CANCER RESEARCH FOUNDATION

Fall 2003

Sharon Swanson, Editor

The Mission of The Cancer Research Foundation Is To Help Find The Cures For Cancer Through Funding Laboratory and Clinical Research.

Advances in Treatment of Colorectal Cancer

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Significant advances in the treatment of colorectal cancer, announced in just the past few months, hold great promise to improve the survival of patients with this common malignancy. Each year approximately 150,000 Americans are diagnosed with colon and rectal cancer and 57,000 individuals die from this disease. Overall, colorectal cancer is the 3rd most common cancer diagnosed in the U.S. and the 3rd most common cause of cancer death in both men and women. Recent advances in early diagnosis, screening and treatment hold great promise for improving the survival of patients with colorectal cancer. In the area of early diagnosis, new molecular diagnostic tests that can detect colorectal cancer at its earliest stages are in development and may eventually enable physicians to detect the disease when only a few malignant cells have developed in the colon and long before bleeding or other symptoms occur.

Although screening for colorectal cancer has been proven to save lives, many people ignore screening recommendations because of concerns about the discomfort of colonoscopy or other invasive tests necessary to examine the full length of the colon. Virtual colonoscopy now provides an option for screening that is less invasive and may, therefore, be more appealing to individuals, particularly those at low risk of having colon polyps or cancer. Virtual colonoscopy is a CT scan examination of the colon that uses sophisticated computer software to reconstruct a three dimensional image of the interior of the colon and allows radiologists to identify polyps or tumors with a high degree of accuracy. Conventional colonoscopy is still necessary if abnormalities are identified but virtual colonoscopy provides an alternative to the more invasive test as an initial screening examination. The technology for virtual colonoscopy has been developed, in part, by University of Chicago radiologists and the test is available at the medical center.

Perhaps the most exciting information about colorectal cancer has come from several recently reported randomized clinical trials that have clearly demonstrated the value of new therapeutic approaches to this disease. A new chemotherapy drug, oxaliplatin (Eloxatin), used in combination with standard chemotherapy (5-FU and leucovorin) has now been shown to provide superior survival for patients with colorectal cancer that has spread throughout the body. In such cases, the FOLFOX chemotherapy program extends median survival into the range of 18-20 months compared to 14-15 months which was the best that could be achieved until now with other chemotherapy programs. The FOLFOX regimen has also been tested as postoperative

We make a living by what we get, but we **make a life** by what we **give**.

– Winston Churchill

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2002 Cancer Research Foundation Fletcher Scholar:

Factors Regulating Metastatic Growth

Carrie Rinker-Schaeffer, Ph.D.
Associate Professor
Department of Surgery
University of Chicago Medical Center

In 1988, the Cancer Research Foundation received $710,265. from the estate of Eugene and Dorothy S. Fletcher. Under the terms of their trust, this money was "to be held as a permanent fund to be known as the ***Eugene and Dorothy Fletcher Memorial Endowment*** *with income only to be used for laboratory research."*

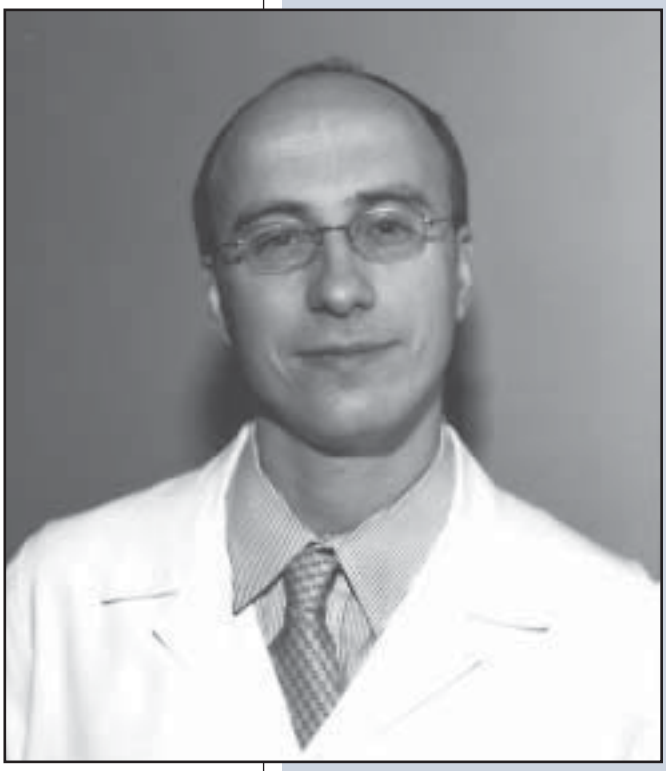
This generous gift was used to establish the Cancer Research Foundation Fletcher Scholars Program, a biennial award of $100,000, to an individual senior cancer scientist doing laboratory research of exceptional import. Dr. Rinker-Schaeffer is our 8th Fletcher Scholar.

