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NCI Cancer Bulletin

Eliminating the Suffering and Death Due to Cancer

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New Nanotech Design Improves Drug Efficacy, Lowers Toxicity

Researchers at the Massachusetts Institute of Technology (MIT) and Brigham and Women's Hospital have revealed a nanoscale molecular design that increases the efficacy of the chemotherapy agent docetaxel against prostate tumors while reducing its toxic side effects in mice. The study, which appeared April 18 in the *Proceedings of the National Academy of Sciences* and was funded in part by NCI, is the first case where aptamers—short strands of nucleic acids—have been used successfully for the targeted delivery of a cancer drug *in vivo*.

"The greatest advantage of our study is in the combination of materials that we used," says Dr. Robert Langer of MIT, who directed the project with Dr. Omid Farokhzad of Harvard Medical School. Their team chose prostate cancer because it is often diagnosed early, when treatment prognosis is good, hoping that a need for safer localized treatments may facilitate the translation of their work to patient care. They designed their drug-delivery vehicle from poly (D,L-lactic-co-glycolic acid) (PLGA) because of the material's demonstrated safety in other FDA-approved

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Director's Update

Promoting the Development and Delivery of Targeted Therapies

Earlier this month at the American Association of Cancer Research annual meeting, impressive data were presented from a phase II trial testing the multitargeted kinase inhibitor dasatinib (BMS-354825) in patients with chronic myeloid leukemia (CML) who had failed to respond to or had developed resistance to imatinib (Gleevec). In chronic-phase CML patients, for instance, 93 percent had a complete hematologic response, meaning normal blood counts and no CML-related symptoms.

Imatinib has rightfully been heralded as a breakthrough drug. Dasatinib is an excellent example, though, of how cancer researchers are learning from the successes and failures of targeted therapies like imatinib to make important advances in the development of next-generation targeted agents. Not only does dasatinib have a 325-fold stronger affinity for its gene target, *BCR-ABL,* than imatinib, it also appears to be effective against 18 of the 19 identified mutated forms of *BCR-ABL*—the very mutations that drive imatinib resistance.

It is this latter observation concerning overcoming the problem of acquired resistance to molecularly targeted therapies that I find most intriguing.

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(Nanotech Design continued from page 1)
medical devices, such as sutures.

To help the vehicles find their targets, the team coated their surfaces with aptamers that bind to a membrane protein found on prostate cancer cells. Aptamers have an advantage over antibody-targeted systems because they can be manufactured independently of biological systems, with less variability. The team added polyethylene glycol to the surface, helping the particles resist the body's efforts to break them down and flush them out. Dr. Farokhzad describes the resulting bioconjugates as "very small tennis balls—small enough that you could put 500 of them side-by-side to span the cross section of a piece of human hair—with molecules on the surface that look like pins."

The addition of aptamers to these nanoparticles gave promising results: *in vitro*, the bioconjugates killed about 30 percent more tumor cells than when docetaxel was given via aptamer-free particles. When mice xenografted with prostate cancer were given just one injection of the bioconjugate at their tumor site, their lesions shrank significantly, and in five of seven mice, the tumors disappeared within 6 weeks. Mice in the comparison groups saw less shrinkage and, in some cases, died.

All of the mice that received the bioconjugates survived the full length of the 109-day study and also maintained their body weight better than those that received straight docetaxel, indicating that the bioconjugate design may have shielded them from toxic side effects of the drug.

"The real advantages here are that the design gets the drug to the right place, and appears to avoid the toxicities and metabolic effects that have hampered some chemotherapy agents up to this point," says Dr. Gregory Downing, director of NCI's Office of Technology and Industrial Relations.

Dr. Farokhzad's group plans to continue their research with aptamer bioconjugates in larger animal models, and he projects human clinical studies in as little as 2 years. His team is pursuing bioconjugates that target atherosclerotic plaques for treatment of cardiovascular disease as well. Other research with aptamers has shown that they can be used to carry imaging agents, which may eventually be used to visualize the location and concentration of drugs at the subcellular level.

