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Gene Silencing Inhibits Tumors in Ewing's Sarcoma Model

Scientists have used a new method of silencing genes to inhibit tumors in mice that have a form of Ewing's sarcoma, a rare and often deadly bone cancer in young adults. The findings were presented April 19th at the annual meeting of the American Association for Cancer Research (AACR) in Anaheim, California.

The project was a collaboration between the laboratories of Dr. Timothy Triche at Childrens Hospital Los Angeles and Dr. Mark Davis at the California Institute of Technology (Caltech). Dr. Triche's team has expertise on Ewing's sarcoma while Dr. Davis' team of chemical engineers has developed ways to deliver gene-silencing molecules to specific cells.

Ewing's sarcoma, which is nearly always fatal once it has spread in the body, has been traced to two chromosomes that break and exchange genetic material, activating a gene called *EWS-FLI1* that is critical to the development of the tumors. Silencing the gene, however, can inhibit Ewing's tumors.

"The purpose of the study was to use the targeting of an oncogene to treat a childhood tumor," says Dr. Siwen Hu, a postdoctoral fellow at Childrens Hospital Los Angeles and the University of Southern California,
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Director's Update

Electricity and Excitement at AACR

Intellectual electricity is always evident at the meetings of the American Association for Cancer Research, but at the annual meeting that began on Saturday in Anaheim, there was also an aura of anticipation. Repeatedly, presentations of progress in cancer research were linked to prospects for improved cancer solutions.

In my presentation, I traced the trajectory that has led to the fusion of progress and purpose. I outlined the National Cancer Institute's (NCI's) commitment to leverage the investment of talent, time, and resources to further accelerate the elimination of the suffering and death due to cancer. Speakers such as Dr. Alfred Knudson, who received the AACR Lifetime Achievement Award,
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Photo © AACR/Todd Buchanan

Dr. von Eschenbach with AACR President Dr. Lynn Matrisian at the AACR annual meeting in Anaheim.

(*Gene Silencing continued from page 1)*
who presented the research at AACR. When the treatment was given over 4 weeks, the results were "striking" and the tumor growth effectively stopped in many animals, according to Dr. Hu.

The delivery method uses a short interfering RNA (siRNA) molecule designed to silence the gene *EWS-FLI1*. The siRNA was packaged with sugar-containing polymers and delivered into tumor cells by a modified protein called transferrin that normally ferries iron into cells.

"We set out to design a delivery system that could work systemically in metastatic disease because you want to reach many different types of locations, wherever the tumors may be," says Dr. Davis.

The ultimate goal is to modify the method for use in people, as an intravenously administered treatment. The sugar molecules, or cyclodextrins, in the polymer that packages the siRNA have been used in pharmaceuticals and are safe for human use.

"The key issue here is that the delivery system is nontoxic and doesn't cause an immune response," explains Dr. Davis. "We've been working on this system for years."

To determine if the system was working as designed, the researchers modified two key elements—the targeting agent that carried the siRNA to tumor cells and the siRNA itself. With each modification, the system failed, suggesting to the researchers that the tumor inhibition they observed was due to the design of the siRNA and the mode of delivery.

The potential of gene silencing approaches in blocking the activity of genes involved in cancer has been suggested by many studies in cell cultures. But a major challenge has been finding ways to target tumor cells and protect the siRNA molecules from degradation so that they can have a therapeutic effect.

The new method "is a real breakthrough in systemic delivery of non-chemically modified siRNAs," comments Dr. John Rossi of the Beckman Research Institute in Duarte, Calif., who was instrumental in bringing the two laboratories together for the study.

"This is a lovely study that combined several technologies to silence a gene," said Dr. John Mendelsohn, president of the University of Texas M.D. Anderson Cancer Center, who moderated the news conference during which the study was presented. He predicted the approach would eventually be tested in human clinical trials.

Drs. Rossi and Davis recently launched a company called Calando Pharmaceuticals to develop siRNA gene-silencing therapies. Dr. Davis selected the word "calando" because in music notation it refers to a gradual decrease in volume, or silencing. ◆

(AACR continued from page 1)
chronicled the exhilarating explosion of knowledge that led from observing cancer's mysterious behavior to now revealing cancer's molecular secrets.

