the expectation that society is on the cusp of a technology-driven revolution in the fight against the disease.

Today, artificial intelligence (AI) is sweeping all facets of our lives — autonomous cars are on roadways, robotic systems are used in surgery, and we can test at home for a range of conditions from pregnancy to glucose levels. We can also imagine a future where these trends converge to transform cancer understanding and care. The past year has shown us the powerful impact of what technology can do — connecting us at a distance, aiding the development of a vaccine, and implementing large-scale testing that is inexpensive, fast, and convenient. Now that our eyes are opened to these possibilities, we must ask ourselves, what more can be done, and what can be done better, for cancer patients?

Progress starts with basic discovery, and discovery depends on innovation, which can be accelerated by using technology to inspire more people from diverse backgrounds to collaborate and apply their talents more effectively. Translating discoveries also increasingly depends on data and analytical methods that grow from AI. This chain of discovery, measurement, analysis, and application can speed the delivery of improved treatments to clinicians and patients.

Technology's potential as a catalyst for transformative change in cancer care has existed for years, but recent progress in AI, and the emergence of precision medicine, makes this focus on technology timely. At the Cancer Center at Illinois (CCIL), we take an even more expansive view of technology by considering how combining diverse fields — from measurement and materials science to chemistry and the biology of networks — will boost progress in cancer research.

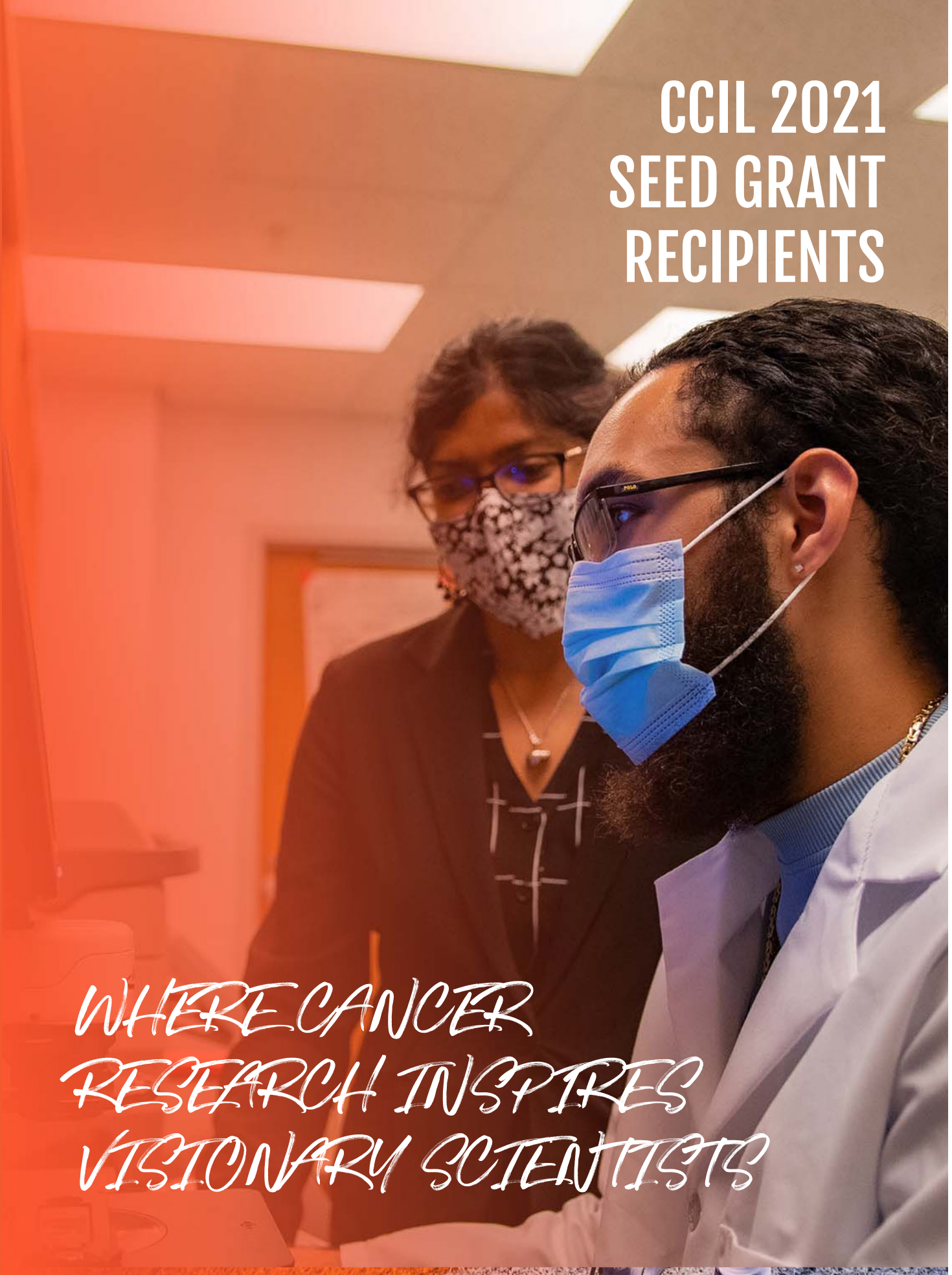
In this issue of Innovation Insider, you will meet many of the CCIL members at the forefront of AI. Using their expertise, they are altering the cancer landscape and rethinking the workhorse of biomedical research. Computer scientists are working alongside CCIL bioengineers, biologists, and chemists to better understand the tumor microenvironment to improve cancer therapeutics and diagnostic technologies. You'll read about new discoveries in glioblastoma research, a groundbreaking cancer drug rapidly moving towards clinical trials, and the progress that CCIL grant recipients have made in taking on cancer.