By building their bioconjugates from material known to be safe in humans, Dr. Downing says the MIT-Harvard researchers may have an advantage when it comes to eventual clinical testing and regulation. "But there are quite a number of questions that will need to be addressed," he says.

"At the nanoscale level, the fundamental properties of materials change," he continued. "The laws of pharmacokinetics are redefined, and the ability of these things to transfer across biological membranes, self-assemble, or take over molecular functions isn't really known yet."

This research was conducted in laboratories that are funded as the MIT-Harvard Center of Cancer Nanotechnology Excellence, part of NCI's Alliance for Nanotechnology in Cancer initiative that accelerates the application of promising nanotechnology to cancer. ◆

By Brittany Moya del Pino

(Director's Update continued from page 1)
From our work on CML resistance to imatinib, and several other molecularly targeted therapies, it appears that the cancer cells become resistant to therapy by the development of further mutations in the targeted pathway and not by mutations or genetic alterations occurring as random events in any critical signaling pathway within the cancer cell. The importance of this, if it holds to be true, is a tremendous economy of scale allowing investigators to focus the study of developing resistance on the original pathway.

Even with the interest and optimism generated by these initial targeted therapies, we must acknowledge that this is a field very much in its infancy. NCI is engaged in efforts on many fronts, intramurally and extramurally, to accelerate the progress in this area. NCI intramural researchers, for example, are identifying important new molecular targets and utilizing high throughput screening of chemical and natural product libraries, developing drugs that inhibit them. Among these is 17-DMAG, a second-generation inhibitor of heat shock protein 90, that has the potential to treat many tumor types.

But NCI's involvement in targeted therapy research goes beyond the work of individual NCI labs or researchers. It is remarkably comprehensive and involves collaborations and partnerships in areas such as molecular imaging, toxicology, drug design, and early phase clinical trials supplemented by intense correlative studies.

One example is the Molecular Targets and Molecular Oncology Center of Excellence, a multifaceted effort that brings together intramural and extramural labs. Through this program we are working with private-sector companies to bring new molecularly targeted screening-platform technologies to NCI. As a result, we already have launched individual projects to screen millions of compounds to
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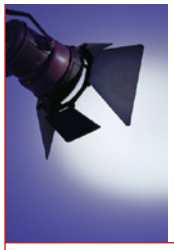

Spotlight

Natural Killer Cells Power Immune System Response to Cancer

Targeted treatments and immunotherapy are two of the most promising approaches to cancer, and each may one day be transformed by basic research on natural killer (NK) cells.

Stem cells in the bone marrow produce most of the immune system's components, including the white blood cells known as lymphocytes. Between 2 and 20 percent of these are NK cells, specialized lymphocytes that continuously patrol the body, eliminating cells that undergo malignant transformation.

Natural killers are aptly named because they act like commandos on a search-and-destroy mission for virally infected and cancerous cells. This streamlined, "ready-to-go" role for NK cells is part of the innate immune system "and makes them well suited for an early defense," explains Dr. Mary Carrington, director of NCI's Basic Science Directorate of NCI's Center for Cancer Research (CCR) in Frederick, Md.

An emerging view of carcinogenesis suggests there is often a long, silent, precancerous period where normal cells begin to undergo alterations, leading eventually to clinical disease. It would make sense if the immune system recognized these threats earlier, when they are easier to combat. "NK cells may have evolved, in part, for this very task," says Dr. Carrington.

How do they do it? Patrolling NK cells first lock onto potential target cells. Then a number of receptors search for complementary molecules on the target. Each receptor finding a match sends an internal signal, which varies not only in its basic message—destroy or ignore—but also in its strength. If the final message says "destroy," the NK makes holes in the target's membrane with the protein perforin, enabling enzymes to enter and destroy the cell's DNA.

Scientists such as Dr. Stephen Anderson, senior principal investigator at NCI-Frederick's Laboratory of Experimental Immunology in CCR, are trying to learn more about how a single cell can make such a complex sequence of calculations and judgments.

