At the University of Chicago Cancer Research Center, our mission is to understand, cure and prevent each of the scores of diseases we collectively call cancer. We pursue this goal by promoting collaboration among a diverse and dedicated team of outstanding laboratory scientists, caregivers, clinical researchers and trainees. These partnerships help us develop solutions tailored to the complexity of individual cancers and the unique needs of each patient. Our faculty and staff are dedicated to mentoring and inspiring the investigators of tomorrow while providing superior care to the people of today.
feel very privileged to introduce this year’s annual report and to thank you for your dedicated, enthusiastic support. I also want to express my appreciation for your help and kindness throughout my first six months as Director of our groundbreaking organization. It has been extremely challenging to follow in the footsteps of our three previous directors – John E. Ultmann, MD; Richard L. Schilsky, MD, and Nicholas J. Vogelzang, MD – and interim director Everett E. Vokes, MD. I only hope that I can meet the high standards they established.

I am also thankful for the support of my colleagues. We have a talented team of dedicated researchers and clinicians with the expertise to push the boundaries of knowledge and achieve fundamental breakthroughs in the prevention, diagnosis and treatment of cancer. The cancer research community recognizes the pre-eminence of our members who have had remarkable success in obtaining funding. Having grown our funding base for five straight years, it now exceeds $101,000,000.

We are doing all we can to make our extraordinary group of professionals even stronger. Our aggressive recruitment campaign is proving successful, in part, because of the generous support of our donors. You can be sure that we will remain at the forefront of cancer research as the pace of scientific discovery accelerates and the number of medical breakthroughs multiplies.

We designed this year’s annual report to give you a sense of the significant progress being made and the electrifying opportunities that lie ahead. Consequently, we have included a brief overview of some of the ways we are “seeking cancer cures on all fronts.” Unfortunately, we could not include all the highlights of this year’s research. A complete accounting would be far too long for this document; thus, we have provided only a few examples of the many excellent efforts underway.

The report also surveys the many activities of the University of Chicago Cancer Research Foundation and the participation of other donors and groups. As our Foundation President Ruth Ann McGuinnis explains, philanthropy provides the seed funding necessary for obtaining additional funding for truly revolutionary research. You enable us to engage in research that will catalyze the discoveries of tomorrow.

Thus, I hope you will read this document with great pride knowing the vital role you play in making this progress possible. You are the core group of supporters who help us meet and overcome tough challenges, and we will be looking for you to come with us as we move forward into a future of enormous promise. The opportunities are there. We intend to pursue them vigorously, and, with your contributions and counsel, we will succeed.

Thank you for your support, your spirit and your sacrifices.

Respectfully,

Michelle M. Le Beau, PhD
Director,
The University of Chicago Cancer Research Center
This is a time of extraordinary promise in medical science, and the University of Chicago Cancer Research Foundation is delighted to play a supporting role in the scientific revolution that is transforming cancer care and prevention. At the University of Chicago Cancer Research Center, the pace of discovery has quickened, and years of diligent, visionary research are culminating in remarkable discoveries that offer hope to cancer victims and their families.

As members of the Foundation, we are investors in innovation. We provide the Center with funding that has a special value because it supports the preliminary research required to obtain financing from other sources. In a sense, we raise the venture capital that gives scientists and clinicians the freedom to boldly pursue their most promising insights. By leveraging our contributions, the Center is able to create pioneering therapies and bring their enormous benefits to patients and communities.

I am pleased to say that the Foundation raised $1,764,672 in funding in Fiscal Year 2003-2004, exceeding last year’s record total by more than $180,000 and the previous year’s by almost $300,000. That is a remarkable achievement, and we all owe a debt of gratitude to the Foundation’s dedicated members and other generous donors.

The Foundation has been able to make significant progress even in difficult economic times, in part, because it can point to a continuing tradition of research success. You can be sure that the breakthroughs of the past year will facilitate our efforts in the decades to come. Our confidence in the future is unshakeable.

Under the dynamic leadership of its new Director, Michelle M. Le Beau, PhD, the Center has developed a comprehensive strategy designed to encourage greater collaboration among researchers, attract new talent to the University of Chicago, and provide its members with new assets to support their vital work. Dr. Le Beau has been a Center member for more than two decades, a program leader for 13 years, and has chaired the Committee on Cancer Biology for the last four years. The remarkable talents she brings to this position will serve her well for this latest and most challenging phase in her career. We congratulate Dr. Le Beau and pledge our unyielding support for her visionary strategy to enhance the Center. Whether our contributions are used to recruit faculty or to equip labs in the new research facility, you can be sure that we will play an important role in implementing her plan. Together, we will help Dr. Le Beau and her team take the Center to the next level.

I encourage you to read this annual report carefully. Although it provides only a small sampling of this year’s advances in fundamental science and clinical research, I am sure it will fill you with great expectations for cancer prevention, diagnosis, and treatment. Your contributions and commitment justify these high hopes. I thank each and every one of you for your generous participation in our essential mission.