Like new technologies, it may have once been difficult to imagine a life without cancer, but CCIL researchers are working together to change that.

Rohit Bhargava

Rohit Bhargava, CCIL Director

CCIL 2021 SEED GRANT RECIPIENTS



WHERE CANCER RESEARCH INSPIRES VISIONARY SCIENTISTS

Nine interdisciplinary projects designed by University of Illinois Urbana-Champaign faculty were selected for the Cancer Center at Illinois (CCIL) annual seed grant awards.

"Due to the proven success of the CCIL Seed Grant Program, we were able to support additional initiatives in 2021 compared to previous years," Paul Hergenrother, CCIL Deputy Director, said. "CCIL scientists are making bold discoveries and leading innovative initiatives that will create technologies and techniques that will translate from labs to clinics."

The nine projects include:

Title: Delineating the Role of Orc6 in Genome Surveillance and Cancer Progression
Principal Investigator: Supriya Prasanth, Cell and Developmental Biology

Title: FORce Control of Cancer Tumor µEnvironment (FORCE)
Principal Investigator: M. Taher Saif, Mechanical Science and Engineering

Title: High-Resolution Magnetic Resonance Spectroscopic Imaging for Adaptive Glioblastoma Multiforme Patient Treatment
Principal Investigator: Hua Li, Bioengineering

"The depth of science, engineering, and technology expertise at the University of Illinois Urbana-Champaign will transform the cancer industry for years to come." - Paul Hergenrother, CCIL Deputy Director

Title: Lipid Droplet Packing: A New Target to Interfere with the Progress of Human Hepatocellular Carcinoma
Principal Investigator: Cecilia Leal, Materials Science & Engineering

Title: Multi-shape 3D Hanging Drop Array for Cancer Drug-screening
Principal Investigator: Rashid Bashir, Department of Bioengineering

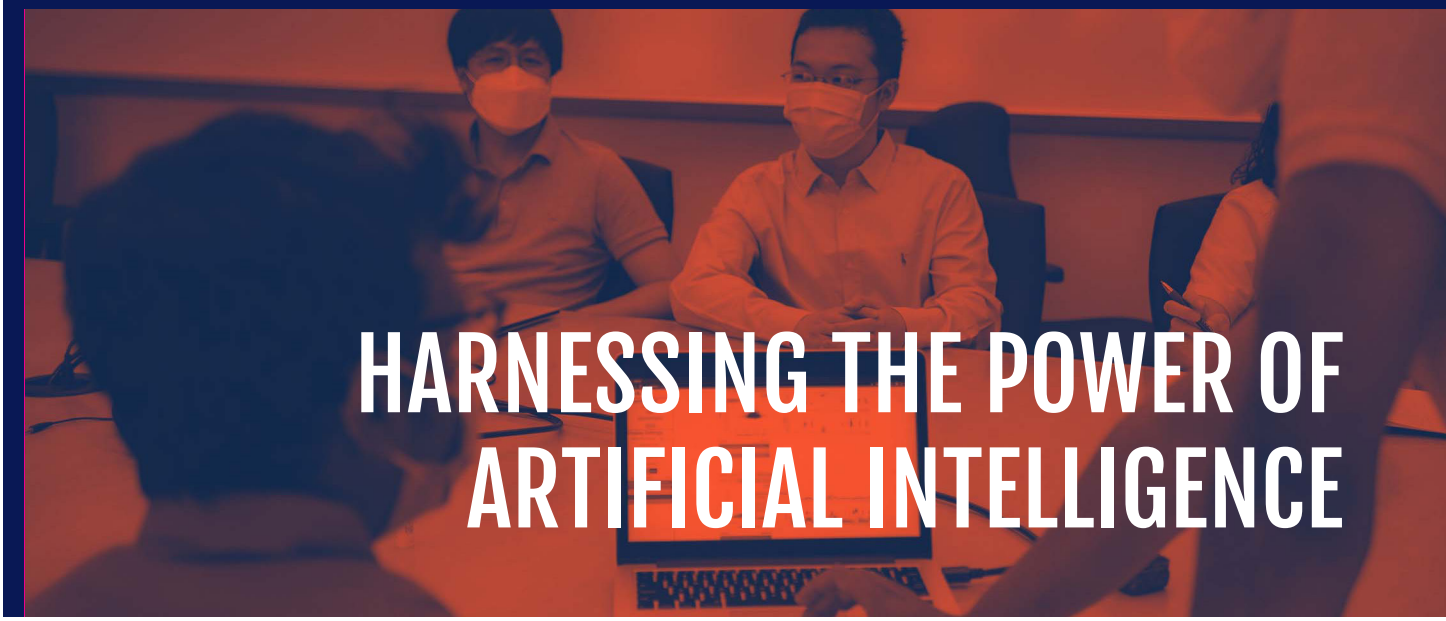
Title: Quantitative Ultrasound for Detection of Lymph Node Metastasis from Oral Melanoma & to Document Tumor Response to Stereotactic Radiosurgery in Dogs as a Large Animal Model of Metastatic Cancer
Principal Investigator: Kimberly Selting, Veterinary Clinical Medicine

Title: Stable Therapeutic Antibody Expression for Cancer Immunotherapy by Liver-directed Gene Editing
Principal Investigator: Shannon Sirk, Bioengineering

Title: Workflows and Tools for Visualizing Tumor Phylogenies in Metastatic Breast Cancer
Principal Investigator: Mohammed El-Kebir, Computer Science

Title: The Role of the Urinary Sterolbiome in Prostate Cancer Risk
Principal Investigator: Jason Ridlon, Department of Animal Sciences

CCIL seed grant funding has supported interdisciplinary cancer research projects that facilitate cross-campus collaboration. Previous grant-supported projects have led to a number of additional external funding awards, including a recent $1.25M NIH grant to further explore breast cancer progression.



HARNESSING THE POWER OF ARTIFICIAL INTELLIGENCE

Computational Genomics. Phylogenetics. Image Construction. The University of Illinois Urbana-Champaign maintains a legacy of excellence in engineering and technology innovation. CCIL scientists are world-renowned experts in artificial intelligence, leading a technological renaissance in cancer research.

Mark A. Anastasio

Professor and Head of Bioengineering

Artificial intelligence (AI), algorithms that teach computers to perform tasks, can efficiently identify patterns and relationships in large amounts of data. These abilities have made AI techniques and tools indispensable in the cancer research community, especially for CCIL scientists who are developing improved imaging tools used to diagnose cancers and guide decisions made in the clinical workflow.

"When we talk about using AI to help us form or reconstruct better images, one of the first things we think about is how we can blend the physics of the imaging system and AI/machine learning (ML)."
— Mark A. Anastasio

READ MORE: GO.ILLINOIS.EDU/AIRESEARCH

Mohammed El-Kebir

Assistant Professor, Computer Science

AI is often employed in the field of cancer genomics, where bits of DNA sequencing data must be identified and further analyzed with statistical, evolutional, and probabilistic models. "Off-the-shelf" computing tools are useful for many cancer researchers, but Mohammed El-Kebir, CCIL scientist, is taking these AI applications a step further.

"Within a single tumor, you have intra-tumoral heterogeneity — different sets or types of mutations — that are intriguing. Evolution of species can be described in a single tree of life, but with cancer, you get a tree for each tumor."
— Mohammed El-Kebir

Saurabh Sinha

Professor, Computer Science

In bioinformatics, ML tools are used to solve problems in molecular biology and genetics. In healthy cells, genes are switched "on" or "off" to carry out specific tasks. Bioinformatics researchers can decode DNA using AI to understand why some of these switches occur inappropriately, leading to disease. At the CCIL, one such expert is Saurabh Sinha, Illinois professor of computer science.

"I'm excited to exploit the incredible revolution happening in machine learning today and adapt it to advance the understanding of human biology. Building black box models is great, but my personal excitement is to marry these tools with the language of science."
— Saurabh Sinha

Celebrating World Cancer Research Day

WINTER 2021

In the fight against cancer, research is our greatest strength.

ASHLIE SANTALIZ CASIANO

TiMe Program Trainee

"Many research labs and groups of scientists are working very hard to tackle cancer from many angles. Finding new therapeutic strategies for patients and creating awareness of existing therapies that do not work effectively can improve disease outcomes and save patients' lives. Support for cancer research ensures that we, as researchers, keep traction as we achieve these scientific goals." — Ashlie Santaliz Casiano, Tissue Microenvironment program trainee and Illinois graduate student.

STEPHEN BOPPART

CCIL Research Program Leader

"The CCIL's approach to addressing the fundamental questions and research challenges in cancer with advances in technologies, computation, and data science will not only enable new tools and techniques for the field, but will also give us the ability to ask and answer new questions that emerge. Looking at long-standing questions and problems through a new lens will allow us to see what had previously been invisible." — Stephen Boppart, Executive Associate Dean and Chief Diversity Officer at the Carle Illinois College of Medicine and professor of electrical and computer engineering.

BIOENGINEERING BETTER PLATFORMS FOR TESTING CANCER

Several CCIL researchers are focused on glioblastomas, a type of brain cancer that is very aggressive, invasive, and incurable. Sara Pedron Haba, a research assistant professor in chemical and biomolecular engineering, is contributing to these efforts with her expertise in biomaterials engineering.

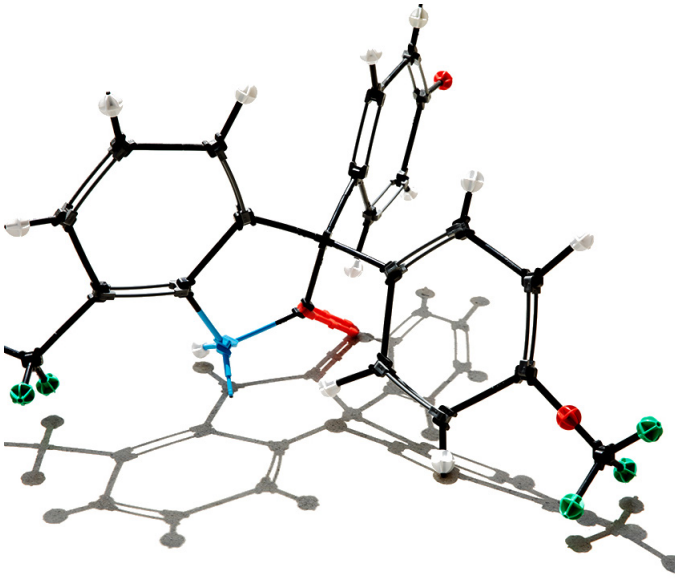
Pedron Haba is developing alternatives to animal models that can grow tumors in vitro, mimic the body's native tissues, and can test cells with drugs and radiotherapy. Developing faster, more effective, and inexpensive techniques for glioblastomas is increasingly important as current therapies have not significantly improved and the patient survival rate remains low for this disease.