Our nation's investment in cancer research, accelerated in 1971, has produced a golden era of progress, but it has also made possible a platinum future if we leverage the resources to match the opportunities. The intellectual electricity and the aura of anticipation evident at AACR will enrich our discovery-development-delivery strategy. Our emerging understanding of the molecular, cellular, and genetic mechanisms of the disease process has created an "inflection point" in cancer research, allowing us to make progress at an incredible pace.

Two important ways to leverage our investment in this effort are to promote Team Science and Big Science. Centers, consortia, and co-principal investigators are creating a culture of transdisciplinary collaborative research that will synergize science in the only way possible to address the unique complexity of cancer. Big Science that integrates science and technology will greatly accelerate the pace of progress in cancer research. This will, in turn, shorten the time it takes to advance from proof of concept to delivery of more effective interventions—from decades to years and from years to months.

We now have more resources devoted to cancer research than ever before. Today, 60 Cancer Centers, more than 4,000 principal investigators, and some of the most talented and brilliant scientists in the world are now simultaneously pursuing promising opportunities such as the integration of clinical research, bioinformatics, imaging, the human cancer genome, integrative systems biology, and nanotechnology.

Over the past 30 years, we have unraveled cancer's complexity and constructed a robust and dynamic cancer infrastructure. We must now nurture this new culture of cancer research to fully realize the fruits of the golden era of the National Cancer Program. By doing so, we can—and will—surge ahead toward a platinum future that is well within our grasp. ◆

Dr. Andrew C. von Eschenbach
Director, National Cancer Institute

NCI at AACR 2005

For more information about NCI presentations at the AACR annual meeting, go to http://www.cancer.gov/aacr2005.

Spotlight

Cancer Imaging: Pictures of the Future of Clinical Oncology

This is the first of a two-part series on cancer imaging. This week's article describes how radiologists more effectively image anatomy to produce more effective diagnoses and improved patient care. Next week's article will discuss new contrast agents that can help illustrate function and aid in drug delivery.

Biomedical imaging of cancer patients has become essential to state-of-the-science oncology practice. Over the last few decades, radiology and imaging sciences have been riding the same wave of discovery and innovation as has the rest of cancer medicine. Imaging advances have powered, demonstrated, and increased understanding of carcinogenesis at the cellular and molecular levels.

"Imaging in the 21st century will follow the historical cycle of innovation in radiology that dates back to Roentgen's X-ray discovery 110 years ago," predicts NIH Director Dr. Elias Zerhouni. Dr. Zerhouni, who was chairman of the radiology department at Johns Hopkins University School of Medicine before coming to NIH, spoke at CCR Grand Rounds on February 15. "You begin with a biological question as a signpost. Then you marry technological advances in scanners and computers to invent new medical devices to approach that question and further interrogate the biology, which suggests how to tailor novel therapeutics. We are heading into a clinical world that will rely profoundly on very powerful, minimally invasive therapeutics. We're at that frontier right now and *in vivo* cellular and molecular imaging beckon us forward."

One of the cardinal tenets of biomedical research holds that "biology is messy." At this month's Sixth Annual National Forum for Biomedical Imaging in Oncology—which focused on the challenge of transforming inherently subjective pictures of biology into repeatable, valid, and quantifiable datasets—Dr. Daniel Sullivan, director of NCI's Cancer Imaging Program (CIP), explained why "segmentation is the mother of all problems."

"The major challenge for oncologists when looking at a structural image is to be able to define what is tumor and what is not," says Dr. Sullivan. "The field or concept of fuzzy mathematics is one approach that can be used to try to pin down the edges of a tumor." Radiologists use highly skilled mental algorithms to perform this task, he notes, and have been remarkably effective, although also notoriously variable, in these judgments. Still, radiologists have done better than early computer attempts to accomplish the same diagnostic task, he adds.

But, once X-ray data became digitized with computerized tomography (CT) in the 1970s, the urge to apply computer algorithms proved irresistible. "You could capture the complexity of reality in a way that just wasn't available before," says Dr. Zerhouni.

Researchers began to dream of the statistical power that could be generated from the images drawn from hundreds of thousands of cancer patients around the country. But before they could begin to put this potential data into a meaningful scientific context, they needed to face the "messy biology" problem and also avoid "comparing apples to oranges," Dr. Sullivan says. The randomized controlled clinical trial is the ultimate scientific framework for turning valid data into meaningful information, he continues, but the obstacles relating to using data derived from thousands of individual, human radiologists reading thousands of images of different tumors from many different machines and technologies were formidable.

