

Pathways to Discovery

At the Forefront of Discovery

THE UNIVERSITY OF
 CHICAGO
CANCER RESEARCH CENTER

Summer/Fall 2008

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UCCRC Transformation Produces Comprehensive Cancer Center Designation



Earlier this year, the ceremonial last beam was hoisted to the top of the Gwen and Jules Knapp Center for Biomedical Discovery. The future home of the UCCRC, the Center is a powerful symbol demonstrating the profound commitment of the UCCRC and the University of Chicago to cancer research. This commitment was instrumental in the decision to award the UCCRC designation as a Comprehensive Cancer Center.

The National Cancer Institute (NCI) has designated the University of Chicago Cancer Research Center (UCCRC) as a Comprehensive Cancer Center. This makes the UCCRC one of only 41 comprehensive cancer centers in the nation and one of two in Illinois. According to the NCI, comprehensiveness signifies that the center has demonstrated “depth and breadth of research activities in each of three major areas: laboratory, clinical, and population-based research, with substantial transdisciplinary research that bridges these scientific areas.” An NCI-designated Comprehensive Cancer Center also has

proven proficiency in “professional and public education and dissemination of clinical and public health advances into the community it serves.”

The designation follows the approval of the five-year competing renewal application for the Cancer Center Support Grant (CCSG). The purpose of these grants is to “foster excellent science and productive interactions within institutions.” The NCI evaluates designated cancer centers every five years to ensure that they are meeting their objectives, investing significant resources, and advancing cancer research. It is a meticulous review that culminates in an on-site evaluation by approximately 30 top researchers. The UCCRC did extremely well in the evaluation, earning its highest score in its 35-year history.

Under the direction of Michelle M. Le Beau, PhD, the UCCRC developed and implemented an aggressive, comprehensive strategic plan that called for the expansion and integration of the basic, translational, clinical, and population research programs. “Our major emphasis for the past 5 years has been the maturation of translational research, and the growth and integration of population research,” said Dr. Le Beau. “The successful implementation of this strategic plan and the extensive expansion and reorganization of our Cancer Risk and Prevention Program were major steps toward achieving comprehensiveness.”

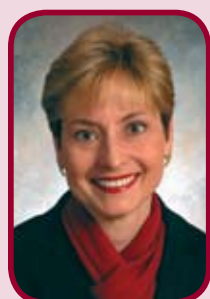
Dr. Le Beau emphasizes that this success is the consequence of years of dedicated effort by the UCCRC members and staff and the

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Funding Opportunity Available for Junior Faculty

The October 31st deadline for the UCCRC American Cancer Society Institutional Research Grant is fast approaching. The grant provides seed money to help junior faculty obtain preliminary data from cancer-related research that will enable them to compete for national peer-reviewed research grants. For more information and eligibility requirements, please visit the UCCRC website at http://funding.uccrc.org/funding_opportunity/detail/289.

A Message from The Director



This is a momentous year for the Cancer Research Center. The National Cancer Institute (NCI) has approved the five-year competing application for our Cancer Center Support Grant, awarding the highest score in our 35-year history. Even more exciting is the decision by the NCI to designate the UCCRC a Comprehensive Cancer Center. These two honors recognize years of dedicated effort by hundreds of people – our members, our staff, our donors, and the leadership of both the Biological Sciences Division and the University.

We spent many long days and nights preparing the competing application. The documentation filled hundreds of pages in a dozen binders, but this material was only a pale reflection of the work and the discoveries of our members and the help of our donors and friends. Words and charts cannot fully express their dedication, vision, and teamwork. Nor can they completely

characterize the expertise and intellectual strengths of our members—the commitment and creativity of our staff—the generosity of our donors—and the support of our leadership.

Everyone associated with the Cancer Research Center has played a role in this success, enabling us to reach the first milestone in the transformation of our organization. Our new comprehensive status is the harbinger of a great future. The University and the Medical Center are committed to building an even greater cancer program. Our members and our staff are prepared to make it happen. And our Foundation and other donors are solid in their support.

Four years ago we set a very high bar for the evolution of our Center—and we cleared it. Today we are working to take the UCCRC to another level of excellence. So, we are setting the bar much higher. But I am confident we will soon soar over this challenge, because our community has proven its capacity for success.

With thanks and warm regards,

Michelle M. Le Beau, PhD

Director, University of Chicago Cancer Research Center
Professor of Medicine

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Focus on UCCRC Scientific Program Five: Advanced Imaging Transforms Cancer Care and Research

“At the Forefront of Medicine” – this motto of the University of Chicago Medical Center also exemplifies the Advanced Imaging Program at the UCCRC. Members in the Program have pioneered advances in imaging that are transforming cancer care. These advances, along with the continued expansion and upgrading of the imaging capabilities for both basic science and clinical researchers on campus, allow physicians to diagnose cancers at earlier stages and attack them with greater precision.

The Advanced Imaging Program is under the leadership of Greg Karczmar, PhD, and Heber MacMahon, MD. (Dr. Karczmar recently succeeded Maryellen Giger, PhD, who founded and led the program for many years.) The Program is comprised of 25 members from the Departments of Radiology and Radiation and Cellular Oncology. The primary goal of the Program is to research and develop new methods of diagnostic image production and analysis, and to translate these findings to the clinical arena.

Dr. Karczmar points out that “there have been extraordinary advances in imaging pioneered by members in the Program. Not only are these advances aiding clinicians in the diagnosis and treatment of cancer, but they are helping basic scientists in other UCCRC Programs analyze their cancer-related experiments.” Major areas of research exist along all aspects of the imaging chain including developing computerized methods of image analysis; designing new imaging techniques for diagnosing and treating cancer, evaluating tumor response to therapy, and supporting basic science research; and developing methods to objectively evaluate newly developed imaging systems.

Computer aided diagnosis (CAD) is a priority research area in the Advanced Imaging Program, and it has seen substantial progress in recent years. CAD involves the use of computer technology to aid in the interpretation of medical imaging scans, including digital mammography, computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) scans. The goal of CAD research is to develop computer systems that can enhance the interpretation of medical images in an effort to detect and diagnose cancers at the earliest possible stage. Radiologists also routinely compare multiple medical imaging scans from a single patient to determine if the patient’s cancer is responding to the therapy being used. A challenge of the routine side-by-side comparison of images is the detection of small changes that are visually subtle, but medically significant. Dr. MacMahon, Samuel Armato, III, PhD, and Kunio Doi, PhD, are working together to develop and test computerized methods for comparing multiple medical images from the same patient in a single combined image. Using chest radiographs and thoracic CT scans, they are working to improve a technique called temporal subtraction imaging where

multiple medical images are combined in a single image that identifies the subtle changes that have occurred in the tissue over time. Recently they have developed a method for automatically creating and analyzing these “temporally subtracted” images that decreases the rate of false positive and negative findings¹.

Several research groups in the Program are also working to develop CAD technology for the detection of breast cancer and the assessment of breast cancer risk. Robert Nishikawa, PhD, Ingrid Reiser, PhD, and Dr. Giger are working to develop automated methods of detecting breast cancer in breast tomosynthesis images. Breast tomosynthesis is an emerging imaging technique where mammographic images of the breast are taken from several angles. These images are then combined to form a detailed 3-dimensional (3-D) image of the breast that has the potential for improving the accuracy of detecting breast cancer. Unfortunately, the current methods for developing the 3-D images are not yet optimal for accurate computerized detection of breast cancers in the final image. To deal with this problem, Drs. Nishikawa, Reiser, and Giger have developed a method that automatically detects candidate lesions at several stages during the 3-D image generation process that has a low false-positive rate².

In addition to helping develop methods of using CAD to diagnose cancer, Dr. Giger is also collaborating with Olufunmilayo Olopade, MBBS, FACP, in the Cancer Risk and Prevention Program on pioneering research that aims to develop computerized medical imaging methods to assess a patient’s risk of developing breast cancer. Dr. Giger’s lab has found that the texture of the breast tissue as it appears on mammograms in women carrying BRCA1/BRCA2 mutations (i.e. breast cancer mutations) is different from the breast tissue in women with a low-risk of developing breast cancer³. Dr. Giger’s lab is now developing methods for combining these image-based biomarkers from mammograms and MR images with genetic analysis to more accurately assess a woman’s risk of developing breast cancer. This project is part of the Breast Cancer Specialized Program of Research Excellence (PI: O. Olopade, Cancer Risk and Prevention Program) that was funded by the National Cancer Institute in 2006.

For computer systems to detect abnormalities on medical images, they need to be “trained” to accurately recognize abnormalities. One of the concerns with CAD is the risk of false-positive identifications. Several research groups in the Program are working to develop methods to reduce this risk. For instance, Kenji Suzuki, PhD, and Abraham Dachman, MD, have developed a training scheme to reduce the number of false-positive identifications of polyps by CAD in CT scans

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1. Armato et al. Med Phys 33:1239, 2006

2. Reiser et al. Med Phys 33:482, 2006

3. Huo et al. Radiology 225:519, 2002

New Procedure Enables Detection of Early Breast Cancers

Demonstrating the enormous potential of advanced imaging, UCCRC researchers and their colleagues have developed a new magnetic resonance imaging (MRI) procedure, which can detect very early breast cancer in mice, including ductal carcinoma in situ (DCIS), a precursor to invasive cancer. Some of the tumors detected were less than 300 microns in diameter, the smallest cancers ever detected by MRI. (A micron is one millionth of a meter.)

This is the first demonstration that very early DCIS can be detected in mouse mammary glands and that the development and progression of DCIS can be followed with serial MR imaging. These methods will place UCCRC investigators in a unique position to study the early events and markers for cancer development, as well as the response of early cancers to therapy, which was not possible in the past due to technical barriers. This breakthrough was made using the new Lynn S. Florsheim 9.4 Tesla MRI scanner in the UCCRC Magnetic Resonance Imaging and Spectroscopy Core Facility. The team was led by graduate student Sunny Jansen; Gregory Karczmar, PhD; Gillian Newstead, MD; Suzanne Conzen, MD; and Thomas Krausz, MD, FRCPath.

The technique is helping researchers study the natural history of DCIS in order to understand which tumors will become invasive cancers and require surgery, and which tumors will not. It will also be used to assess the effects of preventive therapies, such as green tea, on the development of early breast cancers. It may eventually enhance the power of MRI as a breast cancer screening tool.

“We found that MRI can reliably detect the microscopic stages of both in situ and invasive murine mammary cancers with high sensitivity,” researchers reported in the September 9, 2008, issue of *Physics in Medicine and Biology*. “These experiments provide proof of principle that microscopic mammary tumors can indeed be detected and followed in a mouse model of breast cancer.”

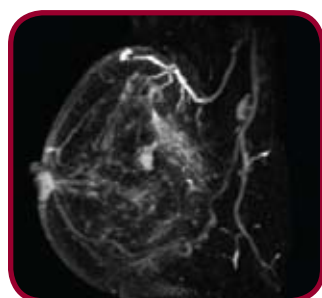
“These are very small tumors,” said study co-author Dr. Conzen. “They are much too small to feel or even to see without a microscope.”

About 20 percent of all newly diagnosed breast cancers are DCIS, which has the best prognosis of any breast cancer with long-term survival rates of 97 to 99 percent. MRI is already used as a screening tool for many women at high risk for breast cancer, but more sensitive tests that could find cancers earlier, when they are more treatable, could increase survival.

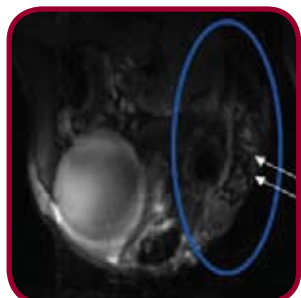
“We decided to try to push the technology a step or two,” said Dr. Karczmar, “to see if we could get good pictures of something people didn’t believe could be imaged.”

Unlike previous MRI studies of tumors in mice, the team was able to detect very tiny naturally occurring cancers, and these tumors were excellent models for human breast cancer. Although the mice used were laboratory animals bred to develop breast cancer, the tumors they developed were “realistic models of the most frequently detected human cancers,” the authors noted. “The morphology of these early murine mammary cancers on MRI is similar to the MR presentation of early human breast cancer.”

“Although still at an early stage,” said Dr. Newstead, “this approach has the potential to produce significant advances in breast imaging, as well as to help us understand cancer development and study the response to therapy.”

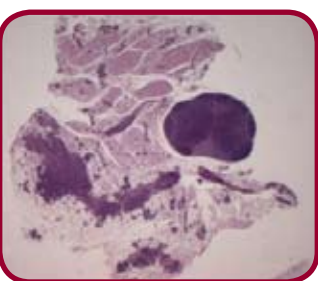


Human DCIS with invasive component - Medved

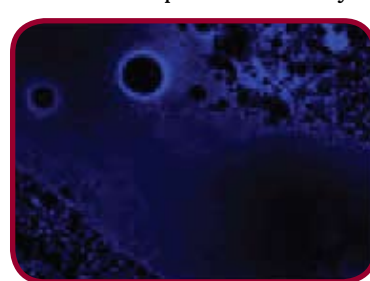


Murine DCIS - Arkani

Mouse mammary gland with DCIS



Mouse DCIS and invasive component; Correlation with histology - Arkani



X-ray fluorescence image of Gd in ducts - Woloschak, Paunescu, Arkani

of the colon. Their method consists of using 4 different sets of 3-D training data designed to reduce four common causes of false positive identifications in these scans. Using this training scheme, the research team was able to reduce the number of false positive identifications of polyps per case without losing the identification of any true polyps.

In addition to improving on the use of existing medical imaging technologies, members in the Advanced Imaging Program are very active in developing new imaging technology to improve the diagnosis and treatment of cancer. For instance, Dr. Karczmar, Gillian Newstead, MD, ChB, FACR, and Hiroyuki Abe, MD, are collaborating in the development of a new approach to breast MRI – high spectral and spatial resolution (HiSS) MRI. This technique gathers information from the water and fat molecules in tissue that are usually ignored by conventional MRI to produce very clear, detailed 3-D images of the breast even before contrast agents are injected. In addition, recent work has demonstrated that HiSS is sensitive to the unusually high concentrations of deoxyhemoglobin (hemoglobin molecules in red blood cells that are not bound to an oxygen molecule) in tumor blood vessels. The images produced by this form of MRI provide enough detail that may allow for the detection of breast cancer lesions, other breast tissue abnormalities, and tumor blood vessels without the injection of contrast agents.

In addition to improving imaging technologies for clinical care, members of the Program are striving to increase the use of imaging in basic science research. For instance, members are using experimental tumor models to develop new imaging technologies that can be used to improve the administration of cancer therapy. It has been observed that a tumor's response to therapy is not homogenous - different areas of a tumor can respond differently to cancer therapy. Early detection of these differences in response could allow doctors to tailor therapy to focus on the areas of the tumor that actually need it while decreasing the damage to healthy tissues. This is referred to as adaptive therapy. Charles Pelizzari, PhD, Howard Halpern, MD, PhD, Hania Al-Hallaq, PhD, and Dr. Karczmar are working to develop an imaged-guided form of adaptive therapy. They are combining a variety of imaging methods to measure changes in hemodynamic parameters, oxygen levels, and the vascular anatomy of a tumor and using this information to change the targeting of local therapy.

In addition, Chien-Min Kao, PhD, and Chin-Tu Chen, PhD, are developing a prototype high-throughput scanner for the imaging of multiple small animals at one time. This technology will make PET imaging an effective tool to be used in drug development or gene expression studies. Brian Roman, PhD, is working to combine the fields of imaging and molecular biology with his research on using MRI to detect and study gene expression. He is currently developing the small equipment required for use in animal models that will allow researchers to examine cellular function *in vivo* and may aid in the identification and monitoring of stem cells in cancer research studies.

These new imaging acquisition and analysis methods are evaluated for clinical accuracy. Charles Metz, PhD, and his colleagues are continuing to develop receiver operating characteristic (ROC) methodology for the objective evaluation of diagnostic techniques in general, and medical imaging techniques in particular. ROC analysis determines the relationship between the numbers of true positive and false positive diagnoses that are generated when different quantitative "thresholds of abnormality" are employed in the diagnosis of a disease such as cancer. This type of analysis plays a vital role in many research areas of the UCCRC, including CAD research. Dr. Metz's team has developed and tested a variety of computer software to analyze the data that are generated by quantitative and image-based diagnostic tests. His new methods have been validated on more than one million simulated sets of diagnostic data and on a broad variety of real diagnostic data from human observers and automated analysis systems. Dr. Metz's software, which is provided free of charge, is now accepted widely as the standard for ROC data analysis and has been obtained by more than 10,000 laboratories in more than 40 countries.

The work of the researchers in the Advanced Imaging Program is groundbreaking. It has the potential to advance the research of many of the clinical and basic studies being conducted on campus. To ensure that the most state-of-the-art imaging equipment is available on campus, members in the Advanced Imaging Program have requested and received funding from the NIH to upgrade and/or develop several imaging technologies. In the past 2 years, Program members have received 3 Shared Instrument Grants and 1 P41 award from the NIH totaling over \$1.2 million (see Program 5 Highlights for details). In addition, the imaging scientists on campus, many of whom are members of the Advanced Imaging Program, are in the process of developing an Imaging Research Institute to expand the use of advanced imaging technologies in basic science, as well as clinical research. The goal of the Institute is to provide a full range of imaging technologies and expertise in both *in vitro* and *in vivo* anatomical, functional, molecular, and cellular imaging for research in the basic and applied biomedical sciences, as well as support and oversight of clinical trials involving the use of human imaging. Not only will the Institute help to integrate and further develop the existing imaging shared resources on campus, several of which are UCCRC shared research facilities, but it will foster and promote collaborative research opportunities between biomedical researchers and imaging scientists, and develop and integrate *in vivo* and *in vitro* imaging technologies that are not currently part of established shared research facilities. The Institute will also help to reliably and accurately incorporate human imaging into clinical research and facilitate the conduct of retrospective imaging research in which post-acquisition images provide the basis for the study.

Through its groundbreaking, collaborative research and the state-of-the-art imaging technology it has helped develop and maintain, the Advanced Imaging Program is poised to remain at the forefront of the imaging revolution. As the Program moves into the future, new collaborative research efforts, the development of new imaging acquisition and analysis techniques, and the translation of advances in imaging science into clinical applications, as well as their application to basic biomedical research, will expedite new cancer research, reduce human error, and improve the diagnosis and treatment of cancer.

Program Five Basics

Program Five Goals:

- Investigate new methods for computerized image analysis to help in the early diagnosis of cancer
- Investigate new methods of image reconstruction for use in computed tomography (CT), single photon emission computed tomography (SPECT), and positron emission tomography (PET) imaging to improve detection of early cancers and pre-cancerous conditions
- Develop new methods of image acquisition such as magnetic resonance imaging and spectroscopy (MRIS) and electron paramagnetic resonance imaging (EPRI) methods to improve detection of early cancers and pre-cancerous conditions
- Identify imaging methods for oncology practice and for the evaluation of response to target-based cancer drugs
- Investigate methods for the evaluation of computer aided diagnosis (CAD), new imaging instrumentation, and other new imaging technologies

Members (2005-2007)

- 25 members representing 2 departments
- 14 new members appointed since 2005: Hania Al-Hallaq, PhD; Hiroyuki Abe, MD; Abraham Dachman, MD; Chien-Min Kao, PhD; Patrick La Riviere, PhD; Gillian Newstead, MD; Charlene Sennett, MD; Michael Vannier, MD; Brian Roman, PhD; Daniel Appelbaum, MD; Richard Baron, MD; Charles Metz, PhD; Kenji Suzuki, PhD; and Aytekin Oto, MD

Publications (2005 – 2007)

- 95 publications
 - 28 Intraprogrammatic publications
 - 13 Interprogrammatic publications

Program Five Highlights

Scientific Accomplishments

- Gregory Karczmar, PhD; Gillian Newstead, MD; and their colleagues are using high spectral and spatial resolution (HiSS) MRI for early detection and staging of breast cancer.
- Robert M. Nishikawa, PhD; Ingrid Reiser, PhD; Maryellen Giger, PhD; and their colleagues have demonstrated that CAD can be used to locate lesions on breast tomosynthesis.
- Maryellen Giger, PhD; Robert M. Nishikawa, PhD; Yulei Jiang, PhD; Charles E. Metz, PhD; and their colleagues are working with breast radiologists to translate their CAD multimodality breast imaging workstations to the clinical arena for evaluation.
- Heber MacMahon, MD; Samuel Armato, III, PhD; and Kunio Doi, PhD; and colleagues are developing and evaluating a technique called temporal subtraction imaging.
- Xiaochuan Pan, PhD; Chin-Tu Chen, PhD; Chien-Min Kao, PhD; Patrick LaRiviere, PhD; and colleagues have made significant contributions to tomographic imaging theory.
- Charles Pelizzari, PhD; Howard Halpern, MD, PhD; and colleagues have made substantial contributions in developing adaptive image-guided therapy based on a combination of Magnetic Resonance Imaging (MRI) and Electron Paramagnetic Resonance Imaging (EPRI) techniques.

Funding Highlights (2005 – 03/2008)

- Members of the Advanced Imaging Program have enhanced imaging at the UCCRC and University of Chicago through the NIH awards of 3 Shared Instrument Grants and 1 P41 award over the past 3 years:
 - Howard Halpern, MD, PhD: (5-P41-EB02034-08) Very Low Frequency EPR Imaging for *In Vivo* Physiology; 08/01/07-07/31/08. Total costs \$683,123
 - Gregory Karczmar, PhD: (1-S10-RR21177-01A1) A 9.4 Tesla MRI magnet for the University of Chicago; 06/01/2006- 05/30/2007. Total costs \$500,000
 - Robert M. Nishikawa, PhD: (1-S10-RR21039-01A2) High-Performance Computer Cluster for Image Analysis; 04/01/07-03/31/08. Total costs \$229,551
 - Chin-Tu Chen, PhD: (1S10RR22520-01A2) Hybrid MicroSPECT/MicroCT for Quantitative Imaging; 03/01/08-02/28/09. Total costs \$500,000
- The Breast Cancer Specialized Program of Research Excellence (SPORE) was funded in October 2006 (PI: O. Olopade, Cancer Risk and Prevention Program; co-PIs: M. Giger, G. Fleming); Maryellen Giger, PhD; Gillian Newstead, MD; and Charlene Sennett, MD; are co-leaders of Project 1: *Imaging-based determination of breast cancer risk*. Gregory Karczmar, PhD; and Gillian Newstead, MD, are co-leaders with Nora Jaskowiak, MD (Cancer Risk and Prevention Program) on Project 2: *Specificity of MRI with optimal temporal, spatial, and spectral sampling in early breast cancer*.

Collaborations

- Maryellen Giger, PhD; Charlene Sennett, MD; and Gillian Newstead, MD; are collaborating with Olufunmilayo Olopade, MBBS, FACP (Cancer Risk and Prevention Program) in developing image-based methods for the computerized assessment of breast cancer risk. The project that involves mammography and breast MRI is one of four in a recently funded Breast Cancer SPORE (PI: O. Olopade). They have found that the radiographic breast parenchyma of women at risk for breast cancer tends to be dense with a pattern that is coarse and low in contrast.
- Samuel Armato, III, PhD, and Hedy Kindler, MD (Clinical and Experimental Therapeutics Program) are evaluating semi-automated methods for assessing mesothelioma tumor response on CT scans.
- Gregory Karczmar, PhD, and Gillian Newstead, MD, are collaborating with Olufunmilayo Olopade, MBBS, FACP, and Nora Jaskowiak, MD (both of the Cancer Risk and Prevention Program) to examine the use of high spatial and spectral MRI in the diagnosis of early breast cancer. The technique has been found to produce very clear 3-D images of the breast even before the injection of contrast agent. The project is one of four in a recently funded Breast Cancer SPORE (PI: O. Olopade).

UCCRC Transformation *Continued from cover*

renewed commitment to cancer research by the University of Chicago Medical Center. “The transformation of the UCCRC has been a collaborative effort engaging the talents and expertise of hundreds of dedicated individuals,” said Marsha Rosner, PhD, UCCRC Deputy Director.

During the last several years, the UCCRC community:

- Developed and implemented a unified strategic plan;
- Expanded and integrated robust basic, translational, clinical, and population research programs;
- Initiated interdisciplinary research programs, such as the Pharmacogenomics of Anti-cancer Agents (PAAR) Consortium, the Center for Interdisciplinary Health Disparities Research (CIHDR), and the Breast Cancer Specialized Program of Research Excellence (SPORE);
- Almost doubled the number of P01 and Center (P-type) Grants held in 2007 as compared to 2002, and secured a Leukemia and Lymphoma Society Specialized Center of Research (SCOR) grant; and
- Increased membership by 26%, peer-reviewed funding by 60%, publications by 31%, and more than doubled early-phase, investigator-initiated clinical trials.

The UCCRC recruited many new faculty members to its Cancer Risk and Prevention Program and to new leadership positions that support this priority program. Habibul Ahsan, MD, MMedSc, joined the UCCRC as Associate Director for Population Research, and Rick Kittles, PhD, joined the UCCRC as Associate Director for Diversity



and Community Outreach. Enhancing population research and community outreach programs was essential to obtaining comprehensiveness.

On August 15, the University celebrated the UCCRC's success in obtaining a record score for its five-year Cancer Center Support Grant and earning designation as a Comprehensive Cancer Center. Among the celebrants were (left to right) Michelle M. Le Beau, PhD, UCCRC Director; Barry Ultmann and his mother Ruth, and Vinay Kumar, MD, Executive Vice-Dean Biological Sciences and the Pritzker School of Medicine and the Alice Hogge and Arthur A. Baer Professor and Chairman, Department of Pathology. Barry and Ruth represented the late John Ultmann, MD, the UCCRC's founder and first director.

and Community Outreach. Enhancing population research and community outreach programs was essential to obtaining comprehensiveness.

“We are very excited about the future of cancer research at the University of Chicago,” said Dr. Le Beau. “Since its beginning, the UCCRC has provided the structure within which cancer research has thrived, and the University’s commitment to cancer studies has intensified.” This renewed commitment to cancer research and therapy is evident in the investment of more than \$1.2 billion in two new research buildings and the New Hospital Pavilion, which will provide complex specialty care with a focus on cancer.

Little Heroes Help Patients Enjoy Days in the Sun

On a recent vacation to Hawaii, Ray Asher mused that his son looked the perfect “surfer dude” with his straw-colored hair. “His hair used to be dark brown,” said Asher. “But it turned blonde following chemotherapy.” His son’s fair hair is one of the few signs that neuroblastoma once threatened his young life.

Arising in immature nerve cells, neuroblastoma is a cancer that affects mostly infants and children. It is one of the deadliest childhood cancers, because it often remains undiagnosed until after the cancer has spread (metastasized) to other parts of the body.

The Asher family has a close relationship with the University of Chicago Medical Center, through Sue Cohn, MD, Director of Clinical Sciences in Pediatric Hematology/Oncology at the Comer Children’s Hospital. Dr. Cohn is one of the world’s foremost experts in neuroblastoma, and she is a leading researcher and a principal member of national pediatric cooperative clinical research groups.

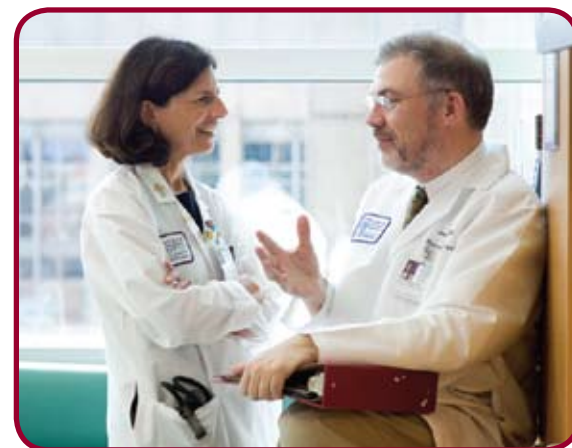
“Sue is a selfless, tremendous person, and, like many of the physicians at the University, she is remarkably approachable,” said Asher.

Asher and his wife Elaine are thankful to Dr. Cohn and other healthcare professionals who helped their son overcome neuroblastoma, and they remain committed to the search for a cure and to helping other families face this challenge. Ray is the president of Little Heroes Pediatric Cancer Research Foundation, a non-profit, volunteer organization that raises money and awareness in the battle against neuroblastoma and provides a resource for families facing this disease.

Founded in 1997 in honor of Steven Newkirk who died from the cancer at 7 years of age, Little Heroes has raised almost \$1.5 million in support of pediatric cancer research. The Foundation has recently committed a \$410,000 gift to the University of Chicago Medical Center, a significant portion of the funds they have raised since 1997. This essential gift will enable Dr. Cohn and her team to approach neuroblastoma from many more angles, in both basic research and clinical research.

“Little Heroes” has enlisted a number of corporate sponsors to support their fundraising activities, such as Comcast and the Chicago Wolves and Blackhawks hockey teams. They hope to establish a long-term relationship with the National Hockey League.

Through the support of Little Heroes board member and “Stand Up to Cancer” liaison Michelle McBride, the national campaign featured the Foundation on its September 5 national telecast, which opened with scenes from the opening of a July 21 Chicago White Sox game. Two additional board members, Kim Green and Jake Marzouk, appeared



Ray Asher and other parents of neuroblastoma patients direct the Little Heroes Pediatric Cancer Research Foundation to support researchers like Sue Cohn, MD, Director of Clinical Research in Pediatric Hematology/Oncology at the Comer Children’s Hospital, and John Cunningham, MD, Chief, Section of Pediatric Hematology/ Oncology.

Continued on back page

Innovative Partnership Brings New Services to Patients

The UCCRC, the Medical Center, and Gilda's Club Chicago have announced a new partnership to bring a wide-range of services to oncology patients.

Gilda's Club Chicago is a support community for men, women and children living with cancer, as well as for their families and friends. It is a free meeting place where people living with cancer join together to build social and emotional support. The organization is located at 537 North Wells Street in Chicago.

"Like our association with the American Cancer Society, our new partnership with Gilda's Club will bring benefits to our cancer patients that will help them enjoy richer, fuller lives and strengthen their resolve in the face of malignancy," said Michelle M. Le Beau, PhD, Director of the UCCRC. "We are pleased that this remarkable organization is supporting our efforts to provide patients with the medical, social, and psychological services that address all of their needs."

Gilda's Club staff members come every Wednesday from 11 AM to 2 PM to the 4th floor atrium of the Medical Center's Duchossois Center for Advanced Medicine. They provide support/networking groups, facilitated by a licensed mental health professional; healing arts and movement workshops such as yoga, tai chi and art classes; and various educational programs, lectures, workshops and social events.

"Gilda's Club Chicago is honored to be in partnership with the UCCRC and the Medical Center in supporting those diagnosed with cancer, as well as their family and friends," said Gilda's Club Chicago CEO LauraJane Hyde. Our shared commitment to the complete care of people living with cancer provides us with the opportunity to create something new within this world-class medical center."

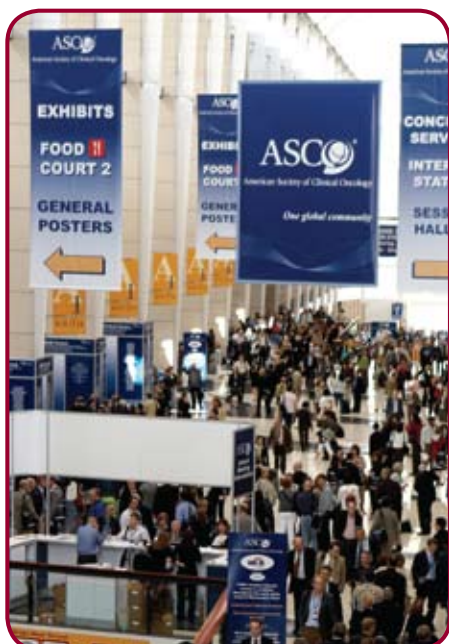
Gilda's Club was founded by the husband and friends of comedienne Gilda Radner who died of ovarian cancer in 1989.

UCCRC Members Take Center Stage as ASCO Comes to Chicago

University of Chicago Cancer Research Center members played key roles at the 44th Annual Meeting of the American Society of Clinical Oncology (ASCO) held in Chicago from May 30 to June 3. ASCO is the world's leading professional organization representing physicians who treat cancer, and its annual meeting attracted more than 34,000 specialists from around the world to discuss the latest advances in cancer care, treatment, prevention and survivorship. Scores of UCCRC members made presentations on groundbreaking research.

Richard L. Schilsky, MD, took office as ASCO President at the conclusion of the meeting. He has announced that "Personalizing cancer care" would be the coming year's ASCO theme (see sidebar) and the focus of the 2009 annual meeting in Orlando, Florida, next spring.

One of ASCO's most prestigious honors went to Everett E. Vokes, MD, who was one of two winners of the Translational Research Professorship. The Professorship provides \$100,000 per year for five years. ASCO developed the award to recognize "oncologists who are dedicated to bringing advances in basic sciences into the clinic and to mentor other translational researchers." Translational research focuses on bridging the divide separating the laboratory and the clinic. UCCRC translational researchers use the discoveries of basic scientists to create new ways to diagnose and treat cancer.



The American Society of Clinical Oncology attracted 34,000 cancer experts to the McCormick Place in Chicago.

According to Dr. Vokes, translational research is flourishing because new technologies are enabling scientists to explore underlying tumor biology, understand the dynamics of carcinogenesis, and identify the molecular targets susceptible to novel therapies. Dr. Vokes has played a key role in the evolution of translational research at the UCCRC, which is gaining worldwide renown for this important form of research.

Richard L. Schilsky, MD, began his term as President of the American Society of Clinical Oncology (ASCO) with great optimism and excitement about the future of cancer prevention, diagnosis, and treatment.

He attributes his enthusiasm, in part, to the remarkable progress he has seen since he began his career in medical oncology three decades ago. The sight of a patient eating a sandwich while receiving the drug Cisplatin intravenously was a vivid reminder for Dr. Schilsky of the extraordinary advances made in recent years. Not too long ago, treatment with Cisplatin caused almost constant nausea and vomiting. Today, we have learned how to mitigate or eliminate some of the harshest side effects of cancer treatment. The nation's 5-year survival rate for all cancers combined has doubled in the last 40 years, in part, because cancer researchers have developed therapies that are safer and more effective.

According to Dr. Schilsky, we can expect the pace of discovery to accelerate as researchers develop new therapies targeted at meeting the unique needs of the individual. The era of customized cancer care is almost upon us, and Dr. Schilsky has made personalized medicine his ASCO theme.

"We are discovering how to identify the therapy most suited for a patient's particular genetic makeup," said Schilsky. "This approach is more effective, safer, and less costly. A drug that is very useful for one patient may be totally ineffective for another. One patient may experience no harmful side effects from a particular drug, while the same therapy might cause another patient to become dreadfully ill. We are committed to discovering the tools physicians need to make the first choice the best choice."

Dr. Schilsky also points out that personalized medicine will create new challenges. Cancer is a remarkably diverse disease, and scientists have not plumbed the depths of this complexity. As scientists discover more about cancer, they reveal new complexities and identify new cancer sub-groups, which have their own characteristics, and treatment. The September 4 issue of *Science* reported that there are often scores of genetic mutations in individual tumors. In an analysis of tumors in pancreatic cancer and brain cancer patients, researchers found the pancreatic tumors carried an average of 63 mutations and one type of brain cancer tumor had an average of 47 DNA mutations.

"Cancer research must become more global, because we are focusing on more specific and rarer types of different cancers," said Dr. Schilsky. "This means fewer patients available for clinical trials and demands more human and technological resources."

These new challenges, however, do not dampen Dr. Schilsky's passion for cancer research. "Oncology is in its infancy; it was not a board-certified specialty until the mid 1960s," he emphasized. "Considering how much we have already accomplished, it is exciting to envision how far we will go in the years to come."

Members News and Notes

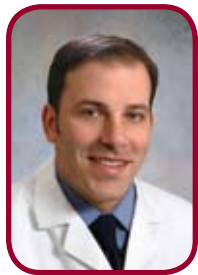
NIA awards Training Grant to Meltzer and Dale



The National Institute on Aging has awarded UCCRC members David Meltzer, MD, PhD, (left) and William Dale, MD, PhD, (right) along with their colleagues Sam Sisodia, PhD and Vineet Arora, MD, MPH, a T-35 training grant. The grant

supported nine students conducting aging-related research; collectively these grants bring the number of NIH-funded student positions in the Pritzker School of Medicine to 54.

School of Medicine Recognizes Roggin and Jaskowiak



The Pritzker School of Medicine recently honored Kevin Roggin, MD, and Nora Jaskowiak, MD. The Gold Humanism Society presented Dr. Roggin with the annual Leonard Tow Humanism in Medicine Faculty Award, which recognizes the faculty member

who most clearly exemplifies “excellence in clinical care, leadership, compassion and dedication to service.” Jaskowiak was one of two faculty members inducted into the University of Chicago chapter of Alpha Omega Alpha, the national medical honor society. Faculty election to the society pays tribute to demonstrated commitment to scholarly excellence and medical education.

AACI Elects Le Beau to Board of Directors

The membership of the Association of American Cancer Institutes (AACI) has elected Michelle M. Le Beau, PhD to the association’s board of directors. Dr. Le Beau has been Director of the UCCRC since April 2004. AACI is comprised of 92 of the leading cancer centers in the United States. AACI’s membership roster includes National Cancer Institute-designated centers and academic-based cancer research programs that receive NCI support.

Rowley Receives Honorary Degree from Harvard University

Janet Rowley, MD, received an honorary degree from Harvard University on June 5, 2008. She shared the spotlight with Senator Edward M. Kennedy, J. K. Rowling (author of the Harry Potter series of books), and eight other recipients.

Lussier Chairs AMIA Program Committee



The American Medical Informatics Association (AMIA) has selected Yves Lussier, MD, to Chair the Scientific Program Committee for its March 15-17, 2009 Summit on Translational Bioinformatics. Held in affiliation with the International Society for Computational Biology (ISCB), the Summit will showcase the use of informatics to enhance translational biomedical

research and the synergy between the medical informatics and bioinformatics communities.

Radiology Team Wins Cum Laude for Poster

Robert Nishikawa, PhD, Ingrid Reiser, PhD, and graduate student Beverly Lau won the Cum Laude poster award in the Physics of Medical Imaging at the Society of Photographic Instrumentation Engineers (SPIE) Medical Imaging Conference. The annual conference is the premier technical meeting on medical imaging. The poster was entitled: “Microcalcification detectability in tomosynthesis.”

Dean Madara Appoints Olopade to New Position

James L. Madara, MD, Dean of the Biological Sciences Division, and CEO of the Medical Center, has appointed Olufunmilayo (Funmi) Olopade, MBBS, FACP, to the newly created position of Associate Dean for Global Health, effective July 1, 2008. According to Dean Madara, “Global Health is an area of expanding opportunity, and it is therefore timely that the BSD provides a coordinating and advisory function to the many faculty members who have developed well-respected independent research programs and to our many students who voice an increasing interest in this growing field of study.”

Alinea Event Recognizes Superior Treatment Team



Chef Grant Achatz (left) chats with guests at the event at his Alinea restaurant, which he sponsored to support the excellent head and neck cancer program led by Everett Vokes, MD (right).

On August 5, world famous chef Grant Achatz and his staff at Alinea, *Gourmet* magazine’s “Best Restaurant in America in 2006”, hosted an extraordinary fundraiser in support of the University of Chicago’s head and neck cancer program. Achatz, a head and neck cancer survivor, has received top honors from the James Beard Foundation, placing him among the very small elite of the world’s culinary artists.

The event raised \$105,000 and was held during Alinea’s summer hiatus. Over 40 hardworking staff donated their time and talents that evening to demonstrate their gratitude to Achatz and the University of Chicago for saving his life.

The spring issue of *Pathways* featured Achatz and his battle against cancer of the tongue, which threatened his career as well as his life. When he discovered he had oral cancer, Achatz consulted with the best oncologists in the nation, all of whom recommended potential career-ending surgery, except for UCCRC Deputy Director Everett Vokes, MD. Achatz chose the team of Vokes, Elizabeth Blair, MD, Ezra Cohen, MD, Daniel Haraf, MD, and their colleagues to



Chef Grant Achatz (foreground right) and his staff at his world-class Alinea busily prepare a fabulous meal to raise funds for head and neck cancer research.

treat his malignancy. The team used an innovative technique combining radiation and chemotherapy to place the cancer in complete remission.

A Message from the Executive Director of the Foundation



This is an ideal time to celebrate past successes and envision new ones. Years of effort, planning, and innovation have resulted in our designation as a comprehensive cancer center. We passed a very rigorous and thorough evaluation with distinction, and have established a solid platform from which to launch new initiatives to improve cancer prevention, diagnosis, treatment, survivorship, outreach, and education.

All of our members and staff are proud of these achievements. However, we are very mindful and appreciative of the essential roles played by the Foundation and our donors. More than four years ago, we developed a strategy to transform the UCCRC, expand its programs, and establish a new level of excellence. Our supporters embraced this ambitious endeavor from the very beginning, providing astute counsel, communicating our mission to the community, and raising invaluable resources.

As I have said many times before, we leverage our contributors' contributions to initiate innovative programs and obtain additional funding from the federal government and other organizations. Of course, their contributions and their guidance were especially vital during this period of renewal and reform. We could not have reached our goal without the wholehearted participation of our most effective and enthusiastic allies. I want to thank them for their commitment and their generosity on behalf of our members, our staff, and, most of all, our patients.

Our collaboration has resulted in a new structure, new commitments, and new expectations. We have the will and the resources to bring cancer under control. The foundation is complete; it is time to build a new future together.

With great appreciation,

Mary Ellen Connellan

Executive Director, University of Chicago Cancer Research Foundation

Research Highlights

Kevin White: New Breast Cancer Marker



Kevin White, PhD, Director of the Institute for Genomics and Systems Biology, reported the discovery of a new protein associated with breast cancer prognosis in the April 15th issue of *Molecular Systems Biology*. Dr. White and his colleagues used an integrated systems biology approach to identify proteins associated with breast cancer prognosis in the complex pathways that turn genes on and off.

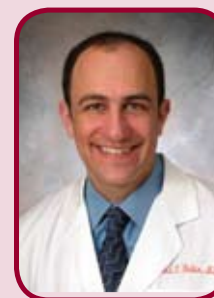
Dr. White's team examined cellular pathways regulated by estrogens to better understand the process by which breast cancers progress to forms resistant to hormone-based therapies. The group found that H2A.Z, a protein never before associated with cancer, was related with breast cancer metastasis and shorter survival. Specifically, they found that estrogen and estrogen-induced MYC (a protein known to be involved in many cancers) could work together to increase the levels of H2A.Z in breast cancer cells, and increased levels of H2A.Z were associated with metastasis of the cancer and shorter patient survival. The authors believe that this protein may represent a marker that physicians can use to identify patients who may need more aggressive treatment. The discovery may also provide a new avenue for developing new cancer therapies.

Chin-Tu Chen and Chien-Min Kao: International Collaboration to Improve PET Technology

Chin-Tu Chen, PhD, and Chien-Min Kao, PhD, are collaborating with a team of researchers in both the Biological Sciences and Physical Sciences Divisions here at the University of Chicago, Argonne National Laboratory, Fermi National Accelerator Laboratory, Lawrence Berkeley National Laboratory, the Stanford Linear Accelerator, the University of Hawaii, and the French Atomic Energy Commission to develop improved positron emission tomography (PET) technology. The group is interested in improving the resolution of PET scans such that cancers are detected when they are smaller and more treatable.

The researchers are pooling their resources and expertise to improve the resolution of "time-of-flight" PET. Time-of-flight PET has the capability of measuring where the signals generated by the radioactive tracer administered to patients during a PET scan go, as well as the time they take to reach the detectors. The combination of these measures allows for the generation of more precise images, however, Drs. Chen and Kao believe these images can be improved even further. The group is testing a variety of detector configurations in an effort to improve the resolution of this technology and cut the amount of computer processing required to generate an accurate image. Not only will these advances improve the detection of cancers, but they will reduce patient scan times and radiation dose, and cut the manufacturing costs for PET equipment.

David Rubin: Colorectal and Urological Cancers as Risk Markers for Each Other



David Rubin, MD, and his colleagues recently published a report in the May issue of the *Archives of Internal Medicine* that suggests colorectal and urological cancers may serve as risk markers for each other. While there has been evidence linking these cancers in specific populations, this is the first report of a link in the general population.

The team analyzed data in the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) database to determine if people diagnosed with colorectal cancer were more likely than the general population to be later diagnosed with urological cancer and vice versa. In general, they found that people diagnosed with certain types of colorectal cancer are at an increased risk of developing urological cancers, and people with certain types of urological cancer are at an increased risk of developing colorectal cancer. This association was particularly strong for individuals in both groups who received their initial cancer diagnosis before the fifth decade of life. While more work needs to be done to understand the pathological link between these two types of cancer, the data suggest that the screening guidelines for these cancers should be examined and possibly modified to account for these observations.

Chuan He: Reveals Structure of Protein that Repairs DNA Damage in Cancer Cells

Chuan He, PhD, and his colleagues reported the crystal structure (the 3-dimensional arrangement of the atoms in the molecule) of both the human DNA repair protein ABH2 and the bacterial DNA protein AlkB bound to double-stranded DNA in the April 24th issue of *Nature*. The research group was interested in understanding the exact molecular contacts these molecules make with damaged DNA in an effort to understand the mechanisms of action of this class of proteins.

The researchers were able to grow crystals of both proteins bound to biologically relevant lengths of double-stranded DNA when other groups have failed at the task, because they chemically cross-linked the proteins to the DNA. This increased the stability of the protein/DNA interaction to allow for the growth of crystals that could be analyzed. Understanding how ABH2 works is of significance to cancer research, because the protein is capable of repairing the type of DNA damage induced by a class of chemotherapy agents (alkylating agents) commonly used in treating cancer. Dr. He believes the structural data will not only provide insight into the functioning of ABH2, but that it can be used to develop agents that specifically block ABH2 in cancer cells to enhance the effectiveness of chemotherapy.

Gifts of Hope

Support for Stem Cell Research a Priority for Hecktman Family

Penny Hecktman will never forget the strengths of her first husband who lost his battle with lymphoma just after he turned 30. Toward the end of his illness, Penny's late husband was treated at the University of Chicago Medical Center by John Ultmann, MD, a former Professor of Medicine and founder and first director of the UCCRC.

Dr. Ultmann suggested that he undergo a bone marrow transplant. However, his condition quickly worsened and surgery was no longer an option. "Even after Dr. Ultmann knew he couldn't do anything for my husband, he was still trying really hard to be there for us emotionally and psychologically," she says. "I'll always have very fond memories of how wonderful he was to us."

Those memories and the generosity of her current husband Jeffrey Hecktman, who regularly contributes to a variety of causes, prompted them to donate \$500,000 in support of Chicago's Pediatric Stem Cell Biology program led by John Cunningham, MD, Professor and Section Chief of Hematology/Oncology in Pediatrics and Harinder Singh, PhD, Professor, Molecular Genetics and Cell Biology. Their gift will fund two new recruits who will be named the Hecktman Senior and Junior Fellow respectively. "My former husband was a very brave, courageous person," Penny says. "My husband today is a fine man, dedicated to hard work that not only contributes to the excellent care of his family, but also to the constant aid of others in need. If you put all the pieces together, it just seemed like a nice fit that we help out in that area."



Hecktman family members (left to right) Jeffrey, Hillary, Candace, Valerie and Penny.

Hecktman's daughter Hillary's interest in stem cell biology highly influenced her parents' decision to support the program. A nursing degree student who is contemplating medical school due to her interest in pediatric oncology, Hillary shadowed Dr. Cunningham last year and had an

opportunity to visit with many of his patients. "Hillary's fascination with Dr. Cunningham's work and his realm of research has had a profound affect toward her future in medicine," Penny says. "This is thrilling for Jeff and me because she's really a special person and very gifted in working with people, especially children."

Golf Pro Hits a Hole in One with Support to Cancer Fellowship Program

According to Jack Nicklaus, the key to golf is aiming for "the heart of the hole." You are more likely to sink the putt if you target the center of the cup rather than the hole itself. Striving to meet the highest standards is the surest way to success.



Jeff Sluman & Linda Sluman

Professional golfer Jeff Sluman and Linda Sluman, MD, a former oncologist at the University of Chicago, have always aimed for perfection. With a half dozen PGA tour wins under his belt including the 1988 PGA Championship, Jeff is passionate about the sport that has brought him success both on and off the course, but he is more pleased with Linda's success. "My wife has been out doing the important stuff like trying to better medicine and cure people."

For the past three years, Jeff and Linda have donated a portion of his PGA earnings to the Hematology/Oncology Fellowship Program at the University. Their support of more than \$200,000 has been instrumental in enabling future scientists and physicians to gain broad and practical exposure to clinical problems of cancer as well as in-depth investigative training. "It was a real easy decision," Jeff says. "When you see the dedication of the doctors and their talents at work, it's a terrific thing."

One of the most sought-after fellowship programs in the country, the University's hematology/oncology program receives more than 300 applications a year for only seven openings. Every year, between 18 and 22 fellows are trained. The Program is currently under the direction of Ezra Cohen who recently replaced Olufunmilayo (Funmi) Olopade, MBBS, FACP, who led the Fellowship Program for many years.

"Of the six to eight graduating fellows each year, more than 75 percent go on to become full-time faculty members at major academic centers," Dr. Olopade says. "This figure speaks to the quality of training they have received here and the opportunity for research collaborations."

In the future, the Slumans say they plan to continue supporting the fellowship program because of the joy they receive knowing they're helping others achieve their goals. "I have to give credit to my wife because she's passionate about healthcare and impacting the lives of others."

Little Heroes Continued from page 4



Crowds jammed Cellular field in Chicago to see Lance Armstrong and Elizabeth Edwards kick-off "Stand Up to Cancer Campaign."

with their children, Ryan Green and Brandon Marzouk, on US Cellular Field with Lance Armstrong, bicycle champion and testicular cancer survivor, and breast cancer survivor Elizabeth Edwards, wife of former Senator and Democratic Vice Presidential candidate John Edwards.

Abigail Mendoza also

appeared in the beginning of the telecast, which raised more than \$131 million. Abigail's mother Judy has been working hard to raise

awareness of neuroblastoma and other cancers affecting primarily children. In September, Childhood Cancer Awareness Month, Judy and her friends distributed more than 2,000 gold ribbons to raise awareness of childhood cancers.

Ryan and Brandon are neuroblastoma survivors and, along with their "Surfer Dude"

friend, they demonstrate the value of advanced cancer care that is creating brighter futures for parents and children confronting cancer.



Neuroblastoma patient Abigail Mendoza (right) and her sister Amanda get a big hug from Elizabeth Edwards at the inaugural event for "Stand Up to Cancer Campaign."

Visit the Funding Opportunity Database Early and Often

Do not forget to visit the Funding Opportunity section of the UCCRC website regularly to remain apprised of cancer-related research funding opportunities. This comprehensive, searchable database offers UCCRC members a convenient pathway to the latest information. You can access the site from the UCCRC website homepage (<http://uccrc.uchicago.edu/>) or the direct link (http://funding.uccrc.org/funding_opportunity).



On August 20, the UCCRC, the American Cancer Society and the Duchossois family celebrated the fourth anniversary of their partnership, which enabled the remodeling of the Cancer Resource Center and its relocation to a more accessible and convenient location. Originally opened in 1997 by the UCCRC, the Center provides counseling, information and other services to cancer patients and their families. Among the attendees were from (left to right) Steve Derks, ACS CEO, Kim Duchossois, Almarie Wagner, Jim Wagner (lung cancer patient) and Ravi Salgia, MD, PhD, member of the Board of Directors of the Illinois chapter of ACS.

Pathways to Discovery

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Editor and Writer

Paul J. Butera, PhD

Staff

Patricia Geiger

Design and Printing

Pixel Print Graphics

University of Chicago Cancer Research Center
5841 South Maryland Avenue, MC1140
Chicago, IL 60637
Phone: 773-702-6180 • Fax: 773-702-9311
E-Mail: pbutera@medicine.bsd.uchicago.edu
uccrc.uchicago.edu

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