In mice, where most experimental work is done, the job of recognizing "self" falls to the Ly49 family of receptors. In humans, killer cell immunoglobulin-like receptors perform this function.

"We have identified a large number of Ly49 inhibitory receptor genes in mice, but a given NK cell does not express them all," explains Dr. Anderson. "The gene for each of these receptors has a unique DNA switch, which turns some 'on' and others 'off' in a random fashion. Thus individual NK cells become 'specialists,' trained to recognize only certain types of threats." The variety of receptors expressed across the population of patrolling NK cells will recognize a number of viruses, as well as signatures characteristic of cancer cells.

Though now a very promising area of immunology and cancer research, two decades ago NKs were underappreciated, often referred to as "null" cells. But a few scientists, such as Dr. Klas Kärre of the Karolinska Institute in Stockholm, saw them as a black box that should be unlocked. The breakthrough idea emerged in 1986 and is now known as the "missing-self" model.

"In vertebrates, nearly all cells express glycoproteins known as HLA Class I, the genes for which are highly variable across the population," explains Dr. Carrington, whose lab has helped fill in the HLA picture. Yet they produce a signature common to all cells within each individual. In the clinical context, this pattern confers a person's tissue type, a crucial factor in whether a transplanted organ will be rejected. Insights from NK cell research may one day lead to more successful bone marrow transplants.

When NK cell inhibitory receptors that recognize "self" detect a person's own HLA on a cell, the basic message: "This one is us and healthy, let it be!" usually prevents the destruction of the cell. Not coincidentally, many cancer cells have downregulated these "self" proteins and are thus recognized as prime targets for destruction.

"The 'missing-self' hypothesis was brilliant and foresighted, but we have been able to refine it in several important ways," says Dr. Lewis Lanier, professor and vice chair of the Department of Microbiology and Immunology at the University of California, San Francisco.

"When NKs and potential target cells meet, we now see the inhibitory receptors acting more like a dimmer switch than an on-off switch. Information is interpreted by an ana-

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Cancer Research Highlights

Prostate Cancer Risk Calculator Available Online

Researchers have developed an online statistical tool for estimating an individual's risk of developing prostate cancer. The risk calculator is designed to help certain men and their physicians evaluate the potential risks and benefits of being screened for prostate cancer. It is available at http://www.compass.fhcrc.org/edrnnci/bin/calculator/main.asp.

The calculator takes into account prostate-specific antigen (PSA) testing, family history, rectal examinations, and history of a prior negative prostate biopsy. Though PSA testing is widely used to assess prostate cancer risk, it does have limitations. Men with normal PSA levels can develop prostate cancer, while some men without prostate cancer can have abnormal levels.

"This risk calculator model uses variables that go beyond only PSA level to help patients and physicians decide whether a prostate biopsy should be performed," write Dr. Ian Thompson, of the University of Texas Health Science Center at San Antonio, and his colleagues in the April 19 *Journal of the National Cancer Institute (JNCI)*.

The calculator was developed using data from 5,500 men in the placebo group of the Prostate Cancer Prevention Trial; it is appropriate for men age 55 or older who have had recent PSA testing and rectal exams but no history of prostate cancer. The researchers say that the calculator improves the accuracy of PSA testing, but the use of PSA testing alone in prostate cancer screening has yet to be shown to save lives.

"The hope is that the risk calculator helps us do a better job selecting patients for biopsy," says co-author Dr. Howard Parnes of NCI, adding, "We need to be careful about how we apply the test." He raises the possibility that the calculator could lead to a large increase in the overall number of biopsies. This, in turn, could increase the overdiagnosis and overtreatment of the disease by detecting and treating cancers that would never have come to clinical attention were it not for screening.

A *JNCI* editorial discusses the critical need for accurate biological markers associated with life-threatening prostate cancer. "Once we have the ability to assess multiple risk factors in populations for which the long-term outcomes are known," approaches like the risk calculator will help identify those men who will benefit from active treatment, writes Dr. H. Ballentine Carter of the Johns Hopkins School of Medicine.