NCI addressed this dilemma by supporting the American College of Radiology Imaging Network (ACRIN). Dr. Carl C. Jaffe, chief of NCI's Diagnostic Imaging Branch, helps to oversee the unique national cooperative group that has been conducting clinical trials in imaging since 1999. ACRIN's trials address the four major uses of imaging in cancer care: screening, diagnosis and staging, image-guided treatment, and measuring response to treatment. Underlying all is the goal of generating information that will lengthen and improve the quality of patients' lives.

The main idea, explains Dr. Jaffe, "is to establish quality control over the process" by developing a model that allows you to aggregate data from widely scattered sites into a truly meaningful process "that rigorously tests biological response in a verifiable, repeatable way."

"We're not using machines to actually read the films," continues Dr. Jaffe. "However, we calibrate the machines and systematize the radiologist's

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Cancer Research Highlights

Avastin with Taxol Slows Breast Cancer Progression

Recent clinical trials have shown that antiangiogenesis drugs—those that inhibit blood vessel growth—can slow progression of colon and lung cancers. Now preliminary results from an NCI-sponsored study reveal that the antiangiogenesis drug bevacizumab (Avastin) has the same effect on recurrent or metastatic breast cancers when it is combined with the chemotherapy drug paclitaxel (Taxol).

These results come from the E2100 clinical trial, which is run by the Eastern Cooperative Oncology Group with the participation of 722 women. "This study is the first to find a benefit of antiangiogenic therapy in patients with breast cancer," said Dr. Kathy Miller, study chair and faculty member at Indiana University Medical Center.

Avastin is a humanized monoclonal antibody approved by FDA to treat metastatic colorectal cancer when combined with chemotherapy. It works by blocking a tumor-released molecule called vascular endothelial growth factor. The drug is manufactured by Genentech, Inc., and provided for use in this clinical trial through a Cooperative Research and Development Agreement with NCI.

Women in the E2100 trial were randomized to receive either paclitaxel alone or in combination with bevacizumab. On average, those who received the combination saw no worsening of their disease for 4 months longer than those who received only the paclitaxel.

Celebrex Alters Gene Activity in the Colon

The drug celecoxib (Celebrex), a COX-2 inhibitor, produces a distinct pattern of gene activity in the normal colons of patients at risk for an inherited form of colon cancer, according to results of a study reported at the AACR annual meeting.

The researchers identified a genetic "signature" based on 173 genes whose activity was altered by the drug, including many genes involved in the immune system and inflammatory response. Overall, celecoxib led to changes in more than 1,400 genes in the colon, according to Dr. Oleg Glebov, an NCI research fellow.

The signature may be the first indicator of whether the drug has effects in the colon. The researchers note that increasing the dose was associated with larger changes in gene activity, suggesting a dose-response effect.

"We can distinguish individuals who take celecoxib on a routine basis from those who do not," says Dr. Ilan Kirsch, Genetics Branch chief in NCI's Center for Cancer Research, who led the study. "The distinct pattern of gene activity implies that there could be a direct or indirect action of the drug on pathways of immune responsiveness, inflammation, and proliferation within the colon."

The researchers tested celecoxib in patients at risk for hereditary nonpolyposis colon cancer. Also known as Lynch Syndrome, the disorder increases the risk of colorectal, ovarian, and endometrial cancers, among others.

DLC-1 Gene Implicated in Prostate Cancer

The tumor suppressor gene *DLC-1* (deleted in liver cancer-1) is often silenced in both prostate cancer and benign prostatic hyperplasia (BPH), according to a study presented at the AACR annual meeting. Dr. Nicholas Popescu and colleagues in NCI's CCR found that the *DLC-1* promoter region was hypermethylated in a high number of prostate tumor and BPH samples, thus keeping the gene turned off and resulting in abnormal cell growth.