Prostate cancer is the most common cancer detected in American men. If prostate cancer is diagnosed when confined to the prostate, it can be cured by surgically removing it. A great challenge lies in treating prostate cancer after it has spread outside of the prostate.

When Dr. Rinker-Schaeffer was a Cancer Research Foundation Young Investigator in 1995, her goal was to identify genes that could block the ability of the cancer cells in the prostate to become metastatic (to escape and carry cancer to other sites in the body), and to identify tumors of high and low metastatic potential.

There is a long-standing belief that once cancer cells spread from the primary tumor, anti- metastatic therapies would be ineffective. The most important clinical need in prostate cancer is to be able to prevent and/or treat bone metastases (the most frequent site of metastases in prostate cancer). Little is known of the underlying mechanisms responsible for bone metastases. Defining the genes and cellular pathways regulating metastatic growth is the first step toward this therapeutic goal.

Development of a Three-Dimensional Magnetic Guidance and Drug Delivery System



$548,000 Grant Award to

Axel J. Rosengart, M.D., Ph.D.
Assistant Professor
Department of Neurology
University of Chicago Medical Center

The goal of this project is to attach drugs to small magnetic particles, carriers called nanoparticles, and to guide the particles through blood vessels to a particular body organ or tissue by using magnets outside the body. A part of this undertaking is the creation of a device implanted into the tumor tissue to "catch" the particles, which would deliver a highly selective payload of anticancer drugs designed to treat and repair damaged cells.

What would make this concept possible is the science of nanotechnology, the ability to create microscopic machines 1,000 times smaller than the diameter of a human hair.

This groundbreaking research project is a collaborative effort. In addition to the University of Chicago departments of Neurology, Neurosurgery, Pathology and Radiology, four divisions within Argonne National laboratory – chemical technology, engineering technology, materials science, mathematics and computer science – have been enlisted. Illinois Institute of Technology, Drexel University and Case Western Reserve University are part of the team.

This research holds the promise of efficient, targeted drug-delivery systems for cancer patients - and for individuals with many other diseases.

CANCER RESEARCH FOUNDATION

Young Investigator Awards

THE USE OF DYNAMIC CONTRAST-ENHANCED MRI TO DIFFERENTIATE BETWEEN RODENT METASTATIC AND NON-METASTATIC PROSTATE TUMORS: COMPARING LOW, MEDIUM AND HIGH MOLECULAR WEIGHT CONTRACT AGENTS

Xiaobing Fan, Ph.D.
Research Associate
Department of Radiology
$49,997. grant award

Contrast-enhanced magnetic resonance imaging (MRI) has the potential to greatly improve the detection and staging of cancer. The rate at which intravenous contrast agent is taken up and washed out of tissue yields important information relating to blood flow that distinguishes dangerous cancers from benign conditions.

However, the clinical use of MRI requires accurate mathematical analysis of the uptake and washout of contrast agents. The methods for analysis that are currently available are not effective. In this project, a new empirical mathematical model for the kinetics of contrast agent uptake and washout detected by MRI will be developed and tested. If the proposed research is successful, the model could be used clinically to analyze patient data and have a significant impact on the diagnosis and treatment of cancer.

REGULATION OF E2A PROTEINS BY THE PHOSPHATIDYL INOSITOL 3-KINASE PATHWAY

Barbara Lynne Kee, Ph.D.
Assistant Professor
Department of Pathology
$50,000. grant award

Dr. Kee is named the Raymond F. Zelko Young Investigator in memory of the Foundation business manager who died of cancer in 1993.