Elderly Female Cancer Survivors Face Functional Limitations

Elderly cancer survivors face quality-of-life issues that currently are not well understood. A large population-based cohort study published in the April 19 *JNCI* sought to clarify the limitations in daily activities faced by older women who have undergone cancer treatment.

In 1986, the Iowa Women's Health Study originally accrued 37,233 postmenopausal cancer-free women who were then followed for cancer occurrence through a link to the regional Surveillance, Epidemiology, and End Results cancer registry. Through a follow-up questionnaire, limitations in daily activities such as walking, housework, or meal preparation were assessed in 1997 for both cancer survivors and women who never had cancer.

Cancer survivors were divided into three postdiagnosis categories for analysis: less than 2 years, between 2 and 5 years, and 5 or more years. Other factors known to be associated with functional limitations, such as smoking, body mass index, and some chronic medical conditions, were included in the analyses.

Women returning the questionnaire less than 2 years after a diagnosis of cancer were significantly more likely to report functional limitations than women who never had cancer. Between 2 and 5 years after diagnosis, women were significantly more likely to report some but not all of the limitations listed on the questionnaire than women who never had cancer. Women who had been diagnosed more than 5 years previously were significantly more likely to report limitations in activities requiring strength and mobility than women who never had cancer.

The investigators conclude that "these findings support the need for interventions to prevent and reverse functional decline among elderly long-term cancer survivors." In an accompanying editorial, Drs. Julia Rowland and Rosemary Yancik from NCI's Office of Cancer Survivorship

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(Highlights continued from page 4)
stress the need for incorporation of quality-of-life interventions into all stages of cancer treatment. They note that, "…with growing numbers of cancer survivors living 5 or more years after their diagnosis, the scope of quality cancer care must broaden beyond the limited focus on cure to one that fosters health promotion and minimizes dysfunction or disability after illness."

Parents Need Help Talking to Children about Their Cancer

"I thought that before…there was no cure from it; that you just died basically." That's what a 10-year-old girl said to British researchers about her mother's breast cancer diagnosis. After conducting the study about communication between children and a parent with cancer, the researchers concluded that parents diagnosed with cancer would likely benefit from support and assistance in talking with their children about their situation.

In the study, an early online release in the *British Medical Journal*, Dr. Alan Stein and colleagues from Oxford University also found that the children in the study—who ranged in age from 6 to 18—often already suspected or knew something was wrong before their parents finally told them about the cancer, and many of the children over 12 wanted more information about it than they got from their parents.

The research team conducted home-based interviews about family communication with 37 women diagnosed with breast cancer being treated at a single cancer center. They then conducted interviews with the women's children (31 altogether) about their experiences with their mothers' illness. Many children found it especially distressing to see the effects of chemotherapy on their mothers, the researchers found, and also had wildly different interpretations of what the different treatments their mothers were undergoing actually meant for their prognosis.

"Parents are often unaware how much their children know and, often reeling from the diagnosis themselves, may not be in the best position to decide what and how to tell them," the researchers wrote. Families "may need considerable help in dealing with communication…and determining how support could be provided for their children as well as themselves."

More information on communicating with children about a parent's cancer is available from NCI and the American Cancer Society. ◆

Funding Opportunities

Small Grants Program for Cancer Epidemiology

Announcement Number: PAR-06-294
New Application Receipt Dates: July 20, 2006; Nov. 20, 2006; March 20, 2007; July 20, 2007; Nov. 20, 2007; March 20, 2008; July 21, 2008; and Nov. 21, 2008.

This is a renewal of PAR-04-159 and will use the R03 award mechanism. For more information, see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3405. Inquiries: Dr. Mukesh Verma—vermam@mail.nih.gov

Mechanisms of Alcohol-Associated Cancers

Announcement Number: PA-06-269
New Application Receipt Dates: June 1 and Oct. 1, 2006; Feb. 1, June 1, and Oct. 1, 2007; Feb. 1, June 1, and Oct. 1, 2008; Feb. 1, 2009.