Loss of *DLC-1* expression has been associated with liver, breast, and ovarian cancer, among others. Because the chromosome region that contains *DLC-1* is often deleted in prostate tumors, *DLC-1* might be associated with prostate cancer as well. DNA methylation is one way to keep genes turned off, and Dr. Popescu's lab identified *DLC-1* hypermethylation in 11 of 20 prostate adenocarcinomas and 15 of 21 BPHs. In studies with two prostate cancer cell lines, the researchers found that histone deacetylation can also result in loss of *DLC-1* expression. Increased *DLC-1* methylation in BPH samples also correlated with increased levels of prostate-specific antigen in the blood.

"Because abnormal methylation is one of the earliest alterations in tumor development, the detection of *DLC-1* promoter hypermethylation may have clinical application for early detection of prostate cancer," noted Dr. Popescu.

Avastin, Immunotoxin Combo Shows Strong Anti-Tumor Effect

Combining the angiogenesis inhibitor bevacizumab (Avastin) with either of two investigational immunotoxins—genetically modified bacterial toxins that can penetrate cancer cells—provides superior tumor reduction in animal models when compared with bevacizumab alone, NCI researchers reported this week at the AACR meeting.

Bevacizumab was used in combination with SS1P and HA22, investigational immunotoxins being developed by Dr. Ira Pastan and colleagues in the Laboratory of Molecular Biology in NCI's CCR.

Mice were treated with a bevacizumab/immunotoxin combination, bevacizumab alone, or immunotoxin alone. The greatest reduction in tumor volume compared with untreated mice was seen with the bevacizumab/SS1P combination, but similar tumor volume reductions were seen with bevacizumab and with either immunotoxin when compared with bevacizumab alone.

According to Dr. Pastan, the rationale for the study came from work by Dr. Rakesh Jain from Harvard Medical School showing that antiangiogenic therapies can transiently "normalize" the abnormal structure and function of tumor vasculature, perhaps allowing for more effective delivery of antitumor agents.

SS1P is now in a phase 1 clinical trial at NCI and trials with HA22 will begin early in 2006. SS1P, which targets the protein mesothelin, has shown strong antitumor activity against mesothelin-expressing tumors in animal models and in tumor cells from patients with mesothelioma and ovarian cancer. HA22 targets the CD22 protein, which is overexpressed in several different B-cell malignancies.

Statin Use Linked to Lower Risk of Advanced Prostate, Colon Cancer

According to a large observational study presented this week at the AACR meeting, the use of cholesterol-lowering drugs, such as statins, may significantly reduce the risk of advanced prostate cancer.

Researchers at NCI, Johns Hopkins University, and Harvard University followed 34,428 U.S. men for more than 10 years. They found that men who used cholesterol-lowering medications had half the risk of advanced prostate cancer and a third of the risk of metastatic or fatal prostate cancer, compared with nonusers. The study did not reveal any effects of cholesterol-lowering drugs on localized prostate cancer.

"This is a promising lead on a class of drugs that may be offering unanticipated benefits, but we need further studies to confirm these findings as well as figure out the mechanisms at work," says Dr. Elizabeth Platz, the study's lead investigator at Johns Hopkins. More than 90 percent of the men who were using cholesterol-lowering drugs reported using statins in particular.

"The next steps will be to examine the relationship between statin use and prostate cancer recurrence, and to conduct studies involving prostate tissue to try to understand how statins might be preventing the progression of early prostate cancer," adds study co-author Dr. Michael Leitzmann of NCI's Division of Cancer Epidemiology and Genetics (DCEG).

Another study by researchers from Rutgers University, the University of Oklahoma, and NCI's Division of Cancer Prevention and CCR showed that a combination of atorvastatin (Lipitor) and celecoxib was more effective at limiting colon cancer development than higher dosages of either agent alone in a rat model. A dosage of 300 ppm of celecoxib and 100 ppm of atorvastatin inhibited 95 percent of the invasive and noninvasive tumors that developed in the untreated rats. In contrast, twice the dosage of celecoxib given alone reduced tumor incidence and number by 80 percent; 150 ppm of atorvastatin alone reduced tumor incidence by 31 to 41 percent.

Researchers Develop Models to Predict Metastatic Potential

While some cancers spread slowly and respond to conventional therapy, others metastasize quickly and become fatal. Being able to determine which type of cancer a patient may have upon initial diagnosis would be invaluable in providing the best treatment possible, according to a pair of studies presented at the AACR annual meeting.