Sincerely,

Ruth Ann McGuinnis
President
The University of Chicago
Cancer Research Foundation
In the last 15 years, we have learned more about the scores of diseases that we collectively call cancer than in the preceding 4,000. This enormous leap in knowledge has deepened our understanding of the complexity of these diseases and underscored the importance of developing a broad range of strategies and solutions to prevent, diagnose, and treat them.

At the University of Chicago Cancer Research Center (UCCRC), we attack these maladies on all fronts. Our scientists and clinicians seek cancer cures in the lab, the clinic, and the community.

In the lab, scientists study these diseases at the molecular level to evaluate how a minute variation in a single chromosome or gene can trigger a process leading to abnormal, devastating cell growth.

In the clinic, researchers apply the knowledge discovered in the lab to create and test promising new treatments and procedures. They bring patients new hope as they analyze novel therapies for effectiveness and to determine optimal dosages.

In the community, investigators implement new approaches to prevention, teach state-of-the-art diagnostics to local physicians, and strive to eliminate health disparities separating one ethnic or social group from the rest of the population.

Tradition, Teamwork and Translation

The UCCRC can pursue this comprehensive approach successfully, because it has the intellectual and technical resources to excel in each of the three arenas. Moreover, its members share a common commitment to build on the University of Chicago’s tradition of excellence, leverage the power of teamwork, and translate fundamental scientific discoveries into practical applications designed to enhance patient care.

A Tradition of Excellence

For more than 100 years, University of Chicago scientists and physicians have consistently pushed the boundaries of knowledge and transformed cancer care and prevention. In fact, their seminal discoveries helped enable the development and introduction of the majority of the cancer treatments we use today. We can trace the beginnings of chemotherapy, hormonal therapy, gene therapy and bone marrow transplantation to the University of Chicago.

These discoveries earned worldwide recognition for the University. Charles B. Huggins, MD, for example, received the 1966 Nobel Prize for Physiology and Medicine for his fundamental work in hormonal therapy. Dr. Janet Rowley’s groundbreaking research, which established the links between genetics and malignancy, earned her a National Medal of Science and the 1998 Lasker Award for Clinical Medical Research (informally known as the “American Nobel prize”). Dr. Rowley is a UCCRC member and the Blum-Riese Distinguished Service Professor of Medicine.
Elwood Jensen, PhD, the Charles B. Huggins Distinguished Service Professor Emeritus in the Ben May Institute for Cancer Research, won the 2004 Lasker Award for Basic Medical Research as one of the three scientists whose discoveries “revolutionized the fields of endocrinology and metabolism,” according to the award citation. Dr. Jensen’s work enhanced the treatment and prevention of breast cancer. The fact that Dr. Jensen and Dr. Huggins both successfully explored the potential of hormone therapy using different approaches underscores the value of a research community that encompasses a diversity of perspectives.

This tradition of excellence is as vibrant today as it has ever been. The UCCRC has a global reputation for superior research in advanced radiation treatments, excels in the development of novel anticancer drugs, brings the enormous potential of advanced imaging to life, and leads the way in the emerging field of pharmacogenomics.

**The Spirit of Teamwork**

Pharmacogenomics combines the disciplines of medicine, genetics and pharmacology to study how a person’s genetic makeup affects his or her body’s response to drugs. This new field offers the promise of developing therapies that account for genetic diversity. Pharmacogenomics also provides an example of how the cooperative interaction of researchers from diverse fields generate productive new approaches for attacking cancer.

Collaboration is fundamental to the mission of our University. The essence of its scholarly tradition is, in the words of University President Don Michael Randel, the “great conversation” that cuts “across traditional disciplines [and] creates not only new knowledge but whole new fields of knowledge.”

The University’s founders embraced collaboration as a core value and designed the campus to facilitate integrated scholarship. Although the institution is among a handful of the world’s top research universities, it is still small enough to promote ongoing interaction among a community of renowned scholars. Working side-by-side, doctors, medical researchers, chemists, physicists, mathematicians, computer experts and environmental and social scientists share expertise, ideas and insights in the search for cancer cures.

The design of the evolving campus continues to reflect this commitment to interdisciplinary research. When it opens next year, the new Interdivisional Research Building (IRB) will bring biologists, physicists and chemists together at one location. The IRB will also be the new home of the Ben May Institute. Construction will begin soon on a second, interdisciplinary research facility: the New Research Building. The NRB will house the Center and provide us with excellent opportunities to interact with colleagues throughout the University. With the Ben May Institute in the IRB, the two adjacent buildings will become the nexus of cancer research. In addition to fostering cross-disciplinary cooperation, these state-of-the-art facilities will strengthen our recruitment efforts. Of course, we need to raise significant new funding to make this happen.

**Translation: Bench to Bedside and Bedside to Bench**

This power of proximity also plays a role in reinforcing another of the UCCRC’s greatest strengths: the translation of lab breakthroughs into practical treatments.

