Pathways to DISCOVERY
At the Forefront of Discovery™

THE UNIVERSITY OF CHICAGO
COMPREHENSIVE CANCER CENTER

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Breakthroughs in Melanoma Research Stress Importance of Personalized Therapeutics

Advanced-stage melanoma is one of the deadliest cancers, with its patients rarely surviving more than a year after diagnosis. Researchers have long struggled to achieve substantial successful outcomes for this complex cancer, but in-depth analysis of its biology reveals that melanoma is not one cancer. It is a disease with many different subsets, each with unique molecular signatures.

Armed with this information, researchers can use molecular tests to identify mutations in specific genes and determine which patients are likely to benefit from therapy. Tailoring the therapy to each patient's specific cancer is making melanoma the "unlikely poster child for personalized cancer therapy," according to Thomas Gajewski, MD, PhD, professor of medicine and pathology.

"The science has been pushed to a very high level," said Dr. Gajewski. "We know a lot more about the details of melanoma's biology than ever before." This information is helping researchers at UChicago and other institutions make significant advancements in melanoma treatment.

New Therapies

Immune therapy, which stimulates the body's own immune defenses to eliminate cancer cells, is showing great promise for melanoma treatment. Scientists have identified a signaling pathway in the T cells of the immune system, called CTLA-4, that turns off the immune response against the melanoma, which, in turn, allows the tumor to grow and escape.

An antibody was developed to block CTLA-4 so that the T cells become reactivated and destroy the tumor. The generic name of the drug is ipilimumab, and it is the first melanoma therapy to show markedly improved survival in a Phase III clinical trial. Compared to the 6-month average survival rate for advanced melanoma, 40% of the patients in the trial were still alive at 1 year.

In about half of melanoma patients, a mutation in the B-Raf kinase, an enzyme that controls the transmission of information from the cell's membrane to nucleus, causes it to be stuck "on" and

Continued on Next Page

Thomas Gajewski, MD, PhD, talks with a patient about her medical history.

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>
> **Thomas Gajewski, MD, PhD**

A LITTLE MORE WITH...

Thomas F. Gajewski, MD, PhD

Professor of Medicine and Pathology

If you were not a physician, what would your profession be?

Playing guitar in a contemporary blues band.

What do you do for relaxation?

In my free time I tend to do physical sports (tennis, running, skiing, biking), artistic things (music), and outdoor activities (gardening, backcountry camping).

If you could visit any research lab in the world, where would it be … and why?

I have a burning curiosity about some of the new Asian institutes with massive technology investments for high throughput genomic studies.

What projects are you working on at home?

I recently finished painting our son's bedroom, which has a domed ceiling onto which we applied spots of fluorescent paint representing major star constellations. It looks fantastic when the lights go out!

Who is the person you most admire?

We are big on Da Vinci in our house—for the balance of science, arts, and creativity.

What was the last book you read?

I just finished John Steinbeck's *Winter of Our Discontent*. It was the last book he wrote before receiving the Nobel prize, and was badly reviewed by the critics at the time. It's actually fantastic.

What is the most daring thing you have ever done?

A shark dive in the Bahamas, which is done at a location where they regularly feed the local sharks in the open sea with a giant frozen block of fish parts. You could almost touch the sharks as they swam by the divers on the way to the chow.

If you had one piece of advice for someone considering your field, what would it be?

Choose interesting and important questions to study, work hard, and maintain balance in life.

Michelle M. Le Beau, PhD

FROM THE DIRECTOR

If not all cancers are the same and not all patients are the same, doesn't it follow that not all cancer treatments can be the same?

This simple idea illustrates how our approach to cancer treatment has evolved as we begin to understand that cancer is a complex set of diseases. We have entered a new era of medical practice in which patients are being treated with individualized therapies that take into account the unique attributes of both their cancer and their own genetic makeup.

In this issue of *Pathways to Discovery*, we highlight some of the ways that the UCCCC is leveraging individualized therapies to help cancer patients. This includes a new approach to treating melanoma—the deadliest form of skin cancer.

Clinical trials are an important part of developing and testing new cancer treatments, but some barriers exist, such as decreased funding, increased regulatory burdens, and difficulty in accruing patients. In this issue, we present ways to overcome these hurdles so we can bring new therapies into standard practice.

A $2.1 million donation from the William F. O'Connor Foundation will help propel new therapies into the forefront. This generous contribution will be used to support the purchase of a new cyclotron for the Molecular Imaging Program and support the Center for Personalized Therapeutics.

As novel therapies are discovered and the number of cancer survivors reaches an all-time high, UChicago is expanded its survivorship resources. In April, healthcare professionals, patients, and caregivers came together to open a dialogue about common issues in breast cancer survivorship and to help them adjust to a "new normal."

Among the many resources available to cancer survivors is the Pain Clinic located in the Duchossois Center for Advanced Medicine. Pain specialists work with our cancer teams to develop individualized pain management plans.

All of these emerging trends in patient-specific treatment are supporting the UCCCC's efforts to help cancer patients live longer and lead better quality lives.

Regards,

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

Conversation, Targeted Approach May Increase Clinical Trial Enrollment

When the National Cancer Act was signed 40 years ago, scientists had just a basic understanding of the origins and progression of cancer. Today, through the use of new tools and technologies, massive computing power, and insights from other fields, we know that cancer is a complex set of diseases that can be controlled in many different ways. We also know that advances against cancer depend on science of many kinds.

Clinical trials are part of the process of developing new treatments. The University of Chicago has the largest cancer clinical trials program in Illinois, leads several national clinical trials study groups, and is one of only a handful of hospitals in the country that provides all three phases of clinical trials through programs funded by the National Cancer Institute.

Yet, barriers remain to expeditiously develop and implement treatment protocols so that new therapies can become standard practice. Some of those barriers include decreased funding, increased regulatory burdens, and difficulty accruing patients.

"I think we have to be innovative and balance science and practicality," said Walter M. Stadler, MD, Fred C. Buffett Professor of Medicine and Surgery and director of the UCCCC's Phase II Clinical Trials Network. "I think this is solvable."

Dr. Stadler welcomed more than 50 researchers and clinical data managers from six states to a Phase II Clinical Trials Symposium held at UChicago's Knapp Center for Biomedical Discovery in April.

Phase II trials pick up where Phase I trials leave off in testing the safety of a drug or procedure. The difference is that Phase II trials are open to a larger group of patients, tend to focus on a particular type of cancer, and begin to evaluate how well a new drug or procedure works.

Improving Patient Accrual

Having frank conversations with patients may be a key to improving patient accrual. A 2003 study in the *Journal of Clinical Oncology* found that only 3% to 5% of adult cancer patients enroll in clinical trials, even though many indicate an interest in doing so if asked.

Hedy Lee Kindler, MD, describes the progress being made in treatment for prostate cancer.

"Talk with your patients," said Victoria Villaflor, MD, assistant professor of medicine. "I try to explain to my patients that trials will help them to help the future of their disease. I also explain that personalized therapies for some cancers are currently available because of clinical trials."

Richard Schilsky, MD, professor of medicine and co-deputy director of the UCCCC, said that molecular medicine will likely increase clinical trial enrollment and decrease the time needed to complete the studies. "The use of biomarkers to identify patients likely to respond to the treatment being tested offers the potential for higher effect sizes in clinical trials," Dr. Schilsky wrote in a commentary in the March 23, 2011, issue of *Science Translational Medicine.*

Progress in the Treatment of Pancreatic Cancer

Throughout the daylong symposium, speakers discussed progress in open clinical trials and hypotheses for new clinical trials. Among those presenting was Hedy Lee Kindler, MD, associate professor of medicine, who discussed progress in treatment for pancreatic cancer—a cancer that has a 5-year survival rate of only 6%, according to the American Cancer Society.

"This cancer has the worst survival of any solid tumor," said Dr. Kindler. "These dismal statistics reflect not only the early distant spread of pancreatic cancer, but also the inadequacy of current therapies."

She explained that it has been difficult to develop drugs to effectively treat pancreatic cancer because it is a highly lethal disease that is usually detected late, is very resistant to most agents, and has poorly understood biology.

"We are now testing two new novel targets—Hedgehog signaling and notch signaling—in Phase II consortium trials," she said. Inhibiting hedgehog signaling appears to enhance delivery of chemotherapy, while inhibiting notch signaling may decrease tumor growth.

Dr. Kindler said she is hopeful that enough patients will enroll in these studies so that new therapies can be developed.

CLOCK Program

In addition to leading national clinical trials and mentoring dozens of researchers, the UCCCC is helping to speed the clinical trials process through its new CLOCK program. CLOCK stands for Clinical Trial Operational Efficiency via Computer-aided Knowledge. The program defines and standardizes the process across multiple treatment sites, utilizes project management and measurement tools, and develops analytical reports and action triggers that will help optimize the process.

Currently, the UCCCC has more than 350 open cancer clinical trials.

Open Cancer Clinical Trials

Patient enrollment is under way for more than 350 clinical trials at The University of Chicago Comprehensive Cancer Center. Our new clinical trials include:

- A Phase III Prospective Randomized Trial of Dose-Escalated Radiotherapy With or Without Short-Term Androgen Deprivation Therapy for Patients With Intermediate-Risk **Prostate Cancer** – Stanley Liauw, MD, principal investigator.
- A Phase I/II Trial of Concurrent RAD001 With Temozolomide/Radiation Followed by Adjuvant RAD001/Temozolomide in Newly Diagnosed **Glioblastoma** – M. Kelly Nicholas, MD, PhD, principal investigator.
- A Phase II Evaluation of Pazopanib in the Treatment of Recurrent or Persistent **Carcinosarcoma of the Uterus** – S. Diane Yamada, MD, principal investigator.
- Treatment of Patients with Newly Diagnosed Standard Risk B-Precursor **Acute Lymphoblastic Leukemia** – Jennifer McNeer, MD, MS, principal investigator.

To learn more about these or any other UCCCC 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.

Breakthroughs in Melanoma Research Stress Importance of Personalized Therapeutics

Continued from Front Page

drives the tumor to grow. A drug called PLX4032 was designed to block the B-Raf protein and has shown significant promise in Phase III randomized clinical trials and may soon become FDA-approved. About 80% of patients with the B-Raf mutation respond to the drug, with their tumors rapidly shrinking.

However, most patients have their tumors grow back, meaning the tumor somehow bypasses the block. Clinical trials are already under way to combine the B-Raf inhibitor with another drug that targets another enzyme in the same pathway.

The UChicago research team has participated in clinical trials for both of these therapies and continues to host clinical trials for investigational drugs to treat melanoma.

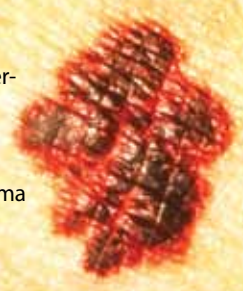
The Future Is Bright

Not only do these therapies show promise to effectively treat the deadly skin cancer, but Dr. Gajewski indicated that other types of cancer could potentially benefit from these discoveries. He predicts that the standard of practice for melanoma will soon involve routine screening of tumors for specific markers to match individual patients to the most appropriate treatment strategy.

Melanoma Risk Factors

Several risk factors may make you more likely to develop melanoma. They include:

- UV radiation exposure from sunlight, tanning booths, and sunlamps
- At least one severe, blistering sunburn
- Fair skin, freckling, and light hair
- Family history of melanoma
- Previous melanoma
- Moles
- Immune suppression



Skin Cancer Prevention

- Protect yourself and children from the sun.
- Avoid tanning beds and sunlamps.
- Check your skin regularly.
- Have suspicious moles removed.
- Consider genetic counseling and testing (if you have a family history of melanoma).

Sources: American Cancer Society and National Institutes of Health

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The University of Chicago Comprehensive Cancer Center
5841 S. Maryland Ave., MC1140, H212
Chicago, IL 60637

PHONE: 1-773-702-6180 • FAX: 1-773-702-9311
feedback@bsd.uchicago.edu

EXECUTIVE EDITOR AND WRITER
Natalie Olinger Boden

MANAGING EDITOR AND WRITER
Jane Kollmer

COPY REVIEWERS
Mary Ellen Connellan, MA
Hoyee Leong, PhD

EDITORIAL ADVISORS
Michelle M. Le Beau, PhD
Marcy A. List, PhD

GRAPHIC DESIGN
Adam Indyk

PRINTING
Service Communications and Solutions, LLC

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UChicago Clinic Takes on Tough Pain for Cancer Patients

Intractable, or uncontrolled, pain takes a devastating toll on the quality of life for the majority of patients in intermediate or advanced stages of cancer. Pain interferes with the activities of daily living and makes the cancer patient uncomfortable, irritable, depressed, and unable to sleep. It can be caused by growing tumors or by radiation, chemotherapy, or surgery that results in nerve damage or other painful side effects.

"We see many causes," said Magdalena Anitescu, MD, PhD, assistant professor of anesthesia and critical care. "We try to tailor pain management toward each specific cause."

Using fluoroscopic guidance, Dr. Anitescu injects pain medication into her patient.

Pain Services at UChicago

As many as 30 patients are treated daily in the Pain Clinic, which is located on the second floor of the Duchossois Center for Advanced Medicine. Other patients, many of them cancer patients, are seen in separate areas of the medical center. The clinic is equipped with five exam rooms and an additional exam room shared with the Perioperative Medicine Clinic. For interventional pain procedures, a dedicated room with a fluoroscopy C-arm allows the physicians to obtain real-time, moving X-ray images during the procedure.

"The patients we see are usually sent to us as a last resort because nobody can figure out what to do about the pain," Dr. Anitescu said. "That's our purpose. We attack the pain as aggressively as possible to try to make patients comfortable."

Pain procedures are individualized to each patient's pain pattern. An outpatient procedure that delivers small, intravenous doses of the anesthetic ketamine is being studied in the treatment of nerve pain caused by chemotherapy. Dr. Anitescu said the treatment is showing promise.

Another promising pain therapy is kyphoplasty for vertebral compression fractures caused by either osteoporosis or cancer, especially multiple myeloma, that has spread to vertebrae. This minimally invasive surgical procedure uses cement to provide instant pain relief for patients suffering from severe pain in their collapsed vertebrae.

"The simple fact is that no one gains anything from being in pain," said Suzanne Conzen, MD, associate professor of medicine, who specializes in breast cancer diagnosis and treatment. "I consider a professional pain management consultation a cornerstone of patient care in oncology."

Implantable Pain Pumps

Although several treatment options exist to help alleviate chronic pain, there is one that has not garnered much attention, according to Gita Rupani, MD, assistant professor of anesthesia and critical care, and one of the founders of the Pain Clinic.

Intrathecal drug delivery systems are battery-operated pumps that are implanted in a patient's abdomen with a soft tube that carries medication to the area around the spinal cord known as the intrathecal space. Because the medication is being delivered directly to fluid surrounding the spine, only a small fraction of the medication is needed (1 mg intrathecal morphine versus 300 mg oral morphine). The decreased dose means fewer side effects, and the round-the-clock delivery provides more consistent pain relief.

Medication refills are needed every few weeks to 6 months, depending on the dosage.

"Most of the time, the pain pump patients are extremely happy with their quality of life because they are more awake and their pain is much better controlled," Dr. Rupani said. "And they can spend quality time with their families."

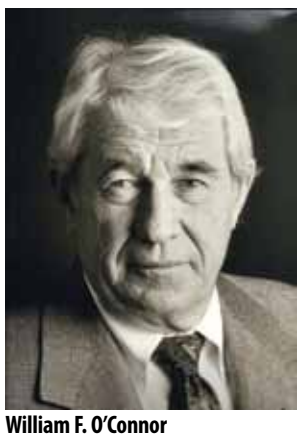
Comfort Team Eases Children's Cancer Pain

When a child has cancer, one of his or her greatest fears is pain. At The University of Chicago's Comer Children's Hospital, a special palliative care service called the Pediatric Comfort Team makes every effort to ease patients' pain during the treatment process. The team comprises a physician, nurse, pharmacist, child life specialist, chaplain, social worker, and psychiatrist, who all work together with the patient and his or her family to achieve pain management goals.

Pediatric Comfort Team Medical Director Melanie Brown, MD, said the team presents the patient with a "cocktail of services" that is very individualized. In addition to medication and narcotics, the patient may also respond favorably to complementary methods, such as hypnosis, sound therapy, massage, and aromatherapy.

$2.1 Million Gift Will Benefit Cancer Patients at UChicago

William F. O'Connor is a legendary figure in financial circles in Chicago. He was a tenacious businessman, an innovative chairman of the Chicago Board of Trade, and an extremely kind and generous person who took care of the people around him.



William F. O'Connor

In 1999, O'Connor died from pancreatic cancer. Before his death, he had the vision to form the William F. O'Connor Foundation to help support cancer research, as well as art and culture in the Chicago area.

His widow, Mary Jane O'Connor, said he wanted The University of Chicago to be one of the primary beneficiaries of the foundation. She said he liked the collaborative process at UChicago and felt that several minds working collectively on a treatment were better than one. That individualized attention, she said, is uncommon at other hospitals.

The William F. O'Connor Foundation is donating $2.1 million over the next 2 years to support the purchase of a new cyclotron for the Molecular Imaging Program and to support the Center for Personalized Therapeutics, under the leadership of Mark Ratain, MD, Leon O. Jacobson Professor of Medicine, who was one of O'Connor's physicians. Mary Jane said O'Connor's faith in Dr. Ratain and his work formed the basis of O'Connor's strong personal belief in the quality of care at UChicago.

> This is significant because it will be the only cyclotron at any academic medical center in Illinois.
>
> **Chin-Tu Chen, PhD**

Center for Personalized Therapeutics

In 2010, Dr. Ratain launched the Center for Personalized Therapeutics (see *Pathways*, Winter 2011). The center aims to discover and incorporate broad genetic information into routine clinical practice allowing for patient-specific treatment decisions regarding both drug and dosage.

The gift will enable further advancement of the center and the "1,200 Patients Project," which will help to identify the genetic variants that influence how individuals metabolize particular drugs.

Molecular Imaging Program

The acquisition of a cyclotron and development of a radiochemistry program at UChicago will help speed the advancement of personalized medicine.

A cyclotron is a particle accelerator that generates radioisotopes used in medical imaging. Imaging at the molecular level, using technology such as positron emission tomography (PET), provides a non-invasive way to monitor and assess a patient's response to treatment and allows that treatment to be adjusted as necessary. Because radioactive isotopes produced by the cyclotron are very short-lived, it is essential that the cyclotron is housed on campus.

This fused PET/CT image, acquired with an F-18 labeled glucose analog (FDG), shows primary squamous cell carcinoma in the left lung with hilar lymph node metastases. UChicago has one PET/CT system in the Duchossois Center for Advanced Medicine. A second system will be installed this summer. Currently, the Clinical PET/CT Center is using FDG supplied by commercial vendors. With the new cyclotron, UChicago will be able to use FDG and many other PET radiotracers produced onsite in the radiochemistry facility.

"This is significant because it will be the only cyclotron at any academic medical center in Illinois," said Chin-Tu Chen, PhD, associate professor of radiology. "The cyclotron will revitalize our radiochemistry program, which had been preeminent from the '50s to the '90s. We will be able to create PET radiotracers that, for example, will not only help to find more accurate ways to apply radiation therapy, but will also allow us to assess the effectiveness of gene therapy."

Dr. Chen said the goal is to have the cyclotron installed by the end of the year. "We've already been contacted by Northwestern University, Rush University, and the University of Illinois at Chicago to see if they can utilize some of our cyclotron-based radiotracers for their own research programs," he said. "I think we will be able to work out some sort of collaborative agreement."

Previous Collaborations

The William F. O'Connor Foundation has made several generous contributions to UChicago over the past 11 years. These contributions have spurred new discoveries in cancer research and treatment, including the development of a simple blood test to predict a patient's response to the powerful chemotherapy drug irinotecan (Camptosar®), which is used to treat people with colon or rectal cancer.

"My husband was a great visionary and he was willing to take risks," said Mary Jane O'Connor. "He participated in clinical trials and he created our foundation because he strongly believed that even if a treatment didn't help him, it would benefit someone else. He was very special."

Breast Cancer Survivorship Conference Connects Patients, Community, and Science

Cancer survivorship has nearly quadrupled over the past 40 years to about 12 million people, according to the latest government statistics. Breast cancer survivors make up the largest proportion of that—at 22%.

A 1-day conference was held in April to give breast cancer survivors and their caregivers the opportunity to discuss complex and emotional issues involving treatment options and resources. The conference, "Surviving Breast Cancer Together: Connecting Survivors, Community, and Science," was at Kennedy-King College and was hosted by the UCCCC Office of Community Engagement and Cancer Disparities and The University of Chicago Specialized Program of Research Excellence (SPORE) in Breast Cancer, as well as other UChicago groups and the University of Illinois at Chicago. More than 130 people attended the free event.

In her opening remarks, UCCCC Director Michelle Le Beau, PhD, Arthur and Marian Edelstein Professor of Medicine, said the goal of the conference was to facilitate a dialogue among everyone involved in breast cancer care. The audience heard unique perspectives from a lawyer, a survivor, researchers, clinicians, a lifestyle and fitness expert, and genetic counselors.

Susan Hong, MD, MPH, assistant professor of medicine and director of the Breast Cancer Survivorship Program, speaks about the state of survivorship among minority and underserved women.

More than 130 people attended the free event.

Karen Kim, MD, MS *(right)*, associate professor of medicine and director of the UCCCC Office of Community Engagement and Cancer Disparities, presents a breast cancer survivor with a raffle prize.

Disparities

According to the Sinai Urban Health Institute, black women in Chicago are 62% more likely to die from breast cancer than white women, and many of the conference speakers discussed factors behind this staggering statistic. Researchers are looking into links between breast cancer, obesity, and other diseases. They are also studying tumor biology specific to black women, as well as cultural and economic factors such as delays in care, inferior treatment compliance, limited access to quality care, and a lack of insurance coverage.

> "Unless we learn to treat breast cancer differently, we're going to keep getting the same results."
>
> **Blase N. Polite, MD, MPH**

Blase N. Polite, MD, MPH, assistant professor of medicine, presented information about the challenges that exist between black breast cancer patients and available clinical trials. He stressed the importance of clinical trials to transform healthcare, saying, "Unless we learn to treat breast cancer differently, we're going to keep getting the same results."

Surviving Breast Cancer

Susan Hong, MD, MPH, assistant professor of medicine and director of the Breast Cancer Survivorship Program, led a breakout session for healthcare professionals to show them how they can provide cancer patients with survivorship care plans. These plans contain treatment summaries, recommendations for follow-up care, and a schedule of surveillance testing.

"I think one of the greatest challenges is helping patients discover what their 'new normal' is," Dr. Hong said. "Many survivors believe once their cancer treatment is completed, they should be right back to their pretreatment baseline. While some survivors do recover fairly quickly, others find that their bodies have undergone significant changes. "

Olufunmilayo Olopade, MBBS, Walter L. Palmer Distinguished Service Professor of Medicine & Human Genetics, addressed emerging trends in breast cancer, encouraging survivors to take a proactive stance on their breast health and not to be afraid of surgery and reconstruction. She also emphasized that breast cancer is not one disease, meaning a personalized approach for each patient is necessary for the best outcome.

Program Teaches the Teachers about HPV Vaccine

MORE THAN A DOZEN MEMBERS of the UChicago staff, who help to educate community groups about various health issues, participated in a February luncheon to learn more about a vaccine for the Human Papillomavirus (HPV), which has been linked to cancer as well as other diseases.

Merck's Gardasil® has been FDA approved to prevent cervical, vulvar, vaginal, and anal cancers caused by HPV.

Karen E. Kim, MD, MS, director of the UCCCC Office of Community Engagement and Cancer Disparities (OCECD) said she is optimistic that vaccines, such as Gardasil®, will help dramatically decrease the risk for cancer, "Just as polio was eradicated by a vaccine, I believe HPV-related cancers can be eliminated."

The luncheon was part of the OCECD's ED-U-CATE program, which stands for Everyone Developing an Understanding of Cancer Awareness, Treatment, and Education. The program provides free wellness sessions about cancer risks, screening behaviors, and treatment options.

ED-U-CATE sessions have also been held at the American Indian Center of Chicago, Chicago Urban League, Chinese American Service League, PepsiCo, and Restaurant Opportunities Center.

Karen E. Kim, MD, MS, director of the UCCCC Office of Community Engagement and Cancer Disparities.

(above) Doriane Miller, MD, director of the Center for Community Health and Vitality, and *(right)* Natalie Elise McClinton, a representative for Merck, which manufactures Gardasil®.

The DreamHome Preview Party was attended by Merchandise Mart Executives, members of the UCCRF Women's Board, and UChicago cancer researchers. *(from left)* Brian Shannon, Mary Ellen Connellan, Jason Garcia, Sam Volchenboum, MD, PhD, MS, Lidia Devonshire, John H. Brennan III, Joan Crouch, Richard Gamble, DreamHome Preview Party Co-Chair Jean Atchison, Chris Kennedy, Jeremy Winter, Kevin Smith, Marsha Rosner, PhD, and Mark Mullen.

DreamHome Inspires Donations to Support Cancer Research

The Design Center at Chicago's Merchandise Mart is hosting its 7th annual DreamHome event through December 9, 2011. Nine elegant and sophisticated rooms, created by the city's top designers, are showcased. A preview gala in April raised more than $100,000 for The University of Chicago Cancer Research Foundation (UCCRF). DreamHome is open to the public. A $5 donation to the UCCRF is requested.

(from left) DreamHome Preview Party Co-Chair Jean Atchison, Sam Volchenboum, MD, PhD, MS, UCCRF Women's Board President Lidia Devonshire, Executive Vice President of Merchandise Mart Properties, Inc., John H. Brennan, Marsha Rosner, PhD, DreamHome Preview Party Co-Chair Joan Crouch.

MEMBER NEWS & NOTES

1 M. Eileen Dolan, PhD, professor of medicine, has received the Purdue Distinguished Women Scholars Award, created by Purdue University to honor alumnae who earned a Purdue doctorate and have made significant scholarly contributions to their respective academic communities. She was honored on Purdue's campus in March, during a Women's History Month celebration.

2 Alessandro Fichera, MD, associate professor of surgery, earned the prestigious Best Video Award at the 2011 annual meeting of the American Society of Colon & Rectal Surgeons. His video, "Single Incision Laparoscopic Total Proctocolectomy for Refractory Crohn's Colitis," documents removing the entire colon, rectum, and anus through the perineum without any visible scars.

3 The American College of Cardiology has presented its 2011 Distinguished Scientist Award to **Stephen Archer, MD,** Harold Hines Jr. Professor of Medicine. Dr. Archer is a clinical cardiologist and translational vascular biologist who studies mechanisms of oxygen sensing and develops experimental therapies for human diseases, including pulmonary arterial hypertension and cancer.

4 President Barack Obama has appointed **Olufunmilayo Olopade, MBBS,** to serve on the National Cancer Advisory Board (NCAB). The NCAB is the highest-level board that oversees the activities of the National Cancer Institute (NCI). Dr. Olopade, Walter L. Palmer Distinguished Service Professor of Medicine & Human Genetics, associate dean for global health, and director of the Center for Clinical Cancer Genetics, has also been named a "Women Deliver 100" honoree for her work in women's health and breast cancer treatment. Women Deliver is a global advocacy organization.

5 Research institutions at 27 sites in the U.S. and Canada have been selected to participate in the Cancer Immunotherapy Trials Network (CITN), a new initiative funded by the National Cancer Institute and headquartered at the Fred Hutchinson Cancer Research Center in Seattle. **Thomas Gajewski, MD, PhD,** professor of pathology, will be the principal investigator at UChicago. This multicenter research trial will investigate promising new agents that boost patients' own immune systems to fight their cancer.

6 Carrie Rinker-Schaeffer, PhD, professor of surgery, received a Pilot Award from the Marsha Rivkin Center for Ovarian Cancer Research for her work "Milky Spot Macrophages: Co-Conspirators in Omental Metastasis Formation." Dr. Rinker-Schaeffer's lab made a novel connection between ovarian cancer metastatic colonization and structures on tissues in the abdomen, called milky spots, that contain immune cells. This discovery could lead to new therapies to suppress metastatic growth, improve quality of life, and extend disease-free survival.

7 Nancy Cox, PhD, professor of medicine, was elected to a 4-year term as a member-at-large of the Section on Biological Sciences for the American Association for the Advancement of Science. Dr. Cox is a geneticist studying common disorders with complex patterns of transmission, including type 1 and type 2 diabetes and polycystic ovary syndrome. She is also a member of the UChicago pharmacogenetics team studying genetic factors that predispose some children to high-risk forms of neuroblastoma and chemotherapy resistance.

8 The American Cancer Society (ACS) has presented **Jianjun Chen, PhD,** assistant professor of medicine, with a Research Scholar Award. The award supports investigator-initiated projects across the cancer research continuum for 4 years. Dr. Chen's research will determine the role of miR-126 in the development of core-binding factor leukemias, as well as critical target genes and relevant pathways. miR-126 is a microRNA molecule that regulates other genes to control angiogenesis (growth of new blood vessels). He said the studies may identify more effective targets for the development of improved treatment strategies.

9 Kay Macleod, PhD, associate professor in the Ben May Department for Cancer Research, will serve a 4-year term on the National Institutes of Health Cancer Molecular Pathobiology (CAMP) Study Section. CAMP reviews grant applications involving the pathology of malignant cells with the emphasis on mechanisms controlling cell growth and death and the molecular events in gene regulation.

10 Mark Ratain, MD, Leon O. Jacobson Professor of Medicine, is the 2011 ASCO Translational Research Professor. The professorship provides flexible funding to outstanding translational researchers who also mentor future translational researchers. Dr. Ratain, director of the Center for Personalized Therapeutics, will use the award to advance the "1,200 Patients Project," an effort to individualize cancer care by charting each patient's genetic variations as a guide to treatment. Dr. Ratain was also named a 2011 honorary fellow of the American College of Clinical Pharmacology.

Bana Jabri, MD, PhD, associate professor of medicine, has been elected to the Association of American Physicians. This honor recognizes Dr. Jabri's important contributions as an international leader in the study of celiac disease and mucosal immunology. She is also studying ways that the immune system can be used to treat cancer.

Dr. Dolan *(right)* receives her award from Beverly Davenport Sypher, Purdue's vice provost for faculty affairs.
Photo courtesy John Underwood

Dean Kenneth S. Polonsky, MD, presents a medal and commemorative case to Marian Edelstein. She is seated next to her grandson Robert Edelstein.

Dr. Le Beau *(center)* celebrates with her husband, Robert Harwood, MD, and her mentor, pioneering cancer geneticist Janet D. Rowley, MD, DSc.

Le Beau Recognized for Significant Contribution to Cancer Research

Cancer Center Director Michelle M. Le Beau, PhD, *was formally presented with the Arthur and Marian Edelstein Professorship of Medicine during an April reception and lecture at the Knapp Center for Biomedical Discovery. A named professorship is the highest academic honor accorded by a university and is awarded only to the most distinguished scientists and clinicians. Dr. Le Beau is credited with several major genetic findings in the diagnosis and treatment of leukemia and lymphoma.*

RESEARCH HIGHLIGHTS

The following represent some of the research by UCCCC members published February–May 2011.

DCIS Patients Who Get Invasive Breast Cancer at Higher Risk of Death

For women who undergo lumpectomy for ductal carcinoma in situ (DCIS), a breast tumor that comes back in the same breast puts them at higher risk of dying from breast cancer than patients who do not develop invasive disease. Researchers evaluated invasive ipsilateral breast tumor recurrence (I-IBTR) and its influence on long-term survival as well as the long-term effects of treatments aimed at avoiding invasive recurrence after lumpectomy.

James Dignam, PhD, associate professor of biostatistics in the Department of Health Studies, was the lead statistician for research that reviewed data from two large randomized trials. The authors conclude that, although I-IBTR increased the risk for breast cancer-related death, radiation therapy and tamoxifen reduced I-IBTR, and long-term prognosis remained excellent after breast-conserving surgery for DCIS. These new findings add to the evidence that adjuvant treatments are warranted, the researchers said.

(Wapnir et al., *J Natl Cancer Inst* 103:478-488, 2011; Schmidt *J Natl Cancer Inst* 103:530-531, 2011)

Dale Shares Personal Reflections

In the *Journal of Geriatric Oncology,* **William Dale, MD, PhD,** associate professor of medicine and director of the Specialized Oncology & Research in the Elderly (SOCARE) Clinic, called attention to common issues in geriatric oncology through a personal narrative of his father's life with and death from lung cancer. Dr. Dale pointed out that while there are many studies about cancer and about aging individually, there is a dearth of information about the intersection of the two. The majority of cancer patients are older and less healthy than the patients who are typically studied in clinical trials.

Through helping care for his ailing father, Dr. Dale bore witness to the problems that older cancer patients face, including accelerated frailty, increased toxicity associated with chemotherapy treatment, delirium and deconditioning after prolonged hospitalization, and the dangers of interactions from comorbidities. He calls for more research to characterize these problems and ways to avoid them.

(*J Geriat Oncol* 2:147-148, 2011)

Drug Combination Yields Excellent Long-term Outcomes in CLL

A new treatment regimen that involves combining a targeted immune-based drug and a chemotherapeutic drug can put some chronic lymphocytic leukemia (CLL) patients in long-term remission without increasing their risk of developing a secondary leukemia, according to a multi-institutional study published in the *Journal of Clinical Oncology.*

Richard Larson, MD, professor of medicine, was among the researchers in the Cancer and Leukemia Group B who reported results from 104 CLL patients being treated only with rituximab and fludarabine. After nearly 10 years of follow-up, 13% of patients had remissions lasting more than 7 years, and patients with certain genetic features in their CLL cells achieved stable long-term remission even when a small amount of disease remained after initial therapy. The results show that the combination of the two drugs is an acceptable first-line treatment for patients with CLL.

(Woyach et al., *J Clin Oncol* 29:1349-1355, 2011)

Journal Focuses on Personalized Cancer Treatment

UCCCC members contributed 13 original research articles to a personalized cancer treatment-themed issue of *Seminars in Oncology.* Articles range from "Tumor Heterogeneity as the Foundation of Personalized Cancer Treatment" to "Individualized Decision-Making for Older Men With Prostate Cancer: Balancing Cancer Control With Treatment Consequences Across the Clinical Spectrum." **Richard Schilsky, MD,** professor of medicine and chief of hematology/oncology, served as the guest editor for the issue.

(*Semin Oncol* 38:163-326, 2011)

Study Reveals Binge Drinking Patterns

Alcohol abuse is a large problem in the United States, but it is not well understood why some individuals accelerate their alcohol consumption to excessive levels while others do not. **Andrea King, PhD,** professor of psychiatry, and colleagues studied how the immediate effects of alcohol relate to a person's susceptibility to future binge drinking.

Among heavy drinkers, alcohol produced greater stimulant and rewarding responses while producing lower sedative and cortisol responses than seen in light drinkers. Among heavy drinkers, greater positive effects and lower sedative effects predicted increased binge drinking frequency during follow-up.

The researchers wrote, "A greater understanding of the factors that contribute to the escalation and maintenance of heavy drinking, especially in young adults, is essential to guide prevention, public education, and early intervention strategies for alcohol use disorders." Heavy consumption of alcohol has been indicated as a risk factor for many types of cancers.

(*Arch Gen Psychiatry* 68:389-399, 2011)

Novel *TP53* Cancer Susceptibility Mutation Uncovered

Whole-genome sequencing conducted on a patient with no other known cancer-susceptibility genes revealed a novel gene variant that could be a key to understanding early onset cancer.

The patient had no family history of cancer but developed breast and ovarian cancer in her late 30s. She subsequently developed therapy-related acute myeloid leukemia (t-AML). The patient tested negative for the *BRCA1* and *BRCA2* mutations. UCCCC Director **Michelle Le Beau, PhD,** Arthur and Marian Edelstein Professor of Medicine, was among researchers who analyzed the bone marrow and skin genome to identify which genetic variants contributed to the patient's cancer and leukemic transformation. They found a deletion in the *TP53* gene—which encodes the p53 tumor suppressor protein. The deletion has not previously been reported in known databases for genetic variants. By testing the patient's mother, they found that the mutation was likely not inherited.

The case illustrates whole-genome sequencing's ability to identify clinically relevant genetic abnormalities that make certain patients more susceptible to developing cancer.

(Link et al., *JAMA* 305:1568-1576, 2011)

Researchers Study How Nicotine Changes the Brain

Tobacco use remains the leading cause of preventable cancer and death in the United States. Despite the many interventions available, at least one-in-five U.S. adults still regularly smokes. Current research is focused on understanding the addictive effects of nicotine, the principal neuroactive component of tobacco. The results indicate that nicotine initiates a series of adaptive changes in the brain at the cellular level.

Daniel McGehee, PhD, associate professor in the Department of Anesthesia & Critical Care, was among the authors of a recent study that aimed to identify important receptor systems that are involved in nicotine-induced long-term changes in the brain. The results provide mechanistic insights into the cellular and synaptic mechanisms of nicotine and tobacco addiction, and reveal remarkable overlap between the effects of nicotine and cocaine on brain reward circuitry. These findings may help identify novel treatment strategies to help smokers quit.

(Mao et al., *J Neurosci* 31:6710-6720, 2011)

Bone Suppression Technology Increases Detection of Lung Nodules

A common problem in diagnosing lung cancer is the obscuration of a lung nodule by the ribs or clavicles on standard X-rays. A new technology aims to overcome this problem by suppressing the bone structures in the chest X-ray to give the radiologist an unobscured view of the lungs.

Heber MacMahon, MB, BCh, professor of radiology, and colleagues conducted a study to evaluate radiologists' ability to detect subtle lung nodules using standard chest X-rays alone compared with bone suppression imaging used with standard chest X-rays. They found that radiologists were better able to detect subtle nodules on chest X-rays using the new technology.

(Li et al., *Am J Roentgenol* 196:W535-W541, 2011)

UCCCC Honors Charles L. Sawyers with 2011 Shubitz Prize

The UCCCC and The University of Chicago Cancer Research Foundation presented the 2011 Simon M. Shubitz Prize to Charles L. Sawyers, MD, a scientist who was instrumental in the development of two drugs for leukemia and who is a leader in the study of drug resistance in prostate cancer. Dr. Sawyers is an investigator at the Howard Hughes Medical Institute and the inaugural director of the Human Oncology and Pathogenesis Program at Memorial Sloan-Kettering Cancer Center in New York. He presented his lecture, "Overcoming Resistance to Targeted Therapy," to UChicago faculty and students on May 23. The Shubitz Cancer Prize and Lectureship is awarded each year to recognize excellence in cancer research and to bring to UChicago internationally respected scientists who have made significant contributions to the study of cancer.

Just the Stats

Kids from 8-to-12 years old participated in a swim-a-thon in March at the Midway Aquatics Club to raise money for pediatric cancer research.

$4,000 *raised*
52 *swimmers*
3.25 *hours*
154,240 *yards*

COMER CHILDREN'S HOSPITAL
THE UNIVERSITY OF CHICAGO

Coaches Mike Cunningham and Laura Thomas from the Midway Aquatics Club at The University of Chicago Laboratory School.

Couple Goes the Extra Mile for Brain Cancer Research

"Life is good" is the mantra that Brian Roman, PhD, assistant professor of radiology, and his wife, Laura, adopted to positively deal with her brain and spinal cancer. Laura, a school psychologist, is being treated for pilocytic astrocytoma, a rare brain tumor that, in her case, has dispersed throughout her cerebral spinal fluid space making it "exceptionally difficult to treat," according to M. Kelly Nicholas, MD, PhD, assistant professor of neurology and director of the Neuro-oncology Program at UChicago.

The Romans told Dr. Nicholas that they preferred an aggressive treatment strategy instead of waiting to see what would happen. The challenge was finding the right treatment. Most available therapies were designed to work on more aggressive cancers. Laura's cancer is slow-growing. Dr. Nicholas presented Laura's case to his colleagues in the Brain Tumor Center, a group of doctors from neurosurgery, radiation oncology, neuro-oncology, neuroradiology, and neuropathology.

"He was so thorough in planning my treatment," Laura said. "He lets you know when he consults with other physicians to compare strategies and see if they agree with the choice of course. As a school psychologist, it fit with my philosophy of problem-solving and helped me feel more confident in those decisions."

Under Steven Chmura, MD, PhD, assistant professor of radiation and cellular oncology, Laura underwent cranio-spinal radiation therapy for 6 weeks, but in the following months began to intermittently experience complications, the most alarming of which were episodes of amnesia. "It's scary when you're walking around and interacting with people, and you have no memory of it," she said.

Presently, Laura is undergoing chemotherapy treatment with an angiogenesis inhibitor called bevacizumab that targets blood vessel growth. It appears to be helping with the leaky blood vessels that may have contributed to her complications. Her tumor appears to be stable. Dr. Nicholas said, "The future is bright for Laura."

Brian and Laura Roman take in a Chicago Cubs baseball game with their 5-year-old son, Joseph.

Team Roman

Because of the excellent care Laura has received, the couple said they decided to express their gratitude through Dr. Roman's participation in the "Fleet Feet Sports Soldier Field 10 Mile" run in May.

"We owe a tremendous debt of gratitude to this group and had been searching for ways to give back to them and other patients," Dr. Roman said. "We wanted to raise public awareness about the program and the great skill and care patients receive."

"Team Roman" has raised more than $6,700 in donations to benefit the Brain Tumor Center at UChicago. The couple said the run is a starting point for more fundraising initiatives that they plan to undertake.

The Brain Tumor Center

Treating brain cancer requires a team of doctors who are experts in many different areas. For example, a brain cancer patient will generally need a neurosurgeon, radiation oncologist, oncologist, neurologist, neuropathologist, neuroradiologist, and a doctor who can coordinate all of the treatment, as well as refer the patient to ancillary services, such as physical, occupational, speech, and cognitive therapies.

> It's scary when you're walking around and interacting with people, and you have no memory of it.
>
> **Laura Roman**

"At UChicago, we have coined the phrase 'Brain Tumor Center' around which all of these activities happen, but it's really a virtual space in which we all work," said Dr. Nicholas.

The Brain Tumor Center is a collaborative group that meets on a weekly basis to discuss all relevant cases, exchange information, and talk about clinical trials that are open. UChicago offers clinical trials for malignant brain tumors, at diagnosis and recurrence, and a variety of rare tumors.

Oncology nurse Jean Arzbaecher, RN, coordinates the clinical activities for the center and runs a monthly support group for patients with brain cancer in the community.

"Dr. Nicholas and Jean are great," Laura said. "We have such confidence in them."

Visit *chicagobraintumors.org* for more information about the Brain Tumor Center.

FOCUS ON CORE FACILITIES

Human Tissue Resource Center Expands, Offers More Services to Researchers

As one of the most widely used core facilities at UChicago, the Human Tissue Resource Center (HTRC) provides research-quality biospecimens to 130 principal investigators from 14 departments. Biospecimens are samples of material—such as tissue, urine, blood, cells, DNA, RNA, and protein—from humans, animals, or plants. One of the HTRC's primary purposes is to collect clinically annotated, or "linked," human tissue in response to investigator-initiated research projects.

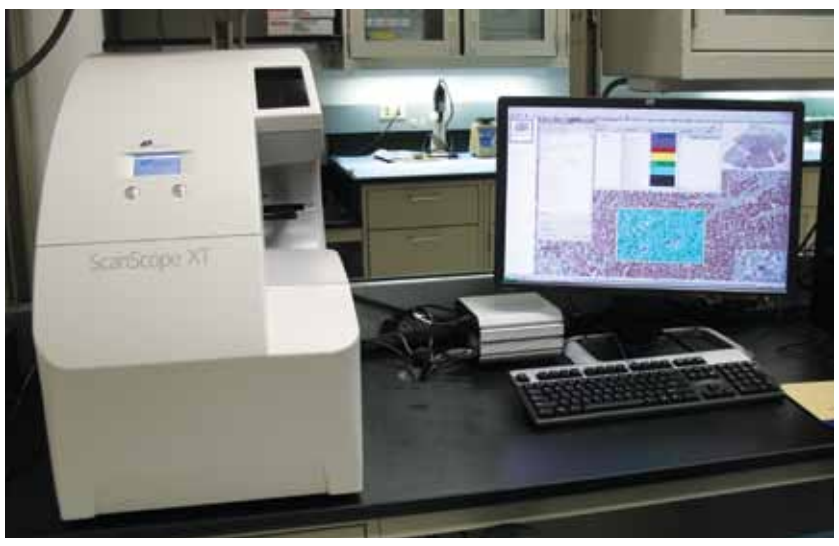
Linked tissue refers to research tissues that are associated with clinical and patient information. Patient information is from individuals who have agreed that certain details of their medical record, such as how they were treated and their response to treatment, can be used in research studies. Access to data from large cohorts of patients is critical to developing more effective personalized cancer treatment and prevention strategies.

A team of research and pathology professionals led by Scientific Director Mark Lingen, DDS, PhD, and Technical Director Leslie Martin operate the HTRC, comprising four integrated facilities: Biospecimen Bank, which is responsible for collecting, processing, storing, and distributing the tissue; Laser Capture Microdissection, which is the dissection of tissues and cells under a microscope; Pathology Image Analysis; and Immunohistochemistry.

Immunohistochemistry, a technique that identifies specific molecules in different types of tissue using antibodies, is used to help diagnose diseases, such as cancer, and to understand how cells grow and differentiate. The merging of the two facilities brings human and animal biospecimens under a coordinated, centralized, and dedicated program for the procuring, processing, dispersing, and assessing of all types of biospecimens.

Upgrades

The ever-expanding facility has been making software upgrades and equipment purchases to further streamline efficiency and help researchers achieve their objectives. For instance, the facility's biospecimen banking database, eSphere, has a new feature that allows users to request samples through a withdrawal process akin to *Amazon.com.* Over a HIPAA-compliant network, investigators can browse through available samples and protocols and make tissue requests.



By integrating image capture, viewing, management, and analysis solutions into a single workflow, the digital pathology image analysis system, Aperio, is helping scientists accelerate basic research and drug discoveries.

> Access to [linked tissue] allows for complex genetic analyses, which is critical to the development of individualized therapies.
>
> **Leslie Martin**

Each sample's unique identifying bar code number corresponds to the pathology report, site of biopsy, and other clinical information, such as diagnosis, metastatic sites, gender, and race.

"Having access to this type of information allows for complex genetic analyses, which is critical to the development of individualized therapies," said Martin.

The HTRC has also made improvements in digital pathology image analysis. An advanced and user-friendly system called Aperio allows researchers to view and quantify images of stained tissue and analyze them using different algorithms that are either pre-populated in the system or created using their own parameters. This can be done via the web with a very high-resolution, user-friendly program that digitally stores images on a secure server. The system enables researchers to distinguish differences in serial sections and measure distances between tissue structures.

Research Technologist Lei-Ann Arceneaux has assembled a manual, available at *pathcore.bsd.uchicago.edu/APERIO/APERIO_Introduction.shtml,* to help UChicago investigators work through the new image analysis process. "By integrating image capture, viewing, management, and analysis solutions into a single workflow, Aperio helps scientists accelerate basic research and drug discoveries," said Martin.

Plans for Expansion

The HTRC space soon will undergo renovations to improve workflow and ensure future College of American Pathologists compliance, according to Martin. As part of the expansion process, the cryostats where frozen specimens are stored will eventually be moved to another room and additional research benches will be installed in the current facility.

Martin also revealed that the HTRC is in the planning stages of renovating space on the 5th floor directly below the HTRC for the establishment of a unified "freezer farm" for the growing collection of biospecimens. These upgrades are being funded via an American Recovery and Reinvestment Act supplement awarded to the UCCCC.

"Upgrading our resources and acquiring more space will facilitate high-quality cancer research in a timely manner," said Martin.

(from left) Jackie Bossu, Steve Bossu, Liz Brandt, and Ted Brandt.

(from left) Ernst Lengyel, MD, PhD, Event Co-Chair Midge Wegener, Event Co-Chair Peggy Tieman, UCCCC Director Michelle Le Beau, PhD, Tara Henderson, MD, MPH, Samuel Volchenboum, MD, PhD, MS, and Auxiliary Board President Laurie Foster Baker.

Event Helps 'Spring Forward' Cancer Research

The University of Chicago Cancer Research Foundation (UCCRF) Auxiliary Board hosted a dinner dance and auction at the Michigan Shores Club in Wilmette in March to support the work of three UChicago physicians and scientists.

Top auction items at the benefit, themed "Spring Forward," included a pig roast, a 5-day stay at a Hyatt Property anywhere in the world, and several spa packages. More than 160 guests raised $110,000 for Tara Henderson, MD, MPH, and her childhood cancer survivors program; Ernst Lengyel, MD, PhD, and his ovarian cancer research; and Samuel Volchenboum, MD, PhD, MS, and his pediatric neuroblastoma research.

***(from left)* UCCRF Executive Director Mary Ellen Connellan and UCCCC Director Michelle Le Beau, PhD, admire one of Paloma Picasso's bracelets.**

***(from left)* UCCRF Women's Board President Lidia Devonshire, Paloma Picasso, Grand Auction Co-Chair Tricia Cox, and Grand Auction Co-Chair Terri Brady.**

Paloma Picasso Dazzles UCCRF Women's Board at Tiffany

More than 100 people attended a cocktail party at Tiffany & Company in April in honor of Paloma Picasso, the daughter of one of the 20th century's most influential artists. Picasso was in Chicago to launch her new Marrakesh jewelry collection, which is offered at Tiffany, one of the premier sponsors of The University of Chicago Cancer Research Foundation (UCCRF) Women's Board Grand Auction, which is held every November.

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COMPREHENSIVE CANCER CENTER

The University of Chicago Medical Center
5841 S. Maryland Ave., MC1140 H212
Chicago, IL 60637
feedback@bsd.uchicago.edu

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