Dr. Gennadi Glinsky and colleagues at Sidney Kimmel Cancer Center used gene microarrays to identify a set of 11 genes known as the "death from cancer" signature. The 11 genes are part of the BMI-1 pathway, which normally is essential for the self-renewal of stem cells. This pathway can also increase renewal in cancer cells and promote tumor progression and metastasis. The researchers tested the predictive power of this gene set in 1,566 patients diagnosed with 10 different cancer types and found that positive expression of the BMI-1 pathway was a consistent predictor of rapid metastasis and poor patient outcome.

An NCI study led by Dr. Kent Hunter in NCI's CCR looked at the genetic make-up of normal cells, rather than which set of genes are turned on in a cancer cell. "Millions of polymorphisms exist between individuals in the population, and studies in mice have shown this genetic polymorphism can influence almost any measurable trait," said Dr. Hunter. "These observations suggest that even a process as complex as metastasis could be influenced by an organism's genetic background."

The researchers collected saliva samples from a panel of backcross transgenic mice—some that develop highly metastatic tumors and the others that do not — and ran protein expression profiles." They observed that the mice can be accurately classified as either low- or high-metastatic phenotypes according to their protein expression profiles. Using the protein classifiers developed in the training set of mice, the researchers were able to prospectively identify mice as high- or low-metastatic in a test set of 17 heterogenous mice. ◆

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approach to the image." Once captured, an image's digital data can be processed by algorithms that further sort and standardize it. "We use blinding and randomization to present the films to the radiologists, and always have a second independent reading, sometimes a third," he notes. "In essence, ACRIN provides a core facility that embodies the rigor and scientific control you need for a national study with geographically distant sites. From all of this quality assurance comes the beginning of quantifiable data in oncology."

While CIP is only one of the five major programs within NCI's Division of Cancer Treatment and Diagnosis, imaging is a crucial part of NCI's long-term strategy. In NCI's budget proposal for fiscal year 2006, imaging was designated an area of "extraordinary opportunity" for the Institute. CIP includes other major projects besides ACRIN, including imaging technology, molecular imaging, and image-guided intervention.

"We're almost like the early explorers," Dr. Zerhouni observes. "We're beginning to explore the frontiers of genetics and biology at the molecular level." He is confident that imaging science will be the primary guide to that terrain because it increasingly enables researchers to look directly into the metabolizing cell. "More and more, the business of clinical medicine will be to deliver treatment drugs and nano-size tools to highly specific sites in the body," such as tumor tissues, he says. "We will use imaging to guide us to the target and then to capture the relevant biological response in real time." ◆

A Conversation with Drs. Denise Aberle and Christine Berg, NLST Co-Directors

The recent announcement of ABC-TV News' Peter Jennings' lung cancer diagnosis has increased public interest in the effectiveness of screening tests to detect and reduce mortality from lung cancer. NCI is supporting the National Lung Screening Trial (NLST) to address this question. NLST compares whether chest X-ray (CXR) or spiral CT scan is more effective in reducing lung cancer deaths among high-risk individuals.

What's the status of NLST?

Dr. Berg: We're in the third and final year of screening for many of the participants. We anticipate we'll be done with screening by late 2006 or early 2007.

Some news reports about Mr. Jennings' diagnosis include statements by physicians recommending spiral CT screens, claiming they are more effective than CXRs. Might this have a negative impact on retention of NLST enrollees?

Dr. Aberle: It's a concern, but one to address by answering questions of our participants individually and through trial updates. There's a difference between screening healthy people and diagnosing symptomatic patients, such as Mr. Jennings. The media focuses on spiral CT because it is new technology and detects smaller lesions, inferring—incorrectly—that CT can prevent lung cancer deaths. We just don't know that. We do know that CT detects many more lung nodules (most benign) and even more cancers, many of which are very slow growing. But we have not seen that CT screening reduces the number of lethal cancers or that it has benefits that outweigh the risks associated with diagnostic work-up of additional nodules.

How do you ensure the safety of participants?

Dr. Berg: We have several protections. First, great care and thought by many experts went into NLST's design. Second, each site has an Institutional Review Board responsible for ensuring thorough consent process and the protection of the subjects. Third, sites report all trial-related events and complications, all of which are regularly reviewed by an independent Data and Safety Monitoring Board that recommends changes or even stopping the trial if trends are seen that suggest possible harm to any group of participants.