The E2A proteins are important in blood cell formation. We know this because mice and human cells that lack these proteins acquire severe immune deficiency and T cell lymphomas. In order to understand how blood cell development is controlled, we propose a series of experiments designed to determine how E2A protein expression is maintained in the precursors of mature blood cells. This information will be essential to evaluate the utility of future therapeutic interventions in T cell lymphoma and possible other cancers and diseases.

INVESTIGATION OF MUTATING T CELLS AND ACTIVATION-INDUCED CYTIDINE DEAMINASE FUNCTION

Somatic hypermutation is highly linked to lymphomagenesis. Mutations are able to either silence or activate a gene, causing loss of function or over-expression of the gene.

Lymphocytes are white blood cells that normally make up about 25% of the total white blood cell count. They occur in two forms: B cells, the chief agent of the humoral immune system, and T cells, the agents of the cell-mediated immune system.

In past studies, a particular gene, BCL-6, has been shown to be highly mutated in both B and T lymphocytes. The factor that causes this is an enzyme called activation-induced cytidine deaminase. This search for the mutation mechanism will help further understanding the relationship between somatic hypermutation and tumor formation.

Hong Ming Shen, Ph.D.
Research Associate
Department of Molecular Genetics and Cell Biology
$50,000. grant award

Mark D. McKee, M.D.
Assistant Professor
Department of Surgery
$25,000. grant award

TRANSFER OF MURINE T CELL RECEPTOR GENES TO HUMAN LYMPHOCYTES FOR RECOGNITION OF HUMAN TUMORS

Cancer vaccines: A natural immune response occurs to many human tumors, but this response is rarely strong enough to slow or prevent the growth of the cancer in patients. Dr. McKee hopes to amplify the natural immune response against many common cancers by identifying the genes that allow immune recognition of proteins found on tumor cells. He has efforts ongoing to identify these genes from human cells, and proposes to identify similar genes from a special mouse strain that carries elements of the human immune system. Human proteins are seen as foreign by mice, and their immune response against these proteins is stronger than the corresponding response of the human immune system. Once Dr. McKee has identified mouse genes that recognize human cancer proteins, he will test his ability to transfer these genes to human immune cells.

Each year, the Cancer Research Foundation accepts grant requests from young men and women engaged in first-project laboratory and/or clinical cancer research. These proposals come to the Foundation already reviewed and ranked by a faculty awards committee, using the National Institutes of Health peer review process. Only the innovative and bold proposals with practicable research plans are considered for funding.

After receipt by the Foundation, our medical consultants, Dr. Joseph B. Kirsner and Dr. Richard L. Schilsky, interpret the complex science to the trustees. Cancer Research Foundation trustees make all funding decisions.

Last October, three young scientists from the University of Chicago Medical Center were awarded young investigator grants:

Xiaobing Fan, Ph.D.
Barbara Lynne Kee, Ph.D.
Hong Ming Shen, Ph.D.

A Cancer Research Foundation Young Investigator from the University of Chicago, class of 2002, applied for 2nd year funding, which was approved for six months:

Mark D. McKee, M.D.

These awards are for one year. At the end of the year, if the hypotheses have proven worthy of further study, this early research will be used as basis for application for major outside funding.

Advances in Treatment of Colorectal Cancer

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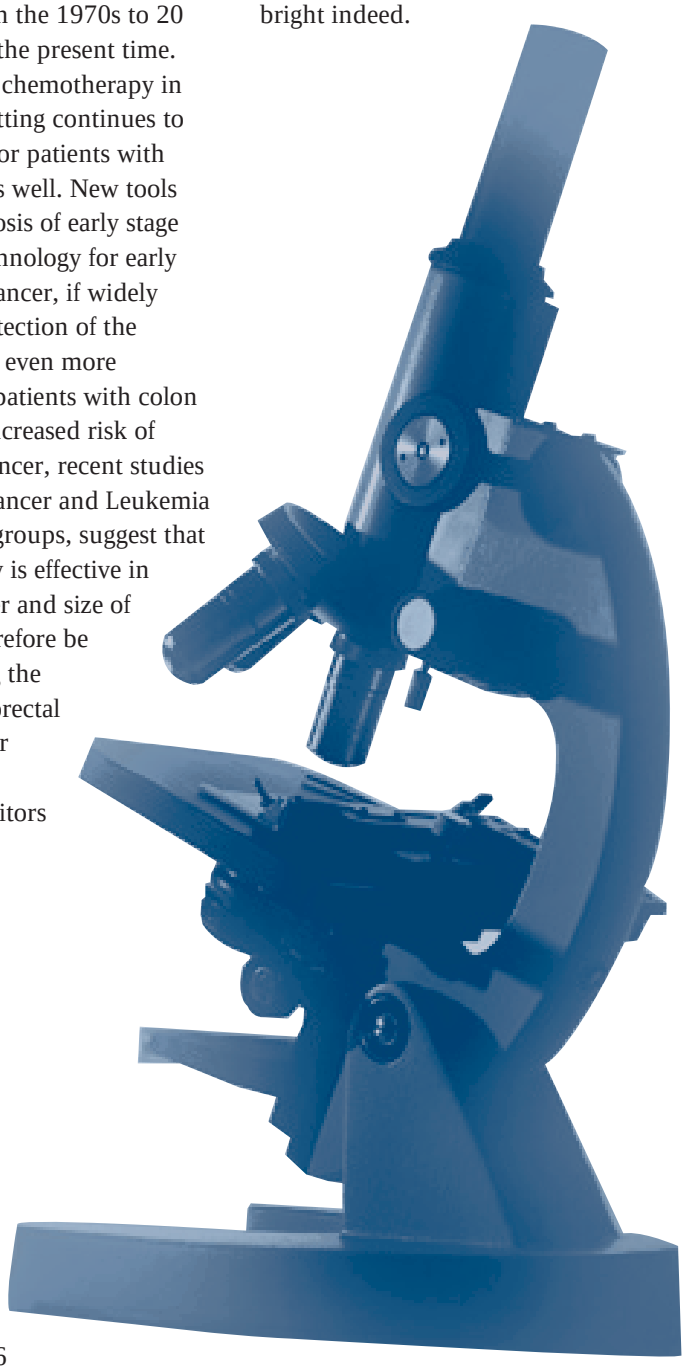
adjuvant chemotherapy for patients with high risk, non- metastatic, colon cancer and has been shown to further reduce the likelihood of tumor recurrence after surgery compared with the prior standard regimen.

In another exciting recent development, study results have shown that adding bevacizumab (Avastin) to chemotherapy significantly improves the survival of patients with metatstaic colorectal cancer. Bevacizumab is a monoclonal antibody directed against the vascular endothelial growth factor (VEGF). VEGF is a molecule produced by tumor cells that stimulates the growth of blood vessels to bring nutrients to the tumor tissue. Blockade of the angiogenic signal by bevacizumab has the potential to cut off the blood supply to tumor cells resulting in tumor shrinkage or slower growth. At the 2003 annual meeting of the American Society of Clinical Oncology held in Chicago, Genentech investigators reported results of a randomized clinical trial showing that adding bevacizumab to chemotherapy improved the median survival of patients with metastatic colorectal cancer by approximately 5 months. This is the first study to clearly demonstrate a benefit from any antiangiogenic strategy and validates this approach as an important new component of cancer treatment. Although bevacizumab is not yet commercially available, it is widely anticipated that the drug will receive marketing approval from FDA in the coming year.

When I first became involved in oncology, 25 years ago, the only drug available for treating colorectal cancer was 5-FU. The average survival of patients with metastatic disease was on the order of 8-10 months. Although it has taken a quarter of a century, the outlook for patients with colorectal cancer is now considerably brighter. Three chemotherapy drugs (5-FU, irinotecan and oxaliplatin) are now commercially available and effective for treating this disease and bevacizumab is another very promising molecule that adds a targeted, antiangiogenic approach to our armamentarium of agents for use in treating colorectal cancer. The median survival of patients with metastatic disease has doubled from 8-10 months in the 1970s to 20 months or better at the present time. The use of adjuvant chemotherapy in the postoperative setting continues to improve outcomes for patients with early stage disease as well. New tools for molecular diagnosis of early stage disease and new technology for early detection of colon cancer, if widely used, will enable detection of the disease at an earlier, even more treatable stage. For patients with colon polyps who are at increased risk of developing colon cancer, recent studies conducted by the Cancer and Leukemia Group B and other groups, suggest that daily aspirin therapy is effective in reducing the number and size of polyps and may therefore be effective in reducing the development of colorectal cancer as well. Other anti-inflammatory drugs, such as inhibitors of cyclooxygenase II (COX-II), also hold great promise for preventing colon polyps and colon cancer.