This funding opportunity will use the R01 award mechanism. For more information, see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3392. Inquiries: Dr. Sharon Ross—rosssha@mail.nih.gov

Mechanisms of Alcohol-Associated Cancers

Announcement Number: PA-06-270
New Application Receipt Dates: June 1 and Oct. 1, 2006; Feb. 1, June 1, and Oct. 1, 2007; Feb. 1, June 1, and Oct. 1, 2008; Feb. 1, 2009.

This funding opportunity will use the R21 award mechanism. For more information, see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3393. Inquiries: Dr. Sharon Ross—rosssha@mail.nih.gov

In Utero Exposure to Bioactive Food Components and Mammary Cancer Risk

Announcement Number: PA-06-277
New Application Receipt Dates: June 1 and Oct. 1, 2006; Feb. 1, June 1, and Oct. 1, 2007; Feb. 1, 2008.

This is a renewal of PA-05-059 and will use the R21 award mechanism. For more information, see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3395. Inquiries: Dr. Cindy D. Davis—davisci@mail.nih.gov

Understanding the Effects of Emerging Cellular, Molecular, and Genomic Technologies on Cancer Health Care Delivery

Announcement Number: PA-06-280
New Application Receipt Dates: June 1 and Oct. 1, 2006; Feb. 1, June 1, and Oct. 1, 2007; Feb. 1, June 1, and Oct. 1, 2008; Feb. 1, 2009.

This funding opportunity will use the R01 award mechanism. For more information, see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3397. Inquiries: Dr. Louise Wideroff—wideroff@nih.gov ◆

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log, not a binary process," he explains. The cell essentially combines signals from a number of inhibitory and activating receptors to arrive at the final destroy-or-ignore decision.

Over time, NK cells have waged a kind of war with viruses in the body. NK cell receptors have evolved to recognize specific molecules that mark certain cancer signatures and viruses, such as human cytomegalovirus.

But viruses—and no doubt some cancers—also persist by evolving to outsmart the immune system of their potential host, and "some of the more deadly cancers have also evolved a way to silence the genes coding for the proteins recognized by NK cell activating receptors," suggests Dr. Lanier.

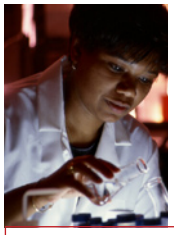
A few years ago, with NCI support, Dr. Lanier's lab identified molecules that are preferentially expressed on tumors for an important activating receptor known as NKG2D. Certain cancers may have evolved a way to turn off genes that encode for these molecules, and thus deceived the NK cell. "If we could develop ways to turn these genes back on, we would be much closer to a vaccine for cancer," says Dr. Lanier. ◆

By Addison Greenwood

CCR Grand Rounds

May 2: Dr. Chi V. Dang, Professor of Medicine, Oncology, Pathology and Cell Biology, The Hopkins Family Professor in Oncology Research; Vice Dean for Research, Johns Hopkins University School of Medicine. "Global Genomic Mapping of the Myc Target Gene Network and Tumorigenesis."

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. ◆



Featured Clinical Trial

Immunotherapy for Advanced Pancreatic Cancer

Name of the Trial
Phase II Study of Anti-Cytotoxic T-Lymphocyte-Associated Antigen-4 Monoclonal Antibody (MDX-010) in Patients with Locally Advanced or Metastatic (Stage IV) Pancreatic Adenocarcinoma (NCI-05-C-0141). See the protocol summary at http://cancer.gov/clinicaltrials/NCI-05-C-0141.

Principal Investigator
Dr. Richard Royal, NCI Center for Cancer Research

Dr. Richard Royal

Why This Trial Is Important
When foreign cells invade the body, the immune system mounts an immune response to the invading cells and kills them. The immune system is also capable of mounting a response to tumor cells. Often, however, the body's immune response isn't strong enough to completely destroy tumors.