When will we know results from NLST?

Dr. Berg: The current schedule is for follow-up to end in 2008 and for final data analysis in 2009.

Dr. Aberle: If we don't see some decrease in advanced-stage, lethal lung cancers with CT, that may also provide early evidence that CT doesn't offer a screening advantage over CXR. We would expect to see that sooner than mortality differences. But, NLST is critically important because it offers the potential to identify a screening test that may reduce the burden of death from lung cancer. ◆

Notes

Gray to Lead NCI Extramural Activities

Dr. Paulette S. Gray was recently named director of NCI's Division of Extramural Activities (DEA). She has served as acting division director since 2003 and as deputy director since 1994. As director, Dr. Gray will be responsible for the scientific, fiscal, and administrative management of the office, as well as strategic planning, development, implementation, and evaluation.

DEA coordinates all NCI extramural programs and grants, provides scientific peer review and oversight of extramural research, and coordinates and administers advisory activities related to the NCI mission. It also establishes and disseminates extramural policies and procedures and tracks the NCI research portfolio.

Dr. Gray earned her B.S. in biology from Tuskegee University and later received her M.S. in mycology and Ph.D. in cellular and developmental biology from Atlanta University. She was a Josiah Macy Jr. Fellow at Woods Hole Marine Biological Laboratory and a Fulbright Scholar at the University of Kaiserslautern in Germany. Dr. Gray joined NCI in 1984 and has held a number of administrative positions at NCI as well as senior advisory posts at HHS.

caBIG Meeting with Commercial Sector Planned for Next Fall

NCI's cancer Biomedical Informatics Grid (caBIG) management is planning a meeting in early fall 2005 to discuss and encourage involvement in the year-old program by the commercial and industrial sectors, caBIG Director Dr. Ken Buetow announced April 12 at the opening session of the caBIG annual meeting (*NCI Cancer Bulletin* April 12). "One of the reasons we're formally exploring how to engage the commercial sector is that we have a fair number of them already knocking at the caBIG door expressing interest in such business models," Dr. Buetow explained. Such private sector involvement will not change the program's fundamental principles of "open source, open access, open development" or lessen the primary role of the Cancer Centers, he added. "However, we're hoping that as caBIG moves forward and matures, industry will see viable business models in the ongoing development and support of caBIG-based tools." The annual meeting attracted 350 attendees and included 47 poster sessions on first-generation caBIG tools and standards.

NCI Launches C-GEMS Project

NCI is launching a strategic initiative that will use the cutting-edge technology of whole genome single nucleotide polymorphism scans to help identify inherited susceptibility genes for breast and prostate cancer. The Cancer Genetic Markers of Susceptibility (C-GEMS) project is an enterprise activity in NCI's DCEG and the NCI Core Genotyping Facility, with collaboration from the Cancer Genome Anatomy Project.

C-GEMS represents a resource for the strategic partnerships between intramural and extramural groups that are joining forces to incorporate genomic and other emerging technologies in large-scale epidemiologic studies (*NCI Cancer Bulletin*, February 24, 2004).

The 3-year project will leverage a series of current intramural and extramural resources—including component studies of the Cohort Consortium, NCI's core genotyping capabilities, and caBIG—at an estimated cost of approximately $14 million. The overall project goal is to accelerate the discovery of susceptibility or modifier genes in these cancers through this collaborative network. The project will be coordinated by Drs. Stephen Chanock and Robert Hoover, along with Dr. David Hunter, an NCI Eminent Scholar. A distinguished panel of extramural scientists is being convened to provide guidance and evaluation.

A key goal of C-GEMS is rapid dissemination of results to the scientific community. The detection of linkage from genome scans will need to be followed by fine mapping and candidate gene inclusion/exclusion studies. For this purpose, the datasets will be made quickly available via caBIG to the entire research community.

Mirkin to Speak at Nanotech Seminar

Dr. Chad A. Mirkin, George B. Rathmann Professor of Chemistry and director of the International Institute for Nanotechnology at Northwestern University, is the next featured speaker in NCI's Nanotechnology Seminar Series. Dr. Mirkin's lecture will take place April 26, from 3:00–4:00 p.m. in the Masur Auditorium on the NIH campus in Bethesda, Md. The presentation will be webcast at http://videocast.nih.gov. For more information, go to http://nano.cancer.gov/events_nanotech_seminar_series.asp. ◆

CCR Grand Rounds

April 26: Dr. John T. Schiller, Senior Investigator, Laboratory of Cellular Oncology, CCR, NCI. "Recent Advances in Prophylactic HPV/Cervical Cancer Vaccines"

May 3: Dr. Curtis C. Harris, Chief, Laboratory of Human Carcinogenesis, CCR, NCI. "Chronic Inflammation and Cancer: Radical Causes of Cancer"

CCR Grand Rounds are held 8:30 to 9:30 a.m. at the NIH campus in Bethesda, Md., in the Clinical Center's Lipsett Amphitheater. ◆

Community Update

Georgia Postal Service Rallies Support for Breast Cancer Research

The idea was both practical and philanthropic: Why not create a campaign promoting the Breast Cancer Research stamp to raise revenue for the U.S. Postal Service's South Georgia District while also raising money to fight the disease? The district marketing team had never tackled such a campaign, but they didn't let that stop them.

They named the campaign "The Circle of Hope," designed artwork for posters and promotional items, and left the rest to postal clerks. Surprisingly, after only 30 days, the district, which administers mail service throughout the lower two-thirds of the state, sold more than three times as many Breast Cancer Research stamps as it had during the same period of time the previous year. The campaign raised $21,378 in net proceeds, which was donated to the Department of Defense Medical Research Program and to the NIH for cancer research during a ceremony in Macon, Ga., last month.

The U.S. Postal Service issued the Breast Cancer Research stamp, its first semipostal fundraiser, in 1998. For every 45-cent stamp sold, 8 cents go to research. To date, more than 606 million stamps have been sold, raising almost $45 million. "When you emphasize a medical issue like breast cancer—one that has relevance for everyone—people don't mind paying the extra money for the stamps," says Donna Ricks, manager of consumer affairs at the district office.

The marketing team had the idea of using pink circles on which people could write the name of someone they wanted to honor who was affected by breast cancer. They initially printed 50,000 circles for the district's 445 postal locations, but soon had to order more. After customers signed the circles, the clerks mounted them in the post office lobbies. "It wasn't long before there were pink circles from one end to the other," Ms. Ricks says.

She says that the key to this campaign's success has been local postal workers who believe in the cause and help their customers believe in it, too. George Barnhill is one such clerk. A postal employee for more than 40 years, he works alone at the office in Port Wentworth, Ga., a town of about 3,200 people a few miles outside of Savannah. Last October, he sold 306 20-stamp postage sheets. "I've been touched by so many peoples' stories about their experience with breast cancer that this has become almost like a crusade for me," he says.

After such a tremendous success in 2004, the district is running Circle of Hope twice this year, in April and again in October to coincide with Breast Cancer Awareness Month. In less than 3 weeks, the district has sold 113,431 individual stamps. Within the district, there's an informal competition to see which office can sell the most. So far, Savannah is in the lead with close to 700 sheets sold. Meanwhile, Mr. Barnhill sold 179 sheets to his customers in only 2 weeks.

On a larger scale, Ms. Ricks says that Lizbeth Dobbins, district manager, is seeking approval from their headquarters to expand the campaign to a national level. If they are successful, Ms. Ricks says, "You will soon be seeing pink circles in post offices nationwide." ◆

Featured Meetings and Events

A comprehensive calendar of cancer-related scientific meetings and events sponsored by NCI and other scientific organizations is available at http://calendar.cancer.gov/ ◆

The *NCI Cancer Bulletin* is produced by the National Cancer Institute (NCI). NCI, which was established in 1937, leads the national effort to eliminate the suffering and death due to cancer. Through basic, clinical, and population-based biomedical research and training, NCI conducts and supports research that will lead to a future in which we can identify the environmental and genetic causes of cancer, prevent cancer before it starts, identify cancers that do develop at the earliest stage, eliminate cancers through innovative treatment interventions, and biologically control those cancers that we cannot eliminate so they become manageable, chronic diseases.

For more information on cancer, call 1-800-4-CANCER or visit http://www.cancer.gov.

NCI Cancer Bulletin staff can be reached at ncicancerbulletin@mail.nih.gov.