Andrew Von Eschenbach, M.D., Director of the National Cancer Institute, has declared a goal of eradicating the pain and suffering due to cancer by 2015. At least for colorectal cancer, we are already well on our way toward meeting that goal and the future is bright indeed.



Discovery of Molecular Determinants that Influence Anticancer Drug Response and Toxicity in Patients with Sarcoma

$500,000 Grant Award to
Ramamoorthy Nagasubramanian, M.D.
Instructor
Department of Pediatrics
University of Chicago Medical Center

This award will establish a Pediatric Pharmacogenetics Program at the University of Chicago. Pharmacogenetics is the study of variations in genes that determine an individualís response to drug therapy.

The goal of this research proposal is to discover inherited traits and molecular determinants that influence anticancer drug response and toxicity in patients with sarcoma (malignant cancer of the bone, muscle and other connective tissues). Dr. Naga proposes that the response and survival outcomes in these patients may be related to levels of expression of various genes that influence tumor properties such as growth rate, invasiveness, metastasis and response to chemotherapy.

A clinical by-product will be the treatment of children and adults with sarcoma according to risk-adapted therapy that involves tailoring the intensity of multi-agent chemotherapy protocols to each patient's risk of relapse and toxicity. Applying the principles of pharmacogenomics to the development of new therapies could lead to improved survival rates.

Special Occasion and Memorial Acknowledgement

Gifts honoring the memory of someone dear who has died, or gifts in celebration of birthdays, anniversaries, a new home, a new baby or many other special occasions arrive at the Cancer Research Foundation daily.

This represents a current philanthropic trend in gift giving. Caring individuals and companies are making donations to CRF in someone's name, in lieu of client or staff gifts. It's truly a way to demonstrate that it is better to give than to receive.

Now it's even easier to give: In addition to personal checks and cash, **you can charge your gift to VISA, MasterCard or American Express** – by mail, by phoning our office, or online.

Online donations to the Cancer Research foundation are run on a Secure E-Commerce Transaction Server. When you enter information on our website donation page, the information is encrypted before it gets sent over the Internet. The transaction remains 100% secured from everyone except you, the donor, and CRF.

Every contribution will receive a timely, personalized acknowledgement from the Cancer Research Foundation.

This Year You Can...

Give To The Cancer Research Foundation Through Payroll Deductions:

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(CFC #2588)
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Cook County Campaign
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The Campaign Books are Large
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The Bernice Goldblatt Fellowship

In 1997, the Cancer Research Foundation established the Bernice Goldblatt Fellowship. This permanent endowment at the University of Chicago provides annual income to support a first year graduate student in the Biological Sciences Division who is a candidate for a Ph.D. to be issued by the Committee on Cancer Biology.

Rebecca Conkling has been chosen by the Committee on Cancer Biology as the year 2002 Bernice Goldblatt Fellow. Rebecca graduated *cum laude* with a degree in Biology from the State University of New York at Binghamton.She entered Binghamton University with a clear goal in mind: to learn everything she could about molecular biology, with the goal of eventually conducting research applicable to human health. Rebecca has worked in research laboratories at Binghamton University as an undergraduate, and, beginning in the summer of 2002, in the laboratory of Dr. M. Eileen Dolan at the University of Chicago.

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Cancer Research Foundation

As a responsible member of the community, the Cancer Research Foundation believes in accountability. We think the more you know about our trustworthy stewardship of funds, the more willing you will be to invest in the future through the Cancer Research Foundation.

Every year, the Cancer Research Foundation files a report with the Internal Revenue Service, IRS Form 990 (Return of Organizations Exempt from Income Tax). This report is available for public inspection in our office. We also make it available by mail, at a nominal cost.

Cancer Research Foundation financial records are audited annually. This report is reprinted in its entirety and included each year in one of our newsletters.

The Cancer Research Foundation is an Illinois 501 (C) (3) not for profit corporation, operating in Chicago. Our mission is to help find the cures for cancer through research.We welcome memorial contributions and gifts in honor of special celebrations. Contributions are deductible to the full extent allowed by law.