The University of Chicago is one of a handful of research universities with the combination of resources and personnel required to follow the process of drug discovery through the complete spectrum of clinical trials. The Center and the hospitals work together to bridge basic and clinical research and deliver the latest therapies to the bedside at a much faster rate. Our programs are genuinely “Bedside to Laboratory” and “Laboratory to Bedside.”

We are working just as diligently to bring the advantages of groundbreaking scholarship to the community. The Cancer Risk Clinic, for example, works in local neighborhoods to identify families and individuals with an increased threat of malignancy. The Clinic’s teams work with the patients developing strategies to lower risk and to help them deal with the medical, psychological and social impacts of their conditions.

**The Lab, the Clinic, the Community**

From the physicist studying the dynamics of three-dimensional imaging to the epidemiologist evaluating the recurrence of breast cancer in a single neighborhood, University of Chicago researchers are developing new tactics to succeed in the war against cancer in all its forms. The members of the UCCRC understand that complex problems demand multifaceted solutions and they aggressively strive to unravel the intricacies of these diseases. They are attacking cancer’s many manifestations from all angles, and they are making significant headway in the lab, the clinic and the community.
In the lab, our scientists explore the infinitesimal world of a single cell to understand the fundamental dynamics of cancer and to design innovative ways to annihilate malignant cells while leaving healthy ones untouched.

As they probe the chinks in cancer’s defenses, UCCRC researchers are developing an arsenal of new procedures for attacking these diseases from all directions. For example, they explore interactions between the immune system and tumors with the expectation of enlisting the body’s own resources in the fight against malignancy.

**Leveraging the Body’s Own Defenses**

Albert Bendelac, MD, PhD, is studying a family of molecules that regulate the immune system’s attack against cancer. His discoveries promote the development of a body of exciting new cancer treatments, including vaccines and adjuvants.

Hans Schreiber, MD, PhD, investigates the fundamental mechanisms governing the immune system. One of his objectives is to determine why some cancer cells are able to elude and survive the immune system’s dragnet and continue to disseminate malignancy. Solving this problem would be an important milestone in the creation of immunotherapies that could seek and destroy cancer cells that have already spread throughout the body.

**Killing Cancer from the Inside Out**

UCCRC scientists are also probing another potential weak point in cancer’s defenses: angiogenesis. Angiogenesis is the process with which tumors induce existing blood vessels to sprout new capillaries, thereby obtaining the blood they need to grow and thrive. By inhibiting vessel growth, therapies that block angiogenesis deny tumors their vital nourishment, literally killing cancer from the inside out. Dr. Walter L. Stadler, MD, and Gregory L. Karczmar, PhD, have formed a unique collaboration using advanced imaging to investigate antiangiogenic drugs in the treatment of prostate and renal cancer. Their goal is to find new anti-tumor agents that function by inhibiting blood flow to the tumor as well as identify new magnetic resonance imaging (MRI) techniques for predicting which patients are most likely to benefit from such therapy.

Developing effective anti-angiogenic therapies, however, is not a clear-cut task. Tumors have many mechanisms that they call upon in their relentless pursuit of growth through angiogenesis. A drug may successfully inhibit one mechanism only to have another jump into the breach to initiate the process of producing new blood flow.

Mark W. Lingen, DDS, PhD, employs traditional and state-of-the-art applications of biology, genetics, biochemistry, and molecular biology to deal with the complexity of this challenge. He and his team are searching for anti-angiogenic agents that can work in concert to effectively attack all the direct and indirect mechanisms involved. He has discovered that evaluating the genetic fingerprint of a tumor (genetic profiling) is a useful tool for determining which agents are able to combine forces in the fight against angiogenesis. Dr. Lingen’s research is essential to the design of comprehensive attacks that can stop angiogenesis in its tracks.
The Genetics of Cancer

Advances in genetics – from the discovery of the chemical structure of DNA to the mapping of the human genome – have had momentous impacts on cancer research. Cancer, after all, begins with genetic abnormalities that destabilize the body’s controls regulating cell growth and division. Armed with technologies that allow them to study cells at the molecular level, researchers can now pinpoint the changes to genes or chromosomes that are the sources of malignancies.

John D. Crispino, PhD, of the Ben May Institute for Cancer Research, has discovered a genetic mutation that occurs in almost all cases of a form of leukemia that affects young patients with Down Syndrome. It also appears in its earliest phase in patients who have a disorder that precedes the leukemia. This insight may someday enable us to intervene and pre-treat this cancer.

Michelle M. Le Beau, PhD, identifies recurring chromosomal abnormalities in patients with cancer and correlates them with physical and clinical aspects of their diseases. This information is used to determine the most appropriate drugs for treating particular tumors and to better assess the unique hazards faced by individual patients. Dr. Le Beau’s current research emphasis is secondary leukemia, which is an unfortunate side effect of some cancer treatments. By delineating the etiology (or molecular basis) of the disease, she hopes to develop procedures to identify patients at greater risks for contracting the disease and to minimize its hazards.
**Molecular Mechanisms and Cancer**

Anning Lin, PhD, Marsha Rosner, PhD, and their laboratories are working together to leverage the wealth of new information enriching our understanding of the underlying molecular mechanisms of cells. They are examining new ways to initiate natural processes that attack cancer. For example, their collaboration is responsible for exploring novel strategies for promoting apoptosis in tumor cells. Apoptosis is genetically programmed cell death, which is the normal physiological process that eliminates DNA-damaged, superfluous, or unwanted cells. Both Dr. Lin and Dr. Rosner are members of the Ben May Institute, and they are enhancing the Institute's superior reputation for basic scientific research that is fundamental to our efforts to understand and treat cancer.