During an immune response, cells signal each other in complex ways that serve to start, stop, or control the intensity of the response. Molecules found on many types of cancer cells stimulate certain immune system cells (called cytotoxic T lymphocytes, or activated T cells) to attack the cancer cells. Once the attack has started, however, the activated T cells produce a molecule called cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4). This molecule then produces a signal that tells the T cells to stop their attack. This T-cell inhibition helps prevent normal cells from being harmed by an immune response, but it may also prevent the immune system from destroying malignant tumors. Researchers hope that blocking CTLA-4's inhibitory signal will lead to a more robust immune response against tumors.

In this trial, researchers are using a monoclonal antibody called MDX-010 to treat patients with advanced pancreatic cancer. MDX-010 binds to and blocks the activity of CTLA-4.

"We know that T lymphocytes infiltrate pancreatic tumors in great numbers, but the tumors present an immunosuppressive environment," said Dr. Royal. "We hope that MDX-010 will help lymphocytes overcome this immunosuppression and allow the patient's own immune system to destroy their cancer."

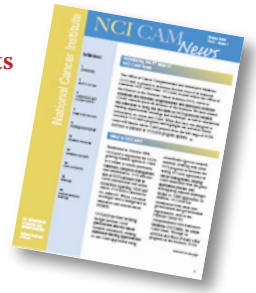
Who Can Join This Trial
Researchers will recruit up to 82 patients aged 18 or over with unresectable or metastatic (stage IV) pancreatic adenocarcinoma. See the list of eligibility criteria at http://cancer.gov/clinicaltrials/NCI-05-C-0141.

Study Site and Contact Information
The study is taking place at the NIH Clinical Center in Bethesda, Md. For more information about this trial, call the NCI Clinical Studies Support Center toll free at 1-888-NCI-1937. This call is confidential. ◆

An archive of "Featured Clinical Trial" columns is available at http://cancer.gov/clinicaltrials/ft-all-featured-trials.

Notes

NCI CAM Newsletter Debuts



NCI CAM News, a new biannual newsletter produced by NCI's Office of Cancer Complementary and Alternative Medicine, features the latest news on NCI's complementary and alternative medicine (CAM) activities. Content includes highlights of NCI-sponsored CAM research; resources for researchers, such as funding opportunities and grant-writing workshops; upcoming meetings and lectures; and information about CAM modalities for cancer. The free newsletter is available online at http://www.cancer.gov/cam/newsletter/home.html. To subscribe, go to https://list.nih.gov/cgi-bin/wa?SUBED1=nci_cam_news&A=1.

Breast Cancer Video Available

A new, free educational video, *Moving Beyond Breast Cancer,* for women finishing breast cancer treatment is now available.

Most women finishing breast cancer treatment are eager to put the cancer experience behind them and get back to normal. However, the time immediately following treatment can be particularly difficult, with a wide range of emotions and reactions.

The 23-minute video features vignettes of women in different life stages who share their concerns and experiences about body changes, emotions, relationships, and new perspectives. Breast cancer surgeon Dr. Susan Love also provides medical insight on common reactions of breast cancer survivors in each of these areas.

The video was funded by an NCI grant to the UCLA School of Public Health and the Jonsson Comprehensive Cancer Center. The Susan G. Komen Foundation provided funding for a portion of duplication and distribution costs. Copies in VHS or DVD formats are available by contacting NCI's Cancer Information Service toll free at 1-800-4-CANCER (1-800-422-6237) or online at http://www.cancer.gov.

NCI Staff Win Plain Language Awards

NCI was well represented among the winners of this year's Plain Language Awards Program, which honors staff whose work best exemplifies the clear and concise writing that helps improve communication within NIH and among NIH, other government entities, and the public. Winners were honored at an April 19 ceremony hosted by NIH Director Dr. Elias Zerhouni.

Nearly a quarter of the winning entries this year were written by NCI staff. Two projects won Outstanding Awards: "Graphic Standards for Use of NCI Logo," by Donna Bonner, Paul LaMasters, Malka Scher, Walt Burroughs, Del Harrod, Kathryn Hollen, Elizabeth Johnson, and David Fridