Pathways to DISCOVERY
At the Forefront of Cancer Care and Discovery®

THE UNIVERSITY OF CHICAGO MEDICINE
Comprehensive Cancer Center

NCI CCC® A Comprehensive Cancer Center Designated by the National Cancer Institute

Winter 2015 | cancer.uchicago.edu

The University of Chicago Launches Historic Campaign

In October, the University of Chicago publicly launched the most ambitious fundraising campaign in its history. The University of Chicago Campaign: Inquiry and Impact seeks to raise $4.5 billion to support faculty and researchers who are shaping fields of inquiry, distinctive educational opportunities for students at all levels, and innovative programs to enhance the University's local and global reach and impact. Of that amount, $1.2 billion will be directed toward new resources for medicine and biological sciences, with $350 million earmarked for cancer research at the University of Chicago Medicine Comprehensive Cancer Center. With this investment, the Comprehensive Cancer Center will tackle cancer's toughest challenges by advancing discovery and developing interventions.

In addition, researchers and doctors are focused on improving cancer prevention programs for individuals at high risk, ground-breaking technologies for early detection, and survivorship programs that better meet the needs of patients, elevating the standard of cancer care.

Pinpointing Cancer Where It Starts

When University of Chicago researcher Janet D. Rowley, MD, established the genetic basis of cancer in 1972, she opened the door for one of the earliest targeted cancer therapies—Gleevec, a drug that has transformed chronic myelogenous leukemia from a fatal disease to a manageable condition. Today, a person's entire genome can be sequenced in just days. Scientists are routinely screening the subtle differences that mark susceptibility to disease across hundreds of genomes. The quest is on to pinpoint the biological drivers behind specific, individual cancers and usher in genome-guided treatment.

"Think of cancer as a picture," said Michelle M. Le Beau, PhD, Arthur and Marian Edelstein Professor of Medicine and director of the Comprehensive Cancer Center. "We're moving from a grainy image of Earth from outer space to a pointillist painting in which every pinpoint is visible."

Collectively, UChicago investigators are steadily filling in these pixels to bring a new, sharper view of cancer into focus. This genetic specificity offers a springboard for new therapies personalized for individual patients.

Importance of Philanthropy

Advances will depend also on the bright ideas and conceptual leaps of dedicated, inquisitive investigators. Philanthropy is critical here too—supplying the seed funding needed to incubate promising early-stage research to the point where it is competitive for major support.

"Donor support allows us to solve the toughest problems, [yet be] more innovative and comprehensive in our approach," said Le Beau.

> The quest is on to pinpoint the biological drivers behind specific, individual cancers and usher in genome-guided treatment.

Cancer genomics is a wide-ranging enterprise: bold team science, new treatment paradigms, intensive sequencing, powerful data-crunching computers, and brilliant investigators committed to generating the next big idea—all of it converging on better, more targeted ways to treat people with cancer. The opportunities to contribute abound. The payback will be profound.

FROM THE DIRECTOR


Michelle M. Le Beau, PhD

In this issue of Pathways, *I am thrilled to report on several major developments that are allowing us to impact the future of cancer care. For one, the University of Chicago Campaign: Inquiry and Impact earmarked $350 million for cancer research at the University of Chicago Medicine Comprehensive Cancer Center. We are optimistic this investment will allow us to tackle cancer's toughest challenges by advancing discoveries and developing interventions.*

Scientific advances will require the computational power to effectively and efficiently mine the growing wealth of "Big Data." In partnership with the National Cancer Institute (NCI), the University of Chicago has recently received funding to establish the nation's most comprehensive computational facility that stores and harmonizes cancer genomic data generated through NCI-funded research programs nationwide. The Genomic Data Commons will expand access for scientists around the country, speeding up research and leading to faster discoveries to benefit patients.

We are also proud to celebrate that Comer Children's Hospital has been serving pediatric patients for the past 10 years and has achieved many milestones in its short history. In addition to providing the best possible care to patients in a kid-friendly environment, Comer is home to some of the world's top researchers. In fact, research conducted by our scientists has led to improvements in the way adolescents and young adults throughout the world are being treated for leukemia and other cancers.

In another exciting development, one of our investigators designed an innovative clinical trial to improve clinical decision-making. The trial addresses the problem of tumor heterogeneity by gathering as much information as possible about the distinct tumor cell populations, and what drives their behavior, and then uses molecularly targeted therapies to eliminate them. This project highlights the potential of personalized medicine, or precision oncology, to tailor therapy to the genetic make-up of both the individual patient and their tumor.

An important facet of our mission is to train the next generation of cancer researchers. That is why we have launched a pipeline program to introduce promising high school and undergraduate students from the Chicago area to cancer research. The CURE program provides a hands-on summer research experience for students from underrepresented populations under the mentorship of Comprehensive Cancer Center faculty.

Also in this edition of *Pathways*, we tell the story of a visionary couple who chose to donate $1 million to accelerate cancer research, as well as a team of radiology experts that assists researchers with the unique medical imaging needs of clinical trials. Enjoy the issue!

Regards,

Michelle M. Le Beau, PhD
Director, The University of Chicago Medicine Comprehensive Cancer Center; Arthur and Marian Edelstein Professor of Medicine

UChicago Medicine to Expand to Orland Park

The University of Chicago Medicine is set to break ground on a 120,000-square-foot medical facility in downtown Orland Park this spring.

The mixed-purpose development will:

- Include a pharmacy and a 580-space parking structure
- Employ more than 100 people
- Create more than 200 construction jobs
- Bring $61 million in private investment and 22,400 annual visitors/patients to the village's downtown
- Bring an estimated $25.5 million to the Southwestern suburb

The hospital's lease-to-purchase agreement is for approximately 4.07 acres of village-owned land at the northwest corner of LaGrange Road and 143rd Street. The public would have free evening and weekend use of the parking garage.

According to research, this southwest suburban area will need to add 370 physicians and more than 400 exam rooms by 2018 to keep pace with population growth and the anticipated impact of the Affordable Care Act.

An artist rendering of the new Center for Advanced Care at Orland Park

Comprehensive Cancer Center at Silver Cross Hospital Adds Second Linear Accelerator

Due to increased demand at the University of Chicago Medicine Comprehensive Cancer Center at Silver Cross Hospital, a second linear accelerator vault has been built which will hold a new TrueBeam™ Linear Accelerator. TrueBeam is an advanced image-guided radiation therapy (IGRT) system used to treat cancer with speed and accuracy while avoiding healthy tissues and organs. The new machine will allow for greater capacity and flexible scheduling to accommodate patient needs and expectations.

"Our radiation oncology volume has grown each year since we opened in July 2012," said Theresa Quinn, executive director at Silver Cross. "In response to patient demand and in an effort to maintain our high levels of patient satisfaction, we found it necessary to invest in a second machine."

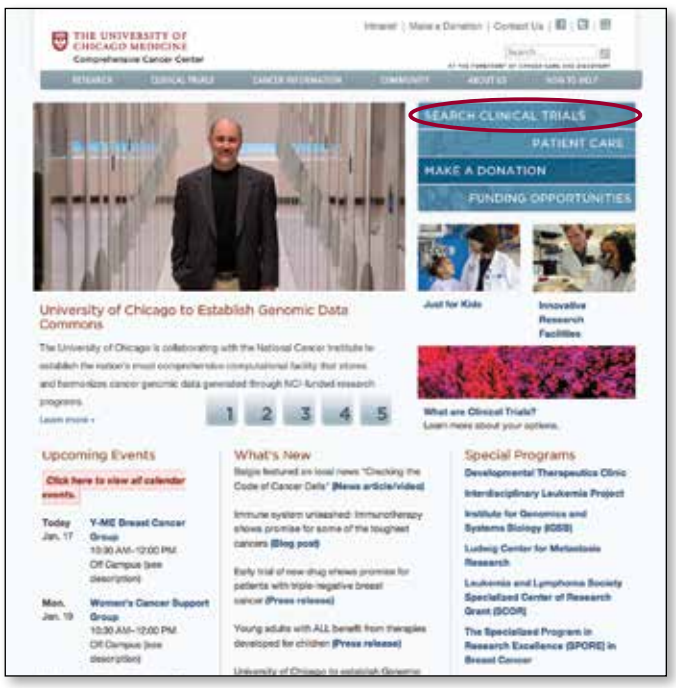
NANCY DAVIDSON AWARDED 2014 SHUBITZ PRIZE


Nancy E. Davidson, MD, receives the 2014 Simon M. Shubitz Cancer Prize from Comprehensive Cancer Center Director Michelle M. Le Beau, PhD, Arthur and Marian Edelstein Professor of Medicine.

The Comprehensive Cancer Center and the University of Chicago Cancer Research Foundation presented the 2014 Simon M. Shubitz Cancer Prize to Nancy E. Davidson, MD, a world-renowned breast cancer researcher best known for her key findings on the role of hormones, particularly estrogen, on gene expression and cell growth in breast cancer. She has led several important national clinical trials of potential new therapies, including chemoendocrine therapy for premenopausal breast cancer. Davidson is the Hillman Professor of Oncology at the University of Pittsburgh School of Medicine, director of the University of Pittsburgh Cancer Institute and UPMC CancerCenter, and associate vice chancellor for cancer research. She presented her lecture, "Breast Cancer in the Age of Precision Cancer Medicine," to University of Chicago faculty and students on October 13. The Shubitz Cancer Prize and Lectureship is awarded each year to recognize excellence in cancer research and to gain knowledge from internationally respected scientists who have made significant contributions to the study of cancer.

Open Cancer Clinical Trials

Patient enrollment is underway for more than 350 clinical trials at the University of Chicago Medicine Comprehensive Cancer Center. A few of our newly launched clinical trials include:



- A phase II, randomized, comparative trial of standard of care, with or without midostaurin to prevent relapse following allogeneic hematopoietic stem cell transplantation in patients with FLT3-ITD mutated **acute myeloid leukemia**–Wendy Stock, MD, principal investigator.
- An open-label, randomized phase IIb/III active control study of second-line Hyperacute®-Lung (tergenpumatucel-L) immunotherapy versus docetaxel in progressive or relapsed non-small cell **lung cancer**–Ravi Salgia, MD, PhD, principal investigator.
- A randomized, double-blind, phase II study of ruxolitinib or placebo in combination with capecitabine in subjects with previously treated advanced or metastatic HER2-negative **breast cancer**–Gini Fleming, MD, principal investigator.
- Phase III study comparing daratumumab, lenalidomide, and dexamethasone (DRd) vs lenalidomide and dexamethasone (Rd) in subjects with relapsed or refractory **multiple myeloma**–Andrzej Jakubowiak, MD, PhD, principal investigator.
- A phase I/II trial of enzalutamide plus the glucocorticoid receptor antagonist mifepristone for patients with metastatic castration resistant **prostate cancer** (CRPC)–Russell Szmulewitz, MD, principal investigator.
- An integrated phase II/III, open-label, randomized, parallel and controlled study of the safety and efficacy of CG0070 oncolytic vector regimen in patients with non-muscle invasive **bladder carcinoma** in situ disease who have failed BCG therapy and refused cystectomy–Gary Steinberg, MD, prinicipal investigator.

To learn more about these or any other Comprehensive Cancer Center clinical trial, call toll-free 1-855-702-8222 for adult clinical trials or 1-773-702-6808 for pediatric clinical trials, or go to *cancer.uchicago.edu* and click on Search Clinical Trials in the blue box.

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NCI Partnership Will Use Big Data to Enhance Cancer Research


Robert Grossman, PhD, professor of medicine and director of the Center for Data Intensive Science, is leading the Genomic Data Commons project.

The University of Chicago is collaborating with the National Cancer Institute (NCI) to establish the nation's most comprehensive computational facility that stores and harmonizes cancer genomic data generated through NCI-funded research programs.

The establishment of the NCI Genomic Data Commons (GDC) will expand access for scientists around the country, speeding up research and, in turn, leading to faster discoveries to benefit patients. The GDC will provide an interactive system for researchers, making the data easier to use; it also will provide resources to facilitate the identification of subtypes of cancers for which specific molecularly targeted therapies may be developed.

"The Genomic Data Commons has the potential to transform the study of cancer at all scales," said Robert Grossman, PhD, professor of medicine and director of the Center for Data Intensive Science, who is leading the GDC project. "It supplies the data that allows any researcher to test his/her ideas, from comprehensive 'big-data' studies to genetic comparisons of individual tumors, to identify the best potential therapies for a single patient."

NCI has funded a number of large research projects that have collected genomic data on tumor types from more than 10,000 patients. However, the data for these studies are scattered across different locations and are in different formats, making it challenging for researchers to perform analyses across datasets. As genome sequencing technology continues to evolve and datasets become increasingly larger and more complex, this situation will become more problematic. According to an Institute of Medicine report, there is an urgent need for a system to store, harmonize and analyze existing cancer genomics data, which currently amounts to roughly 20 petabytes of information—10 times as much as all of the publications currently housed in U.S. academic research libraries.

Data Democracy

To address these challenges, the GDC will provide an expandable, modern informatics framework that applies a set of standards to make raw and processed genomic data broadly accessible. The GDC will integrate and centralize existing NCI datasets through an approach to data storage and analysis similar to what is used by companies such as Google and Facebook. The GDC will eliminate a major bottleneck by streamlining access to data for researchers regardless of their institution's size or budget—effectively democratizing access to the material. It will also enable previously unfeasible collaborative efforts between scientists.

"With the GDC, the pace of discovery shifts from slow and sequential to fast and parallel," said Conrad Gilliam, PhD, dean for basic science at the University of Chicago Biological Sciences Division. "Discovery processes that today would require many years, millions of dollars, and the coordination of multiple research teams could literally be performed in days, or even hours."

The GDC serves as a key step toward the development of precision medicine—targeted treatments that are tailored to individual patients. Once fully developed, it will provide an interactive system for researchers and clinicians to upload their cancer genomics data and identify molecular subtypes of cancer and potential therapeutic targets. Genetic data will be linked to extensive clinical information from patients and their response to treatment.

"The availability of high-quality genomic data and associated clinical annotations is extremely important because this information can be combined and mined repeatedly to make new discoveries," said Louis Staudt, PhD, MD, director of NCI's Center for Cancer Genomics.

Comer Celebrates 10th Anniversary

From boo-boos and bandages to smiles and recoveries, Comer Children's Hospital at the University of Chicago Medicine has experienced many milestones in its short history, many of which can be found in the field of cancer research and treatment. But before acknowledging the accomplishments of the past decade, it is important to know how Comer Children's Hospital came to be.

A Brief History of Pediatrics at the University of Chicago Medicine

Although the University of Chicago began in 1890, it was not until 1898 that the University became involved in medicine. Dedicated on Halloween in 1927, the University of Chicago Medicine quickly began expanding and growing. In 1967, the University of Chicago Medicine's Wyler Children's Hospital opened its doors. The hospital name was later changed to the University of Chicago Children's Hospital. Today, there is a new home for children's medicine. The University of Chicago Medicine Comer Children's Hospital opened in winter 2004.

A Generous Benefactor

The reality of Comer Children's Hospital would not have been possible without the generosity of one man and his family. Gary C. Comer was one of the nation's leading entrepreneurs and philanthropists. With the same energy and vision he brought to founding Lands' End, Gary and his wife, Frances, revolutionized children's healthcare by funding pediatric facilities and programs.

In 2001, the Comers made a generous gift to establish the University of Chicago Medicine Comer Children's Hospital. Two years later, they gave another gift to build the Comer Pediatric Emergency Department, which is the only dedicated emergency room for children on the South Side of Chicago. In January 2006, the couple made a $42-million donation to create the Comer Center for Children and Specialty Care at the University of Chicago. This gift brings the Comers' total support of pediatric medicine at the University of Chicago to more than $84 million.

Recent Research Highlights

In addition to providing the best possible care to patients in a kid-friendly environment, Comer Children's Hospital is home to some of the world's top researchers.

"We're beginning to develop some very interesting and exciting research directions through extensive interactions with faculty, and we're leveraging the intellectual resources of the Division of Biological Sciences to find a cure for pediatric cancer," said John Cunningham, MD, professor of pediatrics and physician-in-chief at Comer Children's Hospital.

One example is the work being done by Susan Cohn, MD, professor of pediatrics and dean of Clinical Research, who conducts research in neuroblastoma, a cancer that typically affects children ages five years and younger. Although some children have high cure rates, approximately half of all patients with neuroblastoma have a highly aggressive tumor that remains difficult to treat. Less than 50 percent of patients with high-risk neuroblastoma can be cured with today's treatments.

Cohn and her team have been conducting clinical trials with investigators at the University of Chicago Medicine and other institutions in North America to evaluate new therapies for children with newly diagnosed and relapsed neuroblastoma. She also co-chairs an international neuroblastoma task force and has developed a web-based interactive database that contains clinical and genetic information from more than 18,000 children diagnosed with neuroblastoma from around the world. Studies conducted using these data have led to seminal findings not previously possible to obtain with smaller patient populations.

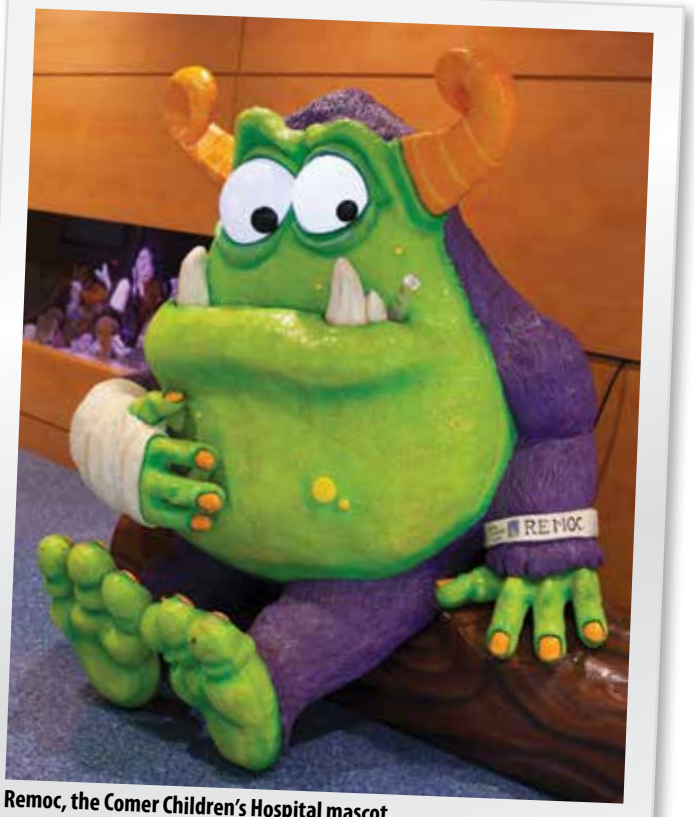
Unique Offerings

Earlier this year, the hospital became the first in Illinois to offer pioneering, targeted, high-dose, intravenous radiation therapy for neuroblastoma and other difficult-to-treat cancers. The hospital is one of only about a dozen across the country equipped to administer this advanced therapy, called metaiodobenzylguanidine or MIBG, which requires a highly-specialized team and a dedicated lead-lined patient room designed to minimize radiation exposure to families, other patients and staff.

Each year, nearly 20,000 adolescents and young adults are diagnosed with leukemia or lymphoma. When facing cancer, this age group often confronts different personal, psychosocial and medical challenges than younger children and older adults with the same diagnosis. That is why the University of Chicago Medicine created the Adolescent and Young Adult (AYA) Oncology Program—a collaborative program offering coordinated care for young adults ages 15-30 with leukemia or lymphoma.

The Program helps adolescents and young adults take an active role in their care, navigate the medical system as well as understand and make decisions regarding their treatments. Its cancer specialists have the clinical experience, the scientific knowledge and the resources to determine which treatment protocol offers the most effective therapy to meet each patient's unique needs. In fact, research conducted by UChicago scientists led to improvements in the way adolescents and young adults throughout the world are being treated for leukemia and other cancers.

The Pediatric Familial Cancer team, which includes a genetic counselor dedicated to cancer risk, helps children and their families who may have known rare cancer syndromes, unknown or unidentified syndromes, or questions about cancer risk. If members of the family are found to be at risk for cancer, the clinic will develop a personalized plan to reduce that risk and will coordinate a child's care with other specialists throughout the hospital.



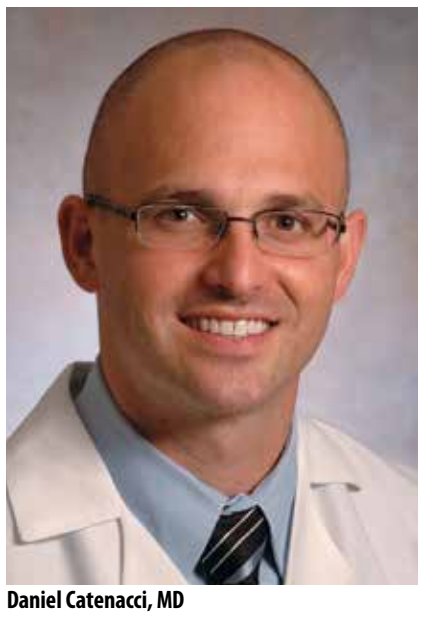
Remoc, the Comer Children's Hospital mascot

The Childhood Cancer Survivors Center for pediatric and adult survivors of childhood cancer is aimed at the prevention and treatment of long-term issues associated with cancer therapy, such as heart, renal and pulmonary complications, endocrine disorders, fertility issues, secondary or recurrent cancer, and social and psychological concerns. The center works closely with patients' primary caregivers and other specialists to ensure that patients are receiving the best possible care.

Fifty years ago, less than 10 percent of childhood cancer patients could be cured. Thanks to the people that make up Comer Children's Hospital and the work being conducted, there is cause for hope. Today, nearly 80 percent of children diagnosed with cancer become long-term survivors, and the majority of them are considered cured.

University of Chicago Investigator Tackles Tumor Complexity with Innovative Clinical Trial Design

When oncologist Daniel Catenacci, MD, assistant professor of medicine, designed a clinical trial, he decided to name it PANGEA, for **P**ersonalized **AN**tibodies for **G**astro-**E**sophageal **A**denocarcinoma. Not unlike the former "supercontinent" that gave rise to the present continents on Earth, this trial represents an almost unrecognizable assembly of the current clinical trial architecture and biomarker-driven approaches to improve clinical decision-making.


Daniel Catenacci, MD

Personalized medicine, or precision oncology, aims to incorporate information about a patient's and/or their cancer's genetic make-up into treatment decisions. However, tumors consist of individual cancer cells with distinct molecular features, including DNA mutations, chromosomal abnormalities, and gene expression profiles. This inherent complexity, also referred to as tumor heterogeneity, is a major challenge to refining treatment strategies for cancer patients so that they are as effective as possible. If a tumor is like a jar full of colored marbles, it is impossible to know if it would be better to take out the blue ones, the red ones, both, or some other color, without knowing which ones are the most important.

The PANGEA trial addresses the problem of tumor heterogeneity by gathering as much information about the distinct tumor cell populations, and what drives their behavior, and then use molecularly targeted therapies to eliminate them. The phase I trial has been approved by the United States Food and Drug Administration and University of Chicago Institutional Review Board to enroll patients with newly diagnosed, stage IV gastric, esophageal or esophago-gastric junction cancer. Upon testing the patient's tumor for its molecular features (biomarkers), the patient will be put on one of five "arms," or treatment groups, and receive the targeted therapy that is most appropriate for him/her. For example, patients with cancers in which a majority of the tumor cells carry amplification of the HER2 receptor will receive the HER2 inhibitor, trastuzumab. Importantly, all patients will be treated with the most advanced treatment available based on their own cancer's characteristics.

What separates this trial from others, however, is that patients may be reassigned to a different arm if they progress on their first therapy and their tumors are revealed to now have a different composition of tumor cell features. Patients could be reassigned as many as three times as a strategy to overcome therapy resistance.

Support for some of the preclinical work necessary for the design and implementation of this innovative clinical trial has come from a Precision Oncology pilot grant funded in 2013 by the University of Chicago Cancer Research Foundation Women's Board. In the fall of 2014, Catenacci successfully leveraged that funding and work to obtain a five-year K23 Mentored Patient-Oriented Research Career Development Award from the National Cancer Institute.

For Catenacci, among the most exciting elements of the PANGEA trial is its flexibility to incorporate new and highly effective treatment strategies as they are developed. In fact, he is currently adding an arm to the trial using pembrolizumab, a promising immunotherapy recently approved for treatment of melanoma. And because of the potential benefit to patients, he sees this biomarker-driven approach as the future of clinical trials, and ultimately, clinical practice for cancer patients.

"The PANGEA clinical trial design has the potential to test tumor profiling and methods for assigning treatment with the intention to tackle the problem of tumor heterogeneity and improve outcomes for these patients," said Catenacci.

A Conversation With…

Daniel Catenacci, MD

Assistant Professor of Medicine

If you were not a physician or researcher, what would your profession be?
In a rock 'n' roll band! Or a teacher of history and philosophy.

What is the most rewarding part of your job?
Patient care and finding new ways to help patients with cancer.

What do you hope to accomplish during your career?
Improve outcomes for patients diagnosed with gastrointestinal malignancies like esophageal, gastric and bile duct cancers.

If you had one piece of advice for someone considering your field, what would it be?
Think outside the box…

In what direction do you see cancer research in general, or your field specifically, going?
Targeted therapy for specific subsets of patients, and immunotherapy including vaccinations and stimulating or re-sensitizing the immune system to attack cancer cells.

How did you get interested in studying cancer and/or treating cancer patients?
A combination of personal family history, exposure to cancer patients during medical school and residency training, the need for better therapies for cancer, and the scientific challenge that cancer poses were all contributing factors to why I chose to pursue oncology and treating cancer patients as a career.

Who inspires you?
My family, including my parents and sister, my wife and my soon-to-be-born daughter! My patients also inspire me to continue to contribute to our understanding of cancer and how to better treat it.

What was the last book you read?
I read a lot, and a few books at a time. Recent books include: *Emotional Intelligence;* 2) *Andrea Pirlo: I Think Therefore I Play;* 3) *La Vida Es Sueño;* 4) *The Price of Civilization;* 5) *The Emperor of All Maladies: A Biography of Cancer.*

What is one thing on your bucket list?
I love to travel – and there are many places on my list that I still have to see (Machu Picchu, Galapagos islands, and the Egyptian pyramids, to name a few!)

Inspiring the Next Generation of Cancer Researchers to Find Cancer "CUREs"


Some of the students, mentors, and research lab assistants who participated in the CURE program

Beyond meeting the needs of patients and conducting state-of-the-art research, training students and fellows in all aspects of basic, clinical, translational and population-based cancer research is a critical component of the University of Chicago Medicine Comprehensive Cancer Center's mission. Unfortunately many of the brightest young minds have no idea what a career in cancer research looks like and cannot visualize such a path in their future because they have not seen it first-hand.

The Comprehensive Cancer Center is taking a bold approach to changing that for promising high school and undergraduate students from the Chicago area. A new program was launched in the spring of 2014 to introduce talented students from underrepresented populations, including ethnic and racial minorities, low income and first-generation college or college-bound students, to cancer research.

"Developing the next generation of innovative scientists requires investing in their future and inspiring them to use their curiosity to tackle the biggest challenges in science and medicine," says M. Eileen Dolan, PhD, professor of medicine and associate director for education of the Comprehensive Cancer Center.

Funded by a Continuing Umbrella of Research Experience (CURE) grant from the National Cancer Institute and the University of Chicago Cancer Research Foundation Women's Board and led by Dolan, the program provided a hands-on summer research experience for students under the mentorship of Comprehensive Cancer Center faculty. For the inaugural summer, the Comprehensive Cancer Center hosted four high school and three undergraduate students.

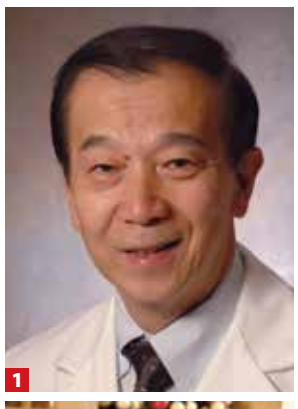
The students' research experience was further enhanced by a cancer research "boot camp," formal faculty and student presentations about cancer research, and career development discussions with faculty. The summer culminated with the students presenting their research findings in a symposium attended by their peers, mentors, program leadership and, in many cases, parents. Even an Advanced Placement Biology teacher from one of the high schools attended the symposium and was amazed at what the students accomplished.

Abidemi Charles, a student at Chicago State University, worked with Mark Lingen, DDS, PhD, on optimizing the detection of a novel biomarker in salivary gland tumors. "My lab experience was surreal, in that those intimidating classroom theories and concepts came to life right before my eyes," she said.

Unlike many programs that end after a summer, the CURE program engages students for a full two years. Throughout the academic year, the students benefit from an additional curriculum aimed at developing skills to read the scientific literature, mine data, discuss data and science ethics, and write proposals.

Sidney Trotter is a student at North Lawndale College Preparatory High School. Her summer project with Patrick La Riviere, PhD, associate professor of radiology, was focused on improving breast cancer screening using a novel transmission ultrasound imaging system. She said, "I hope one day to work as both a doctor and researcher. My time spent doing research has shown me that I can do anything I put my mind to."

COMPREHENSIVE CANCER CENTER NEWS AND UPDATES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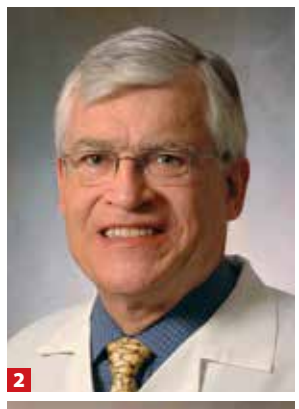
1 Yusuke Nakamura, MD, PhD, professor of medicine, was invited by the Japan America Society of Chicago to deliver a keynote address at their 84th Anniversary Celebratory Dinner.

Nakamura, along with **2 Richard Larson, MD,** professor of medicine, earned the distinction of being ranked among the most cited researchers in their respective fields according to Thomson Reuters' "Highly Cited Researchers 2014."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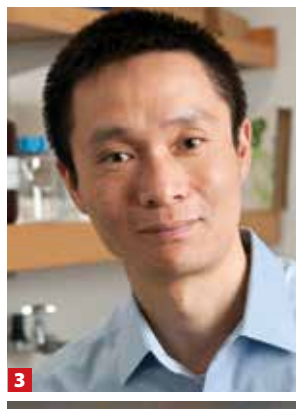
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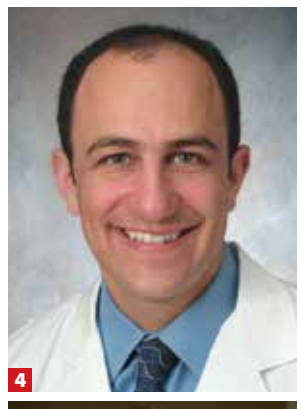
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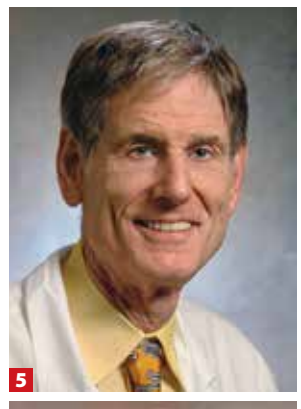
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Several members received named professorships.

- **3 Chuan He, PhD,** was appointed the John T. Wilson Distinguished Service Professor of Chemistry.
- **4 David Rubin, MD,** was appointed the Joseph B. Kirsner Professor of Medicine.
- **5 Ralph Weichselbaum, MD,** D.K. Ludwig Professor and chair of the Department of Radiation and Cellular Oncology, has received the additional designation of Distinguished Service Professor.


6

6 Shutsung Liao, PhD, professor emeritus in the Ben May Department for Cancer Research, died in his Hyde Park home on July 20, 2014. Liao was known as a pioneer in understanding the biochemistry of male hormones and their receptors and how they influenced the development and progression of prostate cancer.


7

7 Jessica Kandel, MD, the Mary Campau Ryerson Professor of Surgery, and Surgeon-in-Chief, the University of Chicago Medicine Comer Children's Hospital, has been named as a master clinician by the University of Chicago Medicine Bucksbaum Institute for Clinical Excellence. The appointment is geared toward recently hired faculty to serve as role models for student scholars and faculty scholars in the delivery of superior clinical care and excellent doctor-patient communications.


8

8 Suzanne Conzen, MD, professor of medicine, was chosen as the recipient of the 2014 Movember-Prostate Cancer Foundation Challenge Award for her project titled, "Use of Selective GR Antagonists in Castration-Resistant Prostate Cancer." The $1 million award was made possible by the thousands of men who grew mustaches to raise money for prostate cancer research as part of the "Movember" movement.


9

9 Michelle M. Le Beau, PhD, Arthur and Marian Edelstein Professor of Medicine, director of the University of Chicago Medicine Comprehensive Cancer Center, has been elected to the national board of directors of The Leukemia & Lymphoma Society. Her term will run through June 30, 2017.


10

10 Olufunmilayo Olopade, MD, Walter Palmer Distinguished Service Professor of Medicine and associate dean for global health, has been selected as the recipient of the Franklin D. Roosevelt Freedom from Want Medal in recognition of her significant contributions to the prevention and treatment of breast cancer and cutting-edge translational research in genetics. She will accept the award in September 2015.


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11 Wendy Stock, MD, professor of medicine; **1 Yusuke Nakamura, MD, PhD,** professor of medicine; and **12 Olatoyosi Odenike, MD,** associate professor of medicine, were awarded a translational grant from the V Foundation for Cancer Research for their proposal studying "TOPK (T-lymphokine-activated killer cell-originated protein Kinase): A new target for FLT3 mutated AML."

13 Megan McNerney, MD, PhD, assistant professor of molecular pathology, has been awarded a two-year V Scholar Research Grant from the V Foundation for Cancer Research. Her research project will focus on transcriptional misregulation in high-risk myeloid neoplasms.

- The University of Chicago Medicine was recognized by Becker's Hospital Review as one of the "100 Hospitals and Health Systems With Great Oncology Programs."
- On Monday, August 11, Senator Dick Durbin (D-IL) visited the University of Chicago campus to deliver a speech about the importance of sustained federal funding for biomedical research and the American Cures Act.

Leukemia & Lymphoma Society Light the Night Walk

The University of Chicago Medicine Heme Team supported the Leukemia & Lymphoma Society by participating in The Light the Night Walk that took place on October 18, 2014 in Grant Park. The team, led by Melissa Spegal, a physician assistant in Stem Cell Transplantation, consisted of 62 physicians, researchers and staff from multiple departments. The team raised over $8,899 for the event that brought together the Chicago community to celebrate blood cancer survivors and shine a light on the need for investing in research to find cures and to provide support services for patients.

Movember Moves Prostate Cancer Research Forward

In October, a team of prostate cancer physicians and scientists from the University of Chicago Medicine, including Suzanne Conzen, MD, Geoffrey Greene, PhD, Walter Stadler, MD, Donald Vander Griend, PhD, Russell Szmulewitz, MD, David VanderWeele, MD, PhD, and Stanley Liauw, MD, was recently recognized at the 21st Annual Prostate Cancer Foundation (PCF) Scientific Meeting as a 2014 Movember-PCF Challenge Award winner. The work funded by this $1M grant, led by Conzen, will test a new drug in patient with prostate cancers that have developed resistance to commonly used hormonal therapy. This Challenge Award was jointly supported by the PCF and Movember Foundation – a leading global organization committed to changing the face of men's health, including prostate cancer, testicular cancer and mental health. During the month of November, Movember supporters grow mustaches to encourage dialogue about men's health and to raise funds to benefit men's health programs and research, like that funded by the PCF. The prostate cancer team, under Conzen's and Stadler's leadership, recruited many of their colleagues, staff and trainees to create the University of Chicago Monsters of the Mo Movember team, grow mustaches and raise more than $5,600 for men's health, including prostate cancer research.

RESEARCH HIGHLIGHTS

The following represent some of the research accomplishments of Comprehensive Cancer Center members published September–November 2014.

New anticancer drug shows promise in preclinical studies

There is a continued need for the development of new therapeutic approaches for cancer in order to personalize therapy and overcome treatment resistance or non-responsiveness. TOPK (T-lymphokine-activated killer cell-originated protein kinase) is a cell signaling protein expressed at low levels in normal cells but overexpressed in many cancer types, including breast and lung cancer. **Yusuke Nakamura, MD, PhD,** professor of medicine, recently discovered a small molecule TOPK inhibitor called OTS514 and optimized its formulation for enhanced anticancer activity and reduced toxicity. In the current lung tumor studies in mice, Nakamura's group demonstrated that the drug effectively caused regression of established tumors, and in the vast majority of animals, the tumors completely disappeared without any adverse reactions. These findings illustrate the potential for TOPK as a therapeutic target and establish some of the necessary preclinical evidence to support an early phase clinical trial. (Matsuo et al., *Sci Transl Med* 6:259ra145, 2014)

This work was supported in part by the Innovation Promotion Program of the New Energy and Industrial Technology Development Organization of Japan and OncoTherapy Science Inc.

Optimizing end points for randomized phase II clinical trials

A significant challenge in the design of randomized clinical trials for cancer therapeutics is to know which end points are optimal, particularly those that are used to inform whether to proceed or not at the end of a phase II study, and can detect a true difference among therapies. Because some currently used end points, such as overall response rate (ORR) and progression-free survival (PFS) have significant limitations, a group led by **Manish Sharma, MD,** assistant professor of medicine, and **Theodore Karrison, PhD,** research associate-associate professor of public health sciences, used computer simulation of phase II trials and compared the power of various end points to detect the superior therapy. Specifically, the group resampled patients from N9741 randomized phase II trial of chemotherapy regimens for metastatic colorectal cancer. They discovered that the time to tumor growth (TTG) was a powerful endpoint in detecting the superior therapy in that it was either comparable or better than PFS and log ratio of tumor size at 18 weeks (a tumor size measurement). Although further analysis is necessary to validate the potential power of TTG over these other end points in other types of phase II trials, these data from the context of a metastatic colorectal cancer trial support its careful consideration. (Sharma et al., *J Clin Oncol* 33:36-38, 2015)

This work was supported by funding from the National Cancer Institute (K12 CA139160) and by the Biostatistics Core Facility at the University of Chicago, a core facility supported by the University of Chicago Medicine Comprehensive Cancer Center CCSG (P30 CA014599).

Alcohol consumption and breast cancer risk among African women

Drinking alcohol has been linked to increased breast cancer risk, although the relationship is poorly understood, as is the effect on different populations. **Dezheng Huo, MD, PhD,** assistant professor of public health sciences and **Olufunmilayo Olopade, MBBS,** Walter L. Palmer Distinguished Service Professor of medicine and human genetics, conducted a case-control study of alcohol consumption patterns and breast cancer risk among women in three sub-Saharan African nations – Nigeria, Cameroon, and Uganda. Their study of more than 4,700 women showed that the women with breast cancer, compared to healthy controls, were more likely to have consumed alcohol, and both past and current drinking were positively correlated with breast cancer risk. Overall, the odds of having breast cancer were 62% higher among women who ever consumed alcohol than those that have not. There was also a dose-response relationship between the duration of drinking and increase in risk so that, for example, women who drank for 20 years or longer were almost twice as likely to have breast cancer compared to non-drinkers. This work indicates that alcohol consumption is a modifiable risk factor for breast cancer that should be addressed in breast cancer prevention programs in Africa. (Qian et al., *PLoS One* 9:e106908, 2014)

The study was supported by grants from the National Institutes of Health (RO1 CA89085 and P50 CA125183), the Dr. Ralph and Marian Falk Medical Research Trust, and Avon Foundation for Women.

Signaling cross-talk in colitis-associated colon cancer

Ulcerative colitis, a type of inflammatory bowel disease of the lining of the colon, is associated with an increased risk of colon cancer, and vitamin D is a promising chemopreventive agent based on preclinical studies. **Marc Bissonnette, MD,** associate professor of medicine, led a multidisciplinary team that included **Vani Konda, MD,** assistant professor of medicine; **John Hart, MD,** professor of pathology; **Gregory Karczmar, PhD,** professor of radiology; **Joel Pekow, MD,** assistant professor of medicine; and **Yan Chun Li, PhD,** associate professor of medicine, to identify the molecular networks involved in colitis-induced colorectal cancer, particularly those involving vitamin D signaling. Using genetically modified mouse models in which the vitamin D receptor gene was disrupted, the investigators discovered that vitamin D inhibits colitis-induced colon cancer development by regulating the renin-angiotensin system. The renin-angiotensin system is a hormone system that controls blood pressure and fluid balance throughout the body. It also contributes to tumor growth in the breast, ovary, lung, prostate and pancreas, but had not been previously linked to colon cancer. These data imply that combining vitamin D and renin-angiotensin system inhibitors may be a promising approach to prevent colon cancer in high-risk patients with inflammatory bowel disease. (Dougherty et al., *Clin Cancer Res* 20:5848-59, 2014)

This work was supported by funding from the National Institutes of Health (P30 DK42086, R01 CA036745; R01 CA141092 R01 CA097540, K08DK090152, R01 CA180087), the Foundation for Clinical Research in Inflammatory Bowel Disease, International Organization for the Study of IBD, Kohut fund, Samuel Freedman Research Laboratories for Gastrointestinal Cancer Research, and NCATS UL1TR000430.

The rising cost of oral anticancer therapeutics

Rapid progress in basic cancer research has led to an explosion of anticancer therapies in the arsenal that oncologists have at the ready; yet, oncologics rank first in national spending on prescription drugs by therapeutic class. Rena Conti, PhD, assistant professor of pediatrics and public health sciences, examined the factors contributing to the high and rising cost of oral oncologics, a growing subclass of all anticancer drugs. Using data representative of the entire United States, Conti and her collaborators assessed oral oncologic use trends and spending spanning the first quarter of 2006 through the third quarter of 2011. They found that the average quarterly national spending on these drugs increased 37%, and that use also increased over that time period but more slowly than spending. These significant increases in spending were primarily driven by spending on new and brand-name, patent-protected oral anticancer drugs, and their associated price increases. Importantly, Conti and colleagues also discovered that when oncologics of all types lose patent protection, patients and society benefit by a dramatic price decrease. (Conti et al., *Health Affairs* 10:1721-7, 2014)

This work was supported by funding from the National Institutes of Health (K07 CA138906).

Deciphering the molecular basis for ibrutinib resistance in CLL

Ibrutinib is a Bruton tyrosine kinase (BTK) inhibitor that has produced a remarkable clinical response in relapsed and refractory chronic lymphocytic leukemia (CLL) and mantle cell lymphoma. However, like many targeted therapies, some patients develop resistance. **Y. Lynn Wang, MD, PhD,** professor of pathology, and her team previously identified a mutation in the *BTK* gene in a CLL patient who progressed after ibrutinib therapy. By analyzing serial samples collected from the patient, Wang's group characterized this mutation's functional consequences, including the impact on signaling, gene expression and cellular behavior changes. They observed that B cell receptor signaling, a network controlled by BTK, over the course of treatment correlated with the disease status and that this mutation confers resistance to ibrutinib by allowing for reactivation of B-cell receptor signaling. In an effort to identify novel therapeutic approaches for these patients, the effectiveness of several other small molecule kinase inhibitors was tested. One drug, a PI3K inhibitor called idelalisib, was found to be particularly effective, suggesting that it may serve as an alternative therapy in the setting of ibrutinib-resistant CLL. (Cheng et al., *Leukemia* Oct 10 Epub ahead of print, 2014)

This study was supported by funding from the Leukemia and Lymphoma Society (LLS 6364-13).

Mesothelial cells promote early ovarian cancer metastasis

Ovarian cancer metastasis to organs in the abdominal cavity, including the omentum – a meshwork that is covered by a single layer of mesothelial cells – is a major clinical challenge. Despite the fact that mesothelial cells are generally considered bystanders to metastasis, **Ernst Lengyel, MD, PhD,** Arthur L. and Lee G. Herbst Professor of Obstetrics and Gynecology, **Diane Yamada, MD,** Joseph Bolivar DeLee Professor of Obstetrics and Gynecology, **Iris Romero, MD,** assistant professor of obstetrics and gynecology, and their team explored whether or not these cells play a more active role. The research team used 3-D culture and tumor cell/mesothelial cell co-culture models, as well as mouse models of ovarian cancer metastasis, to demonstrate that mesothelial cells secrete an extracellular matrix protein called fibronectin. Fibronectin secretion, in turn, was necessary for ovarian cancer metastasis and required activation by the TGFb growth factor pathway in the cancer cells themselves. Uncovering this complex interplay between ovarian tumor cells and the microenvironment, in this case the mesothelial cells of the omentum, identifies potential therapeutic targets for inhibiting the metastatic process. (Kenny et al., *J Clin Invest* 124:4614-28, 2014)

This study was supported by funding from the National Institutes of Health (R01 CA111882) and by an Ovarian Cancer Research Fund Program Development Grant.

Shooting Hoops to Help Kids with Cancer

The Cure It On The Court Foundation held its 7th Annual North Shore 3-on-3 Summer Showdown this summer and raised more than $6,000 to benefit pediatric cancer research at the University of Chicago Medicine Comer Children's Hospital. More than 115 athletes and 100 volunteers, sponsors, and donors were in attendance to support the cause. The annual tournament first began in 2008 when Zachary Bulwa, a graduate of Glenbrook North High School and the University of Illinois, decided to combine his passions for basketball and medicine after shadowing physicians and scientists at UChicago. Bulwa, along with his longtime friends Shane Massel and Jason Krawetz, established the foundation. The funds they raised go toward helping pediatric cancer leaders at the University of Chicago Medicine develop preventive genetic screening, early detection, and better, less toxic treatments for children and young adults with cancer. Visit *www.cureitonthecourt.org* for more information.

Couple Donates $1 Million to Accelerate Cancer Research


Cynthia and Benjamin Chereskin

CANCER IS THE second leading cause of death in the United States. One of two men and one of three women will be diagnosed with cancer in their lifetime. To tackle this disease, Cynthia Chereskin believes more comprehensive research is needed.

Since 1997, Cynthia has been involved with the University of Chicago Cancer Research Foundation Women's Board and now serves as its president. The Women's Board was founded in 1947 and raises funds through its Grand Auction, Annual Appeal, Chicago Hunter Derby, and other events to support world-class programs in basic, clinical, translational, and population research at the Comprehensive Cancer Center. Each year, the Women's Board makes significant contributions, allowing new scientists to generate enough research data to compete for federal funding. Many of the scientists who have received support from the Women's Board have gone on to make important discoveries throughout their career.

Like most of the women on the Women's Board, Cynthia feels strongly about the cause because of personal ties to the disease. Her father, Glen Johnson, was treated for bladder cancer 11 years ago, and her husband, Benjamin Chereskin, was treated for tongue cancer two years ago. Both cases required innovative treatment, and they knew that the most advanced treatment options available were at the University of Chicago.

Other hospitals treat oral cancers by removing portions of the tongue and surrounding tissues, but at the University of Chicago Medicine, surgery is considered after a combination of chemotherapy and radiation therapy is used to shrink the tumor. Fortunately, Benjamin's cancer responded to therapy, and he did not need surgery. Everett Vokes, MD, John E. Ultmann Professor of Medicine, and colleagues used this same approach to save the taste buds of Alinea chef Grant Achatz in 2007.

A community hospital doctor told Cynthia's father there was nothing they could do for his bladder cancer. However, upon seeking a second opinion from the University of Chicago Medicine, he found hope through Gary Steinberg, MD, Bruce and Beth White Family Professor of Surgery. Steinberg is the director of urologic oncology and an internationally known expert in bladder cancer and urinary tract reconstruction. He removed Glen's bladder and reconstructed a new one using intestinal tissue. Steinberg is a pioneer in this technique which, at the time, was not used by many hospitals.

Because of the high level of innovative care, both her father and husband were able to return to full active, healthy lives. Her father passed away this year, but she remembers he always spoke highly of Steinberg, and the compassionate care he received. His treatment for cancer gave him another lease on life, she said.

"Having had loved ones affected by cancer and going through the whole diagnosis and treatment with them really hit a chord," said Cynthia. "I feel incredibly lucky to live in Chicago and have the University of Chicago in our backyard with these amazing doctors who have done so much in the name of research and medical science."

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>
> **Cynthia Chereskin**

In honor of her father, the Chereskins are donating $1 million to the University of Chicago Medicine Comprehensive Cancer Center in the form of an unrestricted gift.

"We believe the greatest challenges and most promising areas of research are best understood by the leadership of the Comprehensive Cancer Center," Chereskin said. "Our goal is to provide flexibility to allocate research dollars to those areas they deem would most rapidly address the most promising areas of cancer research."

There are many ways the funds could be used, including backing young researchers who have yet to become established and are operating at the frontier of technology, research and science; supplementing existing projects to expand and accelerate their impact; acquiring tools that can be leveraged by multiple research teams; developing "Team Science" projects to unite multiple disciplines on a challenging aspect of cancer; or recruiting faculty to bring new disciplines to campus.

"Our work is devoted to finding better ways to prevent, detect, and treat cancer," says Michelle M. Le Beau, PhD, Arthur and Marian Edelstein Professor of Medicine and director of the University of Chicago Medicine Comprehensive Cancer Center. "We are so grateful for this generous gift, which will facilitate the translation of new discoveries from the laboratory to the clinic that extend and improve lives affected by cancer."

Cynthia added, "It is our hope that others will join us in supporting the University of Chicago Medicine Comprehensive Cancer Center with unrestricted gifts to accelerate the pace of innovation and discovery in the fight against cancer." Visit *donatetocancer.uchicago.edu*.

HIRO Serves the Unique Needs of Clinical Trials


(Left to right): **Staff of the Human Imaging Research Office Michael Torno, Jonathan Marino, Susan Fruth, and Nick Gruszauskas (technical director) discuss the imaging portion of a clinical trial.**

CLINICAL TRIALS are an essential part of transforming new laboratory discoveries into improved therapies and bringing about advances in cancer care. The University of Chicago Medicine Comprehensive Cancer Center conducts more cancer clinical trials than any other facility in Illinois. Many of these trials involve the use of some form of medical imaging. However, imaging requirements vary from trial to trial, and research-related imaging techniques may differ from the standard techniques used in the clinic.

"There are probably a hundred legitimate ways that the radiology department could perform a particular scan, yet it's possible that the clinical trial may require one very specific way," said Nick Gruszauskas, PhD, technical director of the Human Imaging Research Office (HIRO).

"One of the biggest requirements for cancer-related imaging is consistency because the investigators are trying to track tumor growth or shrinkage," he continued. "A national clinical trial may be collecting patient scans that are performed at dozens of participating sites across the country, and if every site is doing the imaging in its own way, it becomes extremely difficult—and sometimes impossible—to compare the results and say with certainty that a drug is working."

Failing to meet the imaging guidelines imposed by a clinical trial will result in additional effort for staff and can jeopardize the integrity of the research. It can also cause patient removal from the trial and even tarnish the reputation of the institution.

The HIRO was created to facilitate clinical trials and other research studies that require medical imaging. Another major responsibility of the HIRO is to ensure that the necessary imaging is performed and distributed in compliance with the research protocol, Institutional Review Board requirements, and regulations mandated by the Health Insurance Portability and Accountability Act (HIPAA).

"The Human Imaging Research Office is intended to be the facilitator, or 'go-between,' for clinical trials and research protocols that require imaging exams for their subjects," said Samuel Armato III, PhD, associate professor of radiology and faculty director for the HIRO. "Our goal is to make this process more efficient and accurate and to provide investigators with a wide selection of human research imaging services."

The HIRO is responsible for coordinating the acquisition, analysis, and distribution of images and related data associated with clinical research studies involving human subjects, including de-identified data. It also assists with all imaging-related study initiation activities, including protocol review, completion of imaging-related pre-study documentation, participation in sponsor-mandated training sessions, and completion of test scans for site qualification.

Since opening in early 2009, the HIRO has provided services and assistance for more than 250 cancer-related research studies and clinical trials. Between July 2013 and June 2014, the HIRO processed and delivered more than 2,700 scans for cancer-related research.

The HIRO also partners with the University's Clinical Research Data Warehouse team, which provides the bioinformatics expertise, to facilitate data integration. Equally important to fostering clinical research, senior HIRO staff sit on the Comprehensive Cancer Center's Clinical Trials Review Committee to ensure the imaging-related components of all proposed Comprehensive Cancer Center protocols are feasible and meet institutional and national or best-practice requirements.

Looking ahead, the HIRO has been developing an image storage system that will soon be opened up to the Biological Sciences Division research community. The Biomedical Image Repository (BMIR) aims to provide researchers with a centralized system to store and organize their image data. This will allow researchers to mine and share their data in meaningful ways.

"Our hope is that this system will enable researchers to use their image data more efficiently, which will hopefully lead to faster results, increased collaboration, and adherence to the various legal regulations surrounding image data (like HIPAA)," said Gruszauskas, adding that he expects a majority of the BMIR users to be cancer researchers.

For more information, visit *hiro.bsd.uchicago.edu*.

Grand Auction Raises More Than $1 Million for Cancer Research

The Women's Board of the University of Chicago Cancer Research Foundation hosted the 48th Annual Grand Auction at the Four Seasons Hotel in November. Attendees celebrated this year's theme, "Booth One Ball," with cocktails, dinner, dancing, and a live and silent auction.

Mary Ellen Connellan, executive director of the University of Chicago Cancer Research Foundation, Cynthia Chereskin, president of the Women's Board, Michelle M. Le Beau, PhD, Arthur and Marian Edelstein Professor of Medicine and Comprehensive Cancer Center Director, and Diane Reilly and Karen Slimmon, co-chairs of the Grand Auction.

A table of cancer research supporters toast each other at the Booth One Ball.

Nichole D'Aprile, Lidia Devonshire, and Annemette Clausen take a break from bidding on silent auction items to smile at the camera.

David and Whitley Herbert take their photo at the Booth One replica.

The Women's Board ball chairs and their husbands get into the spirit of Booth One.

Guests show off the pictures they had taken in the Booth One.

SAVE THE DATES!

The University of Chicago Cancer Research Foundation presents a list of upcoming fundraising events:

AUXILIARY BOARD
Lucky 7 Gala
Saturday, March 7, 2015
Michigan Shores Club,
Wilmette, IL

ASSOCIATES BOARD
Fund the Fight Ball
Saturday, April 11, 2015
Moonlight Studios,
Chicago, IL

For more information, please contact kcoady@bsd.uchicago.edu.

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