Geoffrey L. Greene, PhD, also contributes to the Ben May Institute’s tradition of excellence in scientific research. He continues to make breakthroughs in our understanding of how female steroid hormones regulate cellular growth in hormone-responsive tissues and cancers. This research is helping us not only understand the processes that initiate breast cancer, but also to develop novel drugs that can be used to treat and prevent breast and uterine cancers. Some of these drugs might have application in hormone replacement therapy in postmenopausal women.

**Modulating Gene Repair**

Another promising research subject is the mechanics of DNA repair. Healthy cells can repair the damage to DNA molecules, which sometimes occurs during the normal lifespan of a cell. DNA repair helps prevent the inception of cancer because it mends mutations that, if not restored, could lead to the disease. Unfortunately, this process can protect cancer cells themselves against the very treatments designed to kill them. An example is radiation therapy, which works by attacking the DNA in tumor cells. DNA repair can reverse the benefits of these therapies. Clearly, there are times in the fight against these diseases when we want to facilitate DNA repair and other times when we want to inhibit it.

This is why Douglas Bishop, PhD, is intent on expanding our understanding of this process. He recently setup a new method for studying BRCA1, a gene that plays a fundamental role in DNA repair, thus preventing cancer. BRCA1 is best known for its causative role in familial breast cancer. The normal BRCA1 protein helps repair DNA damage and avert cancer. People who inherit defective copies of this gene have a high risk of breast cancer and other malignancies. Dr. Bishop's research into this protein and its role in DNA repair has significant implications for cancer treatment and diagnosis.

Chuan He, PhD, leads a research program that spans a broad range of chemistry and chemical biology. He is probing the mechanism of DNA repair in the search for new DNA repair proteins that initially recognize damage. M. Eileen Dolan, PhD, has also focused on DNA damage and repair. She and her lab are developing modulators of chemotherapy that are being tested clinically as a means to inhibit DNA repair and thus enhance the effectiveness of certain chemotherapy drugs. A chief emphasis of her work has been on the decreasing toxicities associated with chemotherapy. Drs. He and Dolan have joined forces to design better modulators based on the chemical reactions that occur in cells when DNA is damaged and repaired.

Her objective is to identify the genes that can determine an individual’s susceptibility to DNA damaging agents. She is also evaluating how genetic variation influences the effectiveness and toxicity of therapies for individual patients. This information is proving to be extremely valuable in determining which therapies to prescribe to specific patients and at what dosages.

**From the Lab to the Clinic**

Dr. Dolan is just one of many researchers at the UCCRC who are expanding our knowledge of cancer and its dynamics. She and her colleagues are making breakthrough discoveries that build the scientific foundations for numerous advances in the prevention, diagnosis and treatment of cancer. Moreover, they are translating their successes from the lab into the clinic. Thus, they are working diligently to enhance patient care while developing cancer cures that are more effective, less harmful, and increasingly precise when attacking malignant tumors.
obel Laureate and Ben May Institute for Cancer Research founder Charles B. Huggins, MD, affirmed a simple message to his students: the battle against cancer begins with discoveries that illuminate why organisms thrive and why they fail. Thus, cancer cures begin in fundamental research that launches clinical research and culminates in superior cancer care. Whether in the lab or the clinic, our scientists and clinicians share a common goal: to transform discovery into therapy.

Consequently, our researchers often have one foot in the lab and one in the clinic. Like Dr. Huggins, they recognize the usefulness of collaborative research that involves scientists and clinicians. As a result, no clear, bright line separates the lab from the clinic.

**Bringing Advanced Therapies to Patients**

Ben May Institute for Cancer Research investigator Thomas F. Gajewski, MD, PhD, and his team, for example, explore ways to control, manipulate and enhance immune responses against cancer. Their findings enable them to develop vaccines and other immune therapies that they first test in mice bearing established tumors. Approaches that reduce tumors in animals become candidates for human testing. Dr. Gajewski and his team have already shown tumor shrinkage in patients with a vaccine against melanoma. They have new vaccines that are being investigated in patients with pancreatic and kidney cancers. This work relies on the collaboration of basic immunology researchers, medical oncologists, surgeons, and pathologists.

Clinical trials provide the means for bringing the benefits of their advanced research directly to the patients who most need them. More than 1,000 patients participate annually in our clinical trials program, which is one of the most comprehensive and sophisticated in the world. We are one of only a handful of institutions with the expertise, resources and capabilities to take oversight responsibility for trials representing all three phases of clinical research. This three-phase process allows for the orderly gathering of information, ensures patient safety, and maximizes therapeutic value.

**A Three-Phase Process**

Phase I studies involve the fewest number of patients. Their purpose is to determine how to administer new drugs and what are the safest, most effective doses. Phase II trials continue to focus on safety and begin the analysis of the effectiveness of innovative therapies. Phase III trials usually enroll numerous patients and involve numerous institutions under the direction of a lead research center. These trials compare experimental drugs, combinations of drugs or surgical procedures with existing therapies to determine if innovations are superior to the current standards.
Ensuring Patient Safety

Research advances are making clinical trials safer and more beneficial for patients. Pharmacogenomics, for example, enables researchers to identify individuals who are most likely to suffer severe adverse reactions from the drug being tested. Our leadership in the study of cancer and genetics is an invaluable asset in ensuring effectiveness of our clinical trials and in protecting participants. Diet, environment, lifestyle and a myriad of other factors determine how individuals respond to cancer drugs, but genetics arguably is the most powerful factor of all. As a drug enters the body, it reacts with many different proteins, producing both therapeutic and harmful effects.

Since genes determine the structure of each protein, minor disparities in a patient's DNA can cause major differences in how his or her proteins react to a drug. That's why a drug can be effective for one person and ineffective for another. It's also the reason that a drug can be perfectly safe for 99 patients but extremely toxic for one.

Understanding Patient Variability

Mark J. Ratain, MD, has set the standard for studying and understanding human variability in responses to drugs. He chairs the Pharmacogenomics of Anticancer Agents Research Group (PAAR) study. This $14-million, four-year study is investigating how genetic differences affect an individual's response to cancer drugs. The team begins with human tissue samples to evaluate the diverse ways our bodies absorb, distribute, break down and eliminate medications. The most promising compounds are then tested in human trials. The ultimate goal of Dr. Ratain's research is to help tailor medicines to a person's unique genetic make-up, which will ultimately make medicines safer and more effective for everyone.

Dr. Ratain is also the lead investigator on a Phase II trial of a new drug called BAY 43-9006 that has demonstrated significant short-term benefits for patients with advanced kidney cancer. Less than 15 percent of patients with metastatic kidney cancer respond to standard immunotherapy. In the trial, 42 percent of patients had their tumors shrink at least 25 percent within the first 12 weeks.

National Cooperation

As chairman of the Cancer and Leukemia Group B (CALGB), Richard L. Schilsky, MD, oversees clinical trials that are delivering results that are equally spectacular. The CALGB is one of ten national clinical cooperative groups conducting Phase III clinical trials.
A recent CALGB study was so successful that the Data Safety Monitoring Board halted the trial early, because it wanted to accelerate delivery of the treatment to all patients with early stage lung cancer. The study, which enrolled 344 patients, found that adjuvant chemotherapy following surgery decreased the risk of dying from lung cancer by 49 percent.

This is a major breakthrough in the treatment of a particularly deadly cancer that has been resistant to treatment. According to the American Cancer Society, lung cancer is, by far, the most common fatal cancer in men and women. It accounts for 32% of male cancer deaths and 25% of women's deaths from malignancy. Wendy Stock, MD, leads the correlative leukemia studies conducted by CALGB. She studies the disease at the molecular level to evaluate treatment and to determine if any traces remain.

Finding the Best Combinations

Everett E. Vokes, MD, is the principal investigator in a cooperative agreement with the National Cancer Institute (NCI). (A cooperative agreement is a very specific funding mechanism that involves extensive programmatic involvement between the recipient and the NCI.) Only seven other scientists in the nation have this distinction for Phase II trials. Dr. Vokes’ research focuses on malignancies of the chest including lung, chest and esophagus, as well as advanced head and neck cancer. His team is proving the value of therapies that use chemotherapy in combination with radiation. This approach has proven successful in treating cancers that are resistant to more traditional therapies.

Ralph R. Weichselbaum, MD, and his team are exploring the use of radiation in combination with other treatments. Dr. Weichselbaum is using a radiation-activated gene to harness the power of a cancer killing protein called tumor necrosis factor (TNF). The body naturally produces TNF, but it is often lethal when introduced as a therapeutic agent. When attached to the radiation-activated gene, TNF can be targeted precisely, enabling it to seek and kill tumors without affecting healthy tissue. This approach has proven its value in treating breast and pancreatic tumors, and trials are underway to test its effectiveness against pancreatic, esophageal, rectal, and head and neck cancer.

Hedy L. Kindler, MD, is evaluating various combinations of drugs in the battle against pancreatic cancer, a particularly deadly form of cancer. One successful trial investigated the use of an experimental medication, bevacuzimab, in conjunction with a standard chemotherapy drug, gemcitabine. (Bevacuzimab inhibits the growth of blood vessels, which supply the tumors with nutrients.) The striking results of the Phase II trial set the stage for a randomized Phase III trial comparing the effectiveness of the bevacuzimab-gemcitabine combination with gemcitabine alone. It also led to the initiation of several Phase II trials evaluating bevacuzimab in combination with other agents and radiation.

In the Surgical Theater

The surgical theater is another location where we are developing improved cancer treatments. Arieh Shalhav, MD, is employing new robotic systems to remove cancerous prostate glands with less pain, smaller scars, and minimal blood loss. He is using this innovative surgery to increase continence and erectile functional results and shorten recovery time. Patients typically require six weeks of recovery before they can resume normal activities following traditional prostate surgery. The comparable recovery time for robotic surgery is one week.

Dr. Shalhav and his colleagues employ their curiosity and extraordinary expertise to transform scientific discoveries into practical applications. Their efforts in the clinics effectively deliver on the promise of the revolutionary insights made in UCCRC labs.
In the community, we bring our resources and expertise into neighborhoods and engage in community-based research in partnership with local individuals, groups and institutions. Our programs help ensure that all populations benefit from the fruits of our research. They bring clinical, biological, psychological and social scientists together and help them target their efforts in controlling and preventing cancer.

Understanding Population Differences

The Center for Interdisciplinary Health Disparities Research, for example, pursues a collaborative approach to examine population health and to evaluate and eliminate group differences in health. In the first five years, the Center is focusing on understanding population differences in the incidence of and the genetic and environmental factors that contribute to breast cancer in Caucasians, women of African descent living in America and women native to Nigeria.

Sarah Gehlert, PhD, an associate professor at the School of Social Service Administration, where she serves as Deputy Dean for Research, and the Institute for Mind and Biology, leads a diverse team of scientists from the Biological Sciences and Social Sciences Divisions and the School of Social Service Administration. This collaborative approach is creating an integrated, comprehensive analysis of the many factors - social, behavioral, and biological - that are potential causes of the health disparities within diverse communities. UCCRC members lead the four teams and two cores pursuing the specific aims of the research center.

Martha K. McClintock, PhD, and her team are comparing gene regulation in mammary tumors and the ovarian function of socially isolated and group-living rats. They are using an animal model of social regulation of mammary tumor biology developed in her laboratory.

Neighborhood Outreach

In the Center’s first year, Dr. Gehlert’s team conducted community-based focus groups in the 15 neighborhood areas of the South Side that are the focus of the Center’s investigations. Their objectives were to elicit input on breast cancer and its treatment and to explore the suitability of the project’s central constructs and measures with community stakeholders. Suzanne Conzen, MD, and her colleagues are employing rodent models of human breast cancer to investigate the effects of social isolation on the rate of tumor growth, chemotherapy, and chemoprevention effectiveness.

Local and International

In years 2-4 of the project, Olufunmilayo F. Olopade, MBBS, Dr. Gehlert and their colleagues will work with African-American women living in the 15 South Side neighborhoods and women in Ibadan, Nigeria. Since these two groups of women with similar genetics live in very different environments, this comparative analysis will be useful in determining the relative roles of genetics and stress in the early
onset of breast cancer. Dr. Olopade's team will study the molecular characterization of patient samples in these two groups. Dr. Gehlert’s group will examine the influence of social and behavioral factors.

The Tissue Core Laboratory led by Thomas N. Krausz, MD, FRCPath, and Maria Tretiakova, MD, PhD, is responsible for analyzing the mammary tissue for the Center. They utilize the extensive experience of the Human Tissue Resource Core of the Department of Pathology. The University of Chicago has more than 10 years of experience with breast cancer tissue collection and examination, having more than 5,000 archived diagnostic cases and over 150 fresh frozen samples. Dr. Gehlert leads the project’s administrative core.

The Cancer Risk Clinic

Dr. Olopade is also the Director of the Cancer Risk Clinic. This diagnostic and preventive care program offers individuals and families the opportunity to assess their likelihood of acquiring cancer. Teams of experts – physicians, social workers, nurses and genetic counselors – work closely with patients and their families assessing risk and developing strategies for prevention.

Community Partnerships

Another way the UCCRC delivers the fruits of its research directly to local communities is through partnerships with health professionals outside the University. Our association, for example, with Little Company of Mary Hospital Cancer Center in Evergreen Park, Illinois, delivers the advantages of a university-based cancer program to the residents of Chicago’s southwest neighborhoods and suburbs. It also provides them with easier access to clinical trials and the promise of investigational therapies.

Sharing expertise and research findings with community physicians is, of course, invaluable in translating discovery into application. As a leader in advanced imaging (see next page), the UCCRC strives to help general radiologists take advantage of the new imaging techniques and computer-assisted diagnosis that are so helpful in the early detection of cancer. That is why physician researchers Gillian Newstead, MB, ChB, FACR, and Robert A. Schmidt, MD, are developing an intensive training program for radiologists, which will enhance their skills in reading magnetic resonance imaging (MRI), mammography, and ultrasound images.

