THE FUTURE OF CANCER RESEARCH IS HERE
Brilliant ideas. Breakthrough Innovations.
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Innovation Insider is a Cancer Center at Illinois publication that highlights the interdisciplinary and translational work of CCIL faculty, staff, students, and external partners.

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As I was flipping through the draft of this magazine, it became increasingly evident that the story of the Cancer Center at Illinois (CCIL) has deep roots in longstanding cancer research at Illinois. While many innovators have called Illinois home over the past 150 years, we are proud that current CCIL members include scientists who started making seminal breakthroughs in eras when well-known cancers had not been officially identified yet, the importance of specific genes in cancer progression was still a mystery, and targeted diagnostics and therapeutics were in their infancy.

These and other CCIL scientists are unraveling and publishing foundational knowledge that has had a global influence on cancer research. We may have been officially institutionalized in 2017, but our rich history started decades ago, and we’re in the midst of writing some of our most exciting chapters. In this issue of Innovation Insider, you will see how the CCIL is inspired by this rich history to attempt shaping the future of cancer care.

You will meet Benita Katzenellenbogen, a world-renowned expert in endocrinology with an inspirational passion for improving the quality of life for cancer patients. Alongside Prof. Katzenellenbogen’s decades of experience, I’m excited to introduce you to several new members who have recently joined the CCIL. These individuals are bringing knowledge across multiple disciplines, solidifying the CCIL’s strengths in cross-campus collaboration.

The stories of these incredible scientists all culminate towards one thing: discovery. The Cancer Center at Illinois is transforming the cancer research landscape, discovering and developing breakthroughs, and accelerating cancer care improvements. You will learn about how Andrew Smith is wielding quantum dots to improve medical imaging. How Viktor Gruev, in collaborations with other CCIL members, was inspired by the mantis shrimp to create new camera technology. And how Shannon Sirk is bioengineering improved cancer drug delivery methods. Our members are launching exciting technologies that will improve cancer detection and diagnoses as well as improve therapy, lower costs, and increase accessibility.

At our science and technology focused cancer center, the future is in our ideas, in our innovations, and in our labs. CCIL’s interdisciplinary and collaborative initiatives facilitate rapid progress in cancer research. And our commitment to these efforts stretches beyond research. CCIL scientists are training and mentoring the next generation of cancer scientists and oncologists – giving them the creative freedom and tools to develop and lead their own projects and become independent scientists.

Within these pages you will find history, mystery, a bit of intrigue, and inspiration. Please join me in saluting the commitment and excellence of those featured in this issue and all our CCIL scientists, staff and students who are dedicated to solving one of the world’s grandest challenges: cancer.

“All we have to decide is what to do with the time that is given to us.” — J.R.R. Tolkien, The Lord of the Rings

Rohit Bhargava, CCIL Director
CCIL SCIENTIST REFLECTS ON DECADES OF BREAST CANCER RESEARCH
For decades, Benita Katzenellenbogen, Swanlund Professor of Molecular and Integrative Physiology, has focused on understanding breast cancer and women’s health, collaborating with scientists on campus and around the world to develop better treatments and reduce morbidities from the disease. Her research has provided the framework for the development of anti-hormonal therapies used in breast cancer treatment and prevention.

“In the last 25 years, there’s been about a 40% drop in deaths from breast cancer and there have been many exciting breakthroughs and advances both in understanding breast cancer, which is a lot of what I tried to do, and also improving patient care overall,” Katzenellenbogen said.

“In that regard, I would say we’re trying to improve both understanding of the disease and how we can reduce deaths, but also improve the quality of life for people who are on breast cancer treatments, and that means reducing toxicities of some of the treatments.”

Katzenellenbogen, alongside her husband, Swanlund Chaired Professor of Chemistry John Katzenellenbogen, has researched and developed improvements of anti-estrogens, such as the commonly-used Tamoxifen, and the second-line treatment Fulvestrant.

“There are several major subtypes of breast cancer, and the most abundant, about 70% of breast cancers, are called estrogen receptor-positive (ER-positive), meaning they contain the estrogen receptor,” Katzenellenbogen explains. “The estrogen receptor is the main factor that we and others try to target, because if you can turn off the estrogen receptor, you very effectively can suppress these cancers.”

Through their work, the Katzenellenbogens’ labs determined cancers often develop resistance to antiestrogens over time, prompting a closer look at the biology of breast cancer resistance. In particular, they have researched the impact of transcription factor FOXM1 in ER-positive and in triple negative breast cancer, the latter being an aggressive subtype of the disease that lacks the estrogen receptor and frequently metastasizes. The highly upregulated FOXM1 controls many cell activities that lead to cancer progression and metastasis. Their labs found that these inhibitory compounds can suppress the progression of ER-positive and also triple negative breast cancer cells and tumors.

READ MORE: GO.ILLINOIS.EDU/CANCERHISTORY

“While I do think we are understanding cancer much better now than ever, there is so much more to do,” Katzenellenbogen said. “I think it’s an optimistic time because of our treatments and approaches... screening is much better than ever.”
Advances in cancer technologies used to diagnose and treat cancer have revolutionized the cancer research landscape. At the Cancer Center at Illinois, scientists are using their multidisciplinary expertise to develop devices and techniques that address the limitations of current tools.

**Viktor Gruev**
Professor, Electrical and Computer Engineering

Research led by the CCIL’s Viktor Gruev seeks to develop a camera inspired by the mantis shrimp that can visualize cancer cells during surgery. The underwater creatures have exceptional vision - and the ability to see upwards of 12 colors vs. the three perceived by humans. Their visual system inspired the creation of an imaging device that works with tumor-targeted drugs to see cancer in animal and human patients.

“Engineers spend incredible amounts of time and money developing the image sensors in cellphones. These devices can capture pictures that are perfect for social media, but when doctors are examining patients, they don’t care how nice the shot looks – they care how well the picture captures reality. The driving force in the camera market is simply incompatible with the technology required for medical diagnostics.” — Gruev
CCIL scientist, Andrew Smith, is an expert in a complex nanoparticle showing promise at improving medical imaging, the quantum dot. The Smith Lab is publishing work on how they are able to make these quantum dots emit light in an infrared spectrum all for a better quantification and understanding of the cells present in adipose tissue. The information received may uncover why some tissues are more prone to inflammation — leading to diseases like cancer.

“Quantum dots can measure things in the body that are very, very dynamic and complicated and that we can’t see currently. They give us the ability to count cells, detect their exact locations, and observe changes over time. I think it is really a huge advance.” — Smith

Wawrzyniec Dobrucki, also Head of the Experimental Molecular Imaging Laboratory, is a major collaborator on a number of CCIL projects. In addition to working with Viktor Gruev to develop the mantis shrimp-inspired camera, Dobrucki is using molecular imaging to determine the effectiveness of cancer therapies, specifically looking at prostate cancer.

“Our technique would be a way to address the needs for active surveillance when patients are diagnosed with a low-grade cancer and are left with limited tools to observe the switch from indolent to aggressive disease where treatment is needed.” — Dobrucki
Krush Cancer

In Spring 2022, Illinois men's basketball hosted a “Krush Cancer” game, dedicated to raising awareness about the CCIL's groundbreaking cancer research initiatives.
An Illinois research team, led by the CCIL’s Shannon Sirk, assistant professor of bioengineering, is developing a method of producing and delivering monoclonal antibody treatments for breast cancer through commensal microbes in the gut. If successful, this approach could increase accessibility and dramatically decrease the cost of monoclonal antibodies.

The use of bioengineered commensal microbes, bacteria that have a neutral or beneficial effect on our bodies, to produce therapeutics could be incredibly efficacious since they are already perfectly suited to the gut microenvironment. However, there remains a major issue to be solved: how to get the microbially-produced drugs out of the gut and into the bloodstream to the target breast tumor. This new delivery method could remove the necessity for injections of high dose treatments, providing patients with a low-level, steady state rather than a single, large dose.

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“We have an opportunity here to develop a technology that will increase access and decrease cost.” — Sirk
Cancer Center at Illinois and Mount Sinai researchers have developed a low-cost, portable, point-of-care technology capable of diagnosing early-stage liver cancer within 30 minutes. The study, led by Brian Cunningham, CCIL research program leader and professor of electrical and computer engineering, and Carl R. Woese Institute for Genomic Biology (IGB) postdoctoral fellow Bin Zhao, uses a toaster-sized device comprised of a red LED light, microscope objective, and webcam to detect gold nanoparticles (AuNPs) that attach to target RNA.

Researchers from the Mount Sinai group had previously identified three snRNA biomarkers that were relevant for diagnosing liver cancer, and Cunningham’s group developed the technology, a photonic resonator absorption microscopy (PRAM) assay, for detecting low levels of snRNA. This study was the first clinical collaboration testing the technology with human specimens.

“The detection instrument, PRAM, is very inexpensive, small, and has about $7,000 worth of components including the computer, which makes it ideal for point-of-care diagnostic tests for genomic mutations in the clinic,” said Cunningham.
This testing method requires only a few drops of the patient’s blood, is sensitive enough to detect microRNAs (miRNAs) in serum, and is much faster than PCR, the predominant method of detecting snRNAs.

PCR can be very sensitive but requires a laboratory environment where researchers can amplify the molecules with enzymes and multiple thermal cycles that necessitate accurate temperatures in each step of the process.

“The process doesn’t happen all at once, but base by base, almost like a zipper with one link at a time,” Cunningham said. “The cool thing is that when the protector is replaced by the target snRNA, the target is smaller than the protector, so when the protector is removed, the exposed, available nucleic acid bases can be captured by the biosensor that has been specifically designed with a complimentary sequence.”

Cunningham’s team named this biochemical process Activate Capture + Digital Counting, or AC+DC.

The target snRNAs, once captured by the AuNPs and the biosensor, are then counted using a red LED that is reflected into a simple, ordinary webcam. AuNPs are engineered to be very efficient absorbers of red light, so they appear as dark spots that researchers can count.

This testing method could easily be altered to diagnose other cancers or diseases, since there are RNAs associated with every kind of cancer that is thought to be involved in controlling gene expression and used by cancer cells to evade processes of restricting proliferation and metastasis.

The PRAM AC+DC technique may also have applications in monitoring the effectiveness of cancer therapies, where a baseline could be established to determine whether a therapy is having a positive or negative effect. This simple, low-cost blood test would be much less invasive than a biopsy, allowing for close monitoring of treatment efficacy and signs of rejection in patients.

**READ MORE:**
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Bo Wang | Comparative Biosciences

Wang, an assistant professor, specializes in lipid metabolism and applies this knowledge to liver and colorectal cancers. Studies have shown that cholesterol metabolism and high cholesterol levels are linked to colorectal cancer, and Wang’s research with mouse models has uncovered a link between phospholipids and tumorigenesis in intestines. Currently, his work focuses on the enzyme LPCAT3, which controls phospholipid remodeling.

“I noticed a link between phospholipid remodeling and cholesterol metabolism, which regulates the function of stem cells and promote the development of colorectal cancer, so I’m continuing that work to better understand the link between cholesterol metabolism and cancer development.” - Bo Wang
Kevin Van Bortle  
**Cell & Developmental Biology**

Van Bortle’s research questions center around the understudied RNA Polymerase III (Pol III), a complex that transcribes genes encoding t-RNA and small non-coding RNA. In cancers, Pol III is present in elevated levels and is believed to play a role in uncontrolled cancer growth.

“There’s a wide-ranging intersection of Pol III’s cancer relevance, but we do know that it sits at the nexus of cell growth and protein proliferation. We’re behind on our understanding of pol III, but it’s a challenge that I’m excited about since it is clearly so important to cancer development.” - Kevin Van Bortle

Patrick Sweeney  
**Molecular & Integrative Physiology**

As an expert in the brain’s regulation of feeding and body weight, Sweeney is focusing his research on the regulation of obesity, anorexia, and cancer-related cachexia – the loss of lean muscle mass. Cancer patients often experience cachexia, visceral malaise, and late-stage anorexia due to the disease state and chemotherapies.

“Almost all patients show loss of lean mass, and I suspect there are conserved pathways in the brain that are involved in cachexia. My studies suggest that there are circuits in the hypothalamus and hind brain that drives features associated with cachexia – reduced appetite and malaise, which could be interesting targets if we can block them from being activated.” - Patrick Sweeney
Low-carb diets may improve treatment of liver metastases in breast cancer patients

A new study by CCIL education program leader, Zeynep Madak-Erdogan and her team, have found a new mechanism of endocrine resistance in breast cancers metastasized to the liver. The study, published in Molecular Cancer Research, found that liver metastases rely on increased amounts of glucose, revealing the possibility of a dietary intervention to reduce tumor burden and increase treatment efficacy.

“We are so excited about the possibilities, especially in terms of the dietary intervention, where there are not as many regulatory steps. Low-carb diets can easily be tested in the clinic, and one of our near-future goals is to get this to clinical trials,” Madak-Erdogan said.

Neighborhood food environment potential driver of colorectal cancer health disparities

Colorectal cancer is expected to claim more than 52,000 American lives in 2022, and if this year is like most others, Black Americans will bear the brunt of the disease. To understand the disparity in context, University of Illinois researchers looked at the intersection of bile acids, gut microbes, racial identity, and neighborhood food environment in the development of colorectal cancer.

“There is overwhelming evidence those most susceptible to colorectal cancer disparities have inequitable access to high-quality food driven by racist housing policies and predatory marketing strategies,” Patricia Wolf, postdoctoral researcher, said.

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Treating cancer patients and developing biopharmaceutical drugs depends on making the distinction between a healthy live-cell and a sickly dead cell. The state of the cell can indicate whether a cancer treatment is working or a new type of medicine is effective. Groundbreaking research, led by CCIL researchers including Tissue Microenvironment (TiME) program trainee Chenfei Hu, can determine the state of a cell without the limitations inherent to some current methods.
Join us in the fight against cancer.

- To trailblaze discoveries in cancer biology that will transform the cancer research landscape.
- To create state-of-the-art imaging technologies that will detect cancer earlier, quicker, and cost-efficiently.
- To be on the cutting-edge of personalized medicine — allowing clinicians to determine the best treatment plan for their patients.
- To innovate new therapeutics and bioengineer tumor models to ensure that new cancer treatments are safer and more effective than ever before.
- To educate the next generation of cancer researchers, creating a legacy of scientists who will continue to improve cancer patient outcomes.
- To collaborate at the convergence of basic science, technology, and engineering — harnessing the power of world-renowned experts from across disciplines to fight cancer, and ultimately, save lives.

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In 2021, Illinois graduate student Sarah Gardner was awarded a Cancer Center at Illinois (CCIL) Graduate Cancer Scholarship. Today, Gardner is studying cancer stem cells, associated enzymes, and how the tumor microenvironment influences cancer cell phenotype in CCIL member Jefferson Chan’s lab.

Gardner’s work uses a lung cancer cell line that has high concentrations of aldehyde dehydrogenase (ALDH), which is responsible for converting aldehydes to carboxylic acids and may play a role in resistance to chemotherapies with aldehyde intermediates. Gardner believes that ALDH may also be affecting phenotypes such as cancer cell stemness, proliferation, and motility.

Gardner is researching how ALDH and its downstream pathways are affected by the tumor microenvironment and surrounding tissue. For instance, inflammation is common in the lungs due to factors such as second-hand smoke, lung infections, or inhaling air pollutants, and inflammation can be a source of nitric oxide. Gardner hypothesizes that higher concentrations of nitric oxide in the tumor microenvironment could affect ALDH function and contribute to aggressive cancer growth, increased rates of metastasis, and higher rates of cancer recurrence.

“While there are good methods for cancer treatment, they are not perfect… improvements could be made if we understood the effect of external factors, such as the environment, or internal factors, like the tissue microenvironment,” Gardner said.
STUDENT SPOTLIGHT: OPEYEMI AROGUNDADE
Opeyemi Arogundade, Tissue Microenvironment (TiME) program trainee and student in Cancer Center at Illinois (CCIL) scientist, Andrew Smith’s, lab, is applying his academic background in physics to cancer research and improving the penetration of nanoparticles into tissue to obtain three-dimensional images.

As an undergraduate student, Arogundade initially intended to apply for medical school; however, a summer research experience at would change his mind. At first, his study of photonic crystals, nano-fabricated materials that are made using laser light-beams, was directed towards improving the efficiency of solar cells.

Later, Arogundade would pivot his research towards spectroscopy with the goal of using the nanomaterials as biosensors.

When he met Andrew Smith, professor of bioengineering, at the University of Illinois, Arogundade knew that he had found the right lab to build up his knowledge of tissue and cancer biology.

“One of the things that drew me to Illinois and to Dr. Smith’s lab was the chance to explore different opportunities. I was still interested in medical technology, but I realized that I could pursue those interests without becoming a physician,” Arogundade said.

Arogundade has since focused his own research projects on improving the penetration of quantum dots, a type of nanoparticle, for 3D imaging. Most high-resolution tissue images are obtained from thinly sliced tissue, but these generate 2D images, which lack the complexity of 3D images. Other imaging modalities such as MRI and CAT scans can produce 3D images, but often sacrifice high resolutions that can be obtained with 2D fluorescent imaging or microscopy.

“My goal is to try to bridge that resolution gap by imaging whole tissues. The problem is that light doesn’t penetrate 3D tissue very well, and we are trying to address this using our quantum dots, which are bigger than dyes but have a narrower emission,” Arogundade said.

As a TiME program trainee, Arogundade is a member of a community of graduate students who concentrate on the tissue microenvironment through different disciplines and areas of expertise. Arogundade’s current focus is on adipose tissue, which has a strong correlation to breast cancer progression in women.

“My goal is to get a better understanding of how cancer progresses and what factors influence that progression. Knowing this, we could develop better therapies and preventions, leading to improved prognoses for patients,” Arogundade said.