> **"These tumor models are able to integrate different brain cells in a controlled configuration to enable more accurate prediction of effective drugs using patients' biopsied tissue. This is particularly important in cancers with low numbers of patients available for participation in clinical research."**
> **— Sara Pedron Haba**

CCIL SCIENTISTS DISCOVER INNOVATIVE BREAST CANCER THERAPEUTIC

A new approach to treating breast cancer kills 95-100% of cancer cells in mouse models of human estrogen-receptor-positive breast cancers and their metastases in bone, brain, liver, and lungs. The newly developed drug, called ErSO, quickly shrinks even large tumors to undetectable levels.

Led by CCIL scientists, the research team published their findings in the journal Science Translational Medicine. "Even when a few breast cancer cells do survive, enabling tumors to regrow over several months, the tumors that regrow remain completely sensitive to retreatment with ErSO," said U. of I. biochemistry professor David Shapiro, who led the research with Illinois chemistry professor Paul Hergenrother.



3D model of ErSO molecule

"It is striking that ErSO caused the rapid destruction of most lung, bone, and liver metastases and dramatic shrinkage of brain metastases, since tumors that have spread to other sites in the body are responsible for most breast cancer deaths," Shapiro said.

The activity of ErSO depends on a protein called the estrogen receptor, which is present in a high percentage of breast tumors. When ErSO binds to the estrogen receptor, it upregulates a cellular pathway that prepares cancer cells for rapid growth and protects them from stress. This pathway, called the anticipatory Unfolded Protein Response, or a-UPR, spurs the production of proteins that protect the cell.

"It turns out that this pathway shields cancer cells from being killed off by anti-cancer drugs," Shapiro said.

Shapiro and former U. of I. medical scholar Neal Andruska first identified the a-UPR pathway in 2014 and reported the development of a compound that pushed the a-UPR pathway into overdrive to selectively kill estrogen-receptor-containing breast cancer cells.

"Because this pathway is already on in cancer cells, it's easy for us to overactivate it, to switch the breast cancer cells into lethal mode," said graduate student Darjan Duraki, who shares first-author status with graduate student Matthew Boudreau on the new report.

While the original compound prevented breast cancer cells from growing, it did not rapidly kill them, and it had undesirable side effects. For the new research, Shapiro and Hergenrother worked together on a search for a much more potent small molecule that would target the a-UPR. Their analysis led to the discovery of ErSO, a small molecule that had powerful anticancer properties without detectable side effects in mice, further tests revealed.

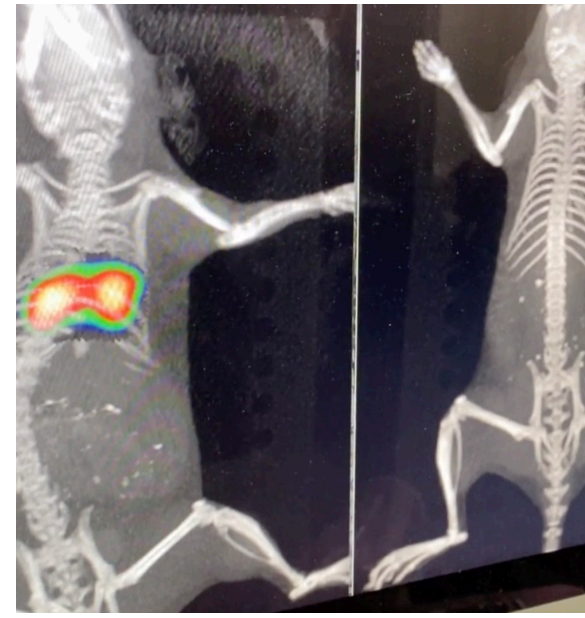
"This anticipatory UPR is estrogen-receptor dependent," Hergenrother said. "The unique thing about this compound is that it doesn't touch cells that lack the estrogen receptor, and it doesn't affect healthy cells – whether or not they have an estrogen receptor. But it's super-potent against estrogen-receptor-positive cancer cells."

ErSO is nothing like the drugs that are commonly used to treat estrogen-responsive cancers.

"This is not another version of tamoxifen or fulvestrant, which are therapeutically used to block estrogen signaling in breast cancer," Shapiro said.

Even though it binds to the same receptor that estrogen binds, it targets a different site on the estrogen receptor and attacks a protective cellular pathway that is already turned on in cancer cells.

"Since about 75% of breast cancers are estrogen-receptor positive, ErSO has potential against the most common form of breast cancer," Boudreau said. "The amount of estrogen receptor needed for ErSO to target a breast cancer is very low,



(Left) Pre-treatment. (Right) After 7 days.

so ErSO may also work against some breast cancers not traditionally considered to be ER-positive."

Further studies in mice showed that exposure to the drug had no effect on their reproductive development. And the compound was well tolerated in mice, rats, and dogs given doses much higher than required for therapeutic efficacy, the researchers found.

ErSO also worked quickly, even against advanced, human-derived breast cancer tumors in mice, the researchers report. Often within a week of exposure to ErSO, advanced human-derived breast cancers in mice shrank to undetectable levels.

"Many of these breast cancers shrink by more than 99% in just three days," Shapiro said. "ErSO is fast-acting and its effects on breast cancers in mice are large and dramatic."

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SUPPORTING THE MOST INNOVATIVE CANCER RESEARCH

Auinash Kalsotra

Auinash Kalsotra, associate professor in biochemistry, leads a lab that is uncovering the intricacies of cell biological mechanisms that may lead to more targeted and improved cancer therapies. Kalsotra, a CCIL seed grant recipient, is an expert in RNA. His lab is currently studying the proteins that cause diseases, like cancer, when RNA splicing is not regulated correctly.

"THE CANCER CENTER AT ILLINOIS HAS ALLOWED SCIENTISTS TO EXPLORE NEW AREAS IN CANCER RESEARCH, MAKE FUNDAMENTAL DISCOVERIES, AND BETTER UNDERSTAND PHYSIOLOGICAL AND PATHOPHYSIOLOGICAL PROCESSES."

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Diwakar Shukla

Diwakar Shukla, associate professor of chemical and biomolecular engineering, received a CCIL grant to study how human growth factor receptors, which play a critical role in numerous cancers, could be selectively targeted using drugs.

The grant funding allowed the research team to demonstrate how cutting-edge experimental techniques and machine learning approaches could provide information that is inaccessible to current experimental approaches for a key class of cancer-related proteins and expand computational research in a new area that will play a critical role in fighting cancer.

Shannon Sirk

Therapeutic antibodies have revolutionized the treatment of many diseases, including cancer. However, these drugs can be prohibitively expensive and are not an option for every patient. Shannon Sirk, assistant professor of bioengineering, is working to address this issue by engineering alternative production and delivery systems for these cancer-fighting drugs.

Sirk's research group is modifying human commensal microbial species to generate therapeutic antibodies from inside the body, circumventing the need for costly manufacturing and providing a means for long-term, low-cost treatment for cancer patients.

CCIL IN THE NEWS

CCIL chemist wins Johnson & Johnson award for breast cancer research

As a Johnson & Johnson 2021 WISTEM2D Scholar Award winner, chemistry professor Hee-Sun Han will be developing a new imaging-based methodology to study RNA-RNA interactions in breast cancer.

Each recipient receives $150,000 in funding and three years of mentorship from Johnson & Johnson. Explaining the project, Han said the majority (more than 90 percent) of RNAs do not encode proteins, and recent studies show that these non-coding RNAs (ncRNAs) are involved in the regulation of most cell processes.

"ncRNAs hold a good potential for next-generation cancer drugs; thus, our study can provide valuable insight into the development of new cancer drugs," Han said.

READ MORE CCIL NEWS AT:
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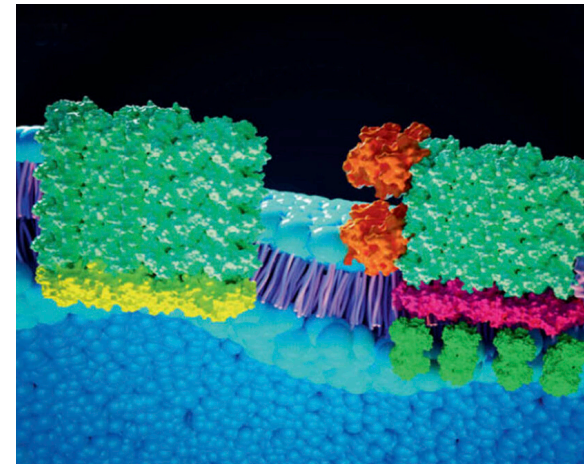


Light can trigger key signaling pathway for embryonic development, cancer

Blue light is illuminating a new understanding of a key signaling pathway in embryo development, tissue maintenance, and cancer genesis.

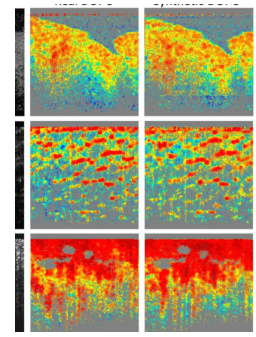
Research led by the CCIL's Kai Zhang, professor of biochemistry, developed an approach using blue light to activate the Wnt (pronounced "wint") signaling pathway in frog embryos. The pathway plays a wide variety of roles in animal and human development, and the ability to regulate it with light will allow researchers to better study its assorted functions, the team says.

"Because cancers often involve overactivated signaling, we envision that a light-sensitive Wnt activator could be used to study cancer progression in live cells," Zhang said.

CCIL member translates virus expertise to cancer research

Nicholas Wu, assistant professor of biochemistry, has spent his career focused on viruses such as influenza and COVID-19 in his research. Wu is now expanding his knowledge to explore opportunities in new fields of study: cancer and immunotherapy.

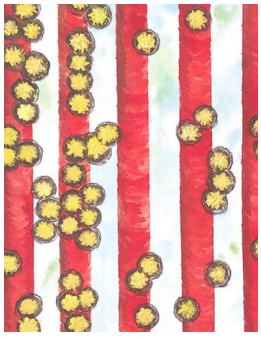
"We've looked at virus evolution – it's similar to how cancer develops; both cancer and viruses gain resistance to drugs since they evolve so fast … I've also researched how flu viruses evolved to resist antibodies and have looked at the antibodies themselves," Wu said.



CCIL scientist uses deep learning to enhance cancer diagnostic tools

An Illinois research team, led by CCIL Research Program Leader Stephen Boppart, explored how deep learning methods can make polarization-sensitive optical coherence tomography, or PS-OCT, more cost-effective and better equipped to diagnose cancer in biological tissues.

"With the increasing use of OCT across medical fields, this advance will likely have a broad impact, and ultimately help to improve the detection and diagnosis of disease," Boppart said.



Compact biosensor microscope built for point of care diagnostics

For several years Brian Cunningham, CCIL Research Program Leader, and his research team have been developing microscopes that use photonic crystal biosensors — nanostructured glass surfaces that brightly reflect only one wavelength of light.

"We are collaborating with researchers at the Mount Sinai Medical Center to diagnose lung cancer, and with the Huntsman Cancer Institute to measure the effects of chemotherapy in prostate cancer," Cunningham said.

CCIL team receives NIH funding to develop imaging device

A team, led by the CCIL's Michael Oelze, is developing a new device that will improve the management of breast cancer using ultrasound imaging. The team has innovated new radiological clips that will increase visibility during imaging, reduce levels of radiation, and offer other new capabilities not previously available.

"Our USID clips would eliminate the need for radioactive seeds and also provide an image for anatomical context through ultrasound," Oelze said.

Annually, millions of individuals are negatively impacted by cancer. Due to the pandemic, the future for cancer patients remains uncertain.

But your gift can change that. Every day, Cancer Center at Illinois researchers walk into their labs with one goal in mind: to save lives. Through your financial support, you can ensure that this lab research continues and new opportunities are funded and explored through Cancer Center at Illinois cancer research grant programs.

Join us in the fight against cancer. Support CCIL research initiatives.

Infrastructure

Cancer Center Research Building

Provide a home for our scientists and their labs to undertake ground-breaking research, supported by world-class physical resources.

Centers of Excellence

Endowing a center of excellence will support cancer changing research, faculty, students, and equipment. Support a specific research focus.

Innovation

Director's Innovation Fund

An unrestricted fund to be used at the Director's discretion to support pioneering, high impact research and translation, new innovative programs, and events.

Directorship

Assist the Cancer Center at Illinois in retaining and supporting our current Director and invest in the recruitment of future leaders.

Instruction

Educational Programming

Train and recruit future cancer researchers. Support high school through postdoctoral students working in cancer research labs.

Professorships

Support faculty excellence, recruitment, and retention.

Learn more about how you can support the Cancer Center at Illinois.

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ILLINOIS STUDENTS RECEIVE CCIL SCHOLARSHIPS TO SUPPORT CANCER RESEARCH

Four Illinois students received 2021 CCIL Graduate Cancer Scholarships to pursue cancer research projects under the mentorship of CCIL scientists.

"A core mission of the Cancer Center at Illinois is to mobilize and inspire students across campus to pursue careers in cancer research," H. Rex Gaskins, CCIL Associate Director for Education, said. "Not only do CCIL scholarships accelerate cancer discoveries at Illinois, but they provide students with real-world laboratory experience with exceptional, interdisciplinary teams."

The four students selected include:

Bashar Emon, graduate research assistant in mechanical science and engineering, is studying the simultaneous biophysical and biochemical cellular interactions in 3D cancer models.

Sarah Gardner, graduate research assistant in biochemistry, is investigating how key enzymes and pathways regulate development of cancer stem cells.

Yoon Jeong, graduate research assistant in bioengineering, is establishing a bacteria-oncological screening strategy based on High-throughput Phenotype Screening (HTPS) and exploring the role of the microbiome in pancreatic cancer recurrence.

You Jin Song, graduate research assistant in cellular and developmental biology, is testing whether Metastasis-Associated Lung Adenocarcinoma Transcript 1 (MALAT1)-mediated SRSF1 activity plays an essential role during hypoxia response in cancer cells.

WHERE ARE THEY NOW?

Joy Chen recently graduated from Illinois with her bioengineering undergraduate degree. Chen participated in the CCIL's researcHStart program and Cancer Scholars Program.

Joy Chen, a graduate student, is attending the University of California, Berkeley (UC Berkeley) and University of California, San Francisco (UCSF) Joint Bioengineering Program this fall, where she hopes to continue conducting research.

Chen, a recently graduated bioengineering student from the University of Illinois, is especially eager to gain experience in more focused fields of research during her time at UC Berkeley and UCSF. Cell and tissue engineering, for example, is one area of research which she hopes to further explore in the upcoming semester.

"Cell and tissue engineering, like disease modeling with microfluidics, are areas that I don't really have experience in yet," Chen said. "[This past year], there were no in-person labs and we didn't get to do any of the higher level cell and tissue engineering labs, so I'm hoping to rotate through some of the tissue engineering labs over at Berkeley."

In addition, Chen is gaining experience in breast cancer-focused labs, an area of research with which she is already familiar due to her time at the CCIL.

A rotation program and a school that would allow her ample time in the research lab were factors that were especially important to Chen in her search for a graduate school. She hopes that this structure will allow her to discover which fields of research are the best fit.

"I think a rotation program was especially important to me because we didn't get to do in-person things [due to COVID], like seeing the school or seeing the lab, or meeting professors and students in-person [last year]," Chen said. "Having options and seeing what you like in the first year is important."

While excited to enter a new learning environment, Chen is appreciative of the skills and experiences she gained during her undergraduate career at the University of Illinois, and states that the CCIL's Cancer Scholars program was especially impactful.

As a Cancer Scholar, Chen was able to continue working with Erik Nelson, assistant professor of molecular and integrative physiology, who she began to work with as a high-school student in the CCIL's researcHStart summer program.

An especially memorable project in the Nelson lab involved breast cancer dormancy, which focused on examining cholesterol and its effects on breast cancer.

"I did a lot of work with animal models, looking at different dormancy models, and how 27-hydroxycholesterol plays a role in the recurrence of cancer from dormancy — which is a tricky thing to study," Chen said.

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