These are just a few of the ways the UCCRC and the University of Chicago are establishing productive links with the surrounding neighborhoods and communities. We are committed to ensuring that the people of the Chicago metropolitan area have access to the state-of-the-art medical care available at one of the world’s premiere research, teaching and medical institutions.
Exploring the Potential of Advanced Imagery

The UCCRC is at the forefront of the radiology revolution that is transforming cancer care. Extraordinary advances in imaging pioneered at the Center are enabling specialists to diagnose cancer in its early, less harmful stages and attack cancerous tumors with greater precision.

For example, Gregory L. Karczmar, PhD, Gillian Newstead, MB, ChB, FACR, and their colleagues are exploring an enhanced form of magnetic resonance imaging (MRI). High spectral and spatial resolution MRI is proving instrumental in the early detection and staging of breast cancer. Dr. Karczmar and Milica Medved, PhD, are pursuing another new technology that will likely prove invaluable in early diagnosis of breast cancer. The scans they have produced using three-dimensional MRI reveal breast tissue with extraordinary clarity.

The UCCRC is also pushing the boundaries of computer-aided diagnosis (CAD). These sophisticated technologies give radiologists a significant advantage in the vital and difficult task of image interpretation. Identifying lung cancers through visual interpretation is very challenging. For this reason, Samuel Armato III, PhD, and Kunio Doi, PhD, are developing automated techniques to identify lung nodules in computerized tomography (CT) scans. (X-ray Tomography produces three-dimensional images of internal structures of the body.)

The UCCRC is pushing the boundaries of computer-aided diagnosis.

Robert M. Nishikawa, PhD, Ingrid Reiser, PhD, Maryellen Giger, PhD, and their colleagues are investigating computerized detection of mass lesions on breast tomosynthesis images. Breast tomosynthesis is a promising new technology that offers a three-dimensional perspective. Conventional mammography, which is two-dimensional, often results in false positives and negatives because overlapping breast tissues can either obscure or mimic cancers.

Dr. Giger, Dr. Nishikawa, Yulei Jiang, PhD, and their colleagues are working with mammographers to translate their multimodality breast imaging workstations to the clinical arena for evaluation. Developing optimal methods for combining computer output from the analysis of multiple images and presenting the information to the radiologist are crucial steps in CAD research.

Drs. Armato and Heber MacMahon, MD, are developing automated methods for comparing multiple chest radiographs. Clinicians often use multiple images of the same patient to identify changes in anatomy and pathology. Drs. Armato and MacMahon are evaluating a technique called temporal subtraction (a procedure for layering images) to accurately integrate serial radiographs and help radiologists identify subtle, but critically significant changes.

Xiaochuan Pan, PhD, and colleagues have made significant contributions to developing high-quality CT images. These new concepts and algorithms facilitate the design of innovative imaging protocols that may have significant clinical implications, e.g., breast imaging, liver imaging, and cardiac imaging.

Our imaging researchers are taking full advantage of new technologies that offer enormous promise in supporting our search for cancer cures. They are using advanced imagery to unravel cancer’s complexity.
The University of Chicago Cancer Research Center thanks those who contributed in 2003-2004 to cancer and cancer-related programs at the University of Chicago.

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The University of Chicago Cancer Research Center thanks those who contributed in 2003-2004 to cancer and cancer-related programs at the University of Chicago.
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Ms. Mary Ellen Reynolds
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| UCCRC Annual Report 2003-2004 | Seeking Cancer CureS On All Fronts |
Boards and Auxiliaries

As this year’s annual report makes clear, the members of the University of Chicago Cancer Research Center are successfully fighting cancer in the lab, the clinic and the community. Among their most valuable allies in these efforts are the University of Chicago Cancer Research Foundation and other supporting boards and auxiliaries. We see the evidence of their participation in state-of-the-art equipment, enhanced hospital and laboratory facilities, fellowships for young scientists, and essential funding for some of our most distinguished researchers. These scientists rely on this essential support because it provides them with the freedom necessary to pursue their most visionary investigations and break new ground.

The next several pages introduce you to these committees and their members and review some of the many ways they have supported cancer research in FY 2004.

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The Women’s Board has become central to the pursuit of the Center’s mission. This year the members exceeded their record successes of past years and provided the Center with a remarkable donation of $625,000. This funding is being used for a variety of purposes.
The Ben May Institute for Cancer Research

Since 1951, the Ben May Institute has advanced cancer research by addressing fundamental issues in biological sciences. As Marsha Rosner, PhD, the Institute's current director, has said, "Every advance in the war against cancer has its origin in basic scientific research. High quality research leads to new treatments and eventually cures." As this report documents in the numerous references to its accomplishments, the Institute sets the standard for excellence.

The Women’s Board has long been a staunch supporter of the Institute. This year, the Board is focusing its contributions in support of an innovative effort to create a core laboratory dedicated to enhancing our drug discovery program. Geoffrey Greene, PhD, is leading the development of this facility. The Women’s Board’s funding is underwriting recruitment of a talented professional to manage this new facility.

Advanced Technology and Resources for the Genetics, Proteomics and the Drug Discovery Continuum

Research has opened a vast new world of scientific discovery. We are searching for solutions in the minute worlds of individual cells, genes, chromosomes and proteins. Such exploration requires instruments and materials of incredible sophistication and precision. In 2004, the Women’s Board enabled the acquisition of resources that support every step of the process, which begins with highly specialized analysis of genes and proteins and culminates in the development of innovative drug therapies.

For example, the Board provided funds for matrix-assisted, laser-desorption-ionization, time-of-flight (MALDI-TOF) mass spectrometry. This complex, innovative technology for protein profiling allows our researchers to compare cancerous and normal tissue and serum samples. The Board’s past support of the Human Tissue Core helps ensure that our researchers have tissue samples and derivatives (i.e. RNA, DNA and proteins) available for study. This year, its contribution is helping staff this facility with a qualified technologist. Thanks to the Board, our scientists also have a new bioreactor that is used to obtain target proteins for research.

Drug screening is at the heart of drug discovery. This process enables researchers to identify the compounds most effective for inhibiting the growth of tumors. This year, the Board supported the purchase of libraries containing 50,000 compounds for study. High performance liquid chromatography (HPLC) is an analytical technique that enables precise quantification of drug levels in plasma, serum and urine samples from patients treated with investigational drugs. By enabling the Center to acquire this advanced technology, the Board has enhanced the Center’s capacities for analyzing new compounds and determining the most effective, least toxic dosages of investigational drugs.

Committee on Cancer Biology

The Board has long been a friend of the Committee on Cancer Biology, which is one of the premier cancer research degree-granting programs in the nation. Private funding from the Women’s Board ensures that Committee is able to attract and educate the most promising students in the world. This year, the Women’s Board is helping in the recruitment of young scholars who will bring fresh perspective and enthusiasm to the pursuit of the Center’s mission.

cGMP Facility

The University of Chicago cGMP (current Good Manufacturing Practice) Core Facility provides investigators with a state-of-the-art facility in which to prepare cellular-based products and drugs for the treatment of cancer patients. This facility must meet daunting standards for quality. In 2004, the Women’s Board provided funding for the recruitment of a top professional to lead a strong quality assurance program. The Food and Drug Administration (FDA) requires that such a program is in place before therapies can be released for patient treatment.

UCCRC AdvanceLink

The Women’s Board has been instrumental in the development of the AdvanceLink information technology system, which is proving invaluable in the management of the voluminous information generated by our clinical trials program. Managing this data is essential to protecting patients, meeting regulatory requirements, and guaranteeing effectiveness. This database allows all researchers and their teams to audit, analyze, and report data more effectively and efficiently. This advanced tool frees them to focus on their patients.
In 2004, the Auxiliary Board provided $90,000 to support three cancer researchers: Mark D. McKee, MD; Karen M. Frank, MD, PhD; and Miriam B. Rodin, MD, PhD.

Dr. McKee is exploring new approaches to immunotherapy. Many studies have focused on developing vaccines that stimulate T cells (a type of white blood cells) to attack tumors. Dr. McKee’s approach skips many of the intermediate steps and is less problematic than the more common method. He uses gene therapy to modify the patient’s own T cells and return them to the body to attack the cancer cells. This more efficient treatment also provides new opportunities to examine how cancer-fighting T cells travel through the body and interact with tumors.

Dr. Frank investigates both the immune system and the mechanisms of cancer development. Her research studies how the immune system creates antibodies to fight infections. This process, managed by white blood cells, breaks DNA and rearranges it in a controlled manner. Leukemia or lymphoma can result if the process fails to rearrange the DNA correctly. She also studies how defects in DNA repair pathways create abnormal genes that can lead to the development of cancer in any organ. Understanding these fundamental cellular mechanisms is the first step in the process of developing more targeted therapeutic strategies.

Dr. Rodin studies the effects of cancer treatments on the memory, attention and thinking faculties of cancer survivors. She and her team also have implemented a clinical database useful in the examination of the health care needs and health outcomes of elderly cancer survivors.

The Associates Board provided $110,000 in funding to support the cGMP facility and mesothelioma research.

Although it is the UCCRF’s newest Board, the Associates Board has already made significant contributions to advance cancer research and has helped the University of Chicago maintain its reputation as a pioneer in the study and treatment of malignant mesothelioma. It has provided funding support for Hedy L. Kindler, MD, Ravi Salgia, MD, PhD, and the cGMP facility, which this report describes on page 22.

The Junior Cancer League

Mrs. Kenneth Rabin, President

The League supports the work of Dr. Melvin L. Griem.

Income

UCCRF Beginning Balance July 1, 2003  $434,984

<table>
<thead>
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<td>Junior Cancer League</td>
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<td>Simon M. Shubitz</td>
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Total Income  $1,764,672

Operating Expenses and Allocations

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Operating Expenses and Allocations $1,822,302

Ending Balance June 30, 2004  $377,354

UCCRC Funding Sources

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<tr>
<td>NSF</td>
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Income

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Operating Expenses and Allocations $1,822,302

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Seeking Cancer Cures
On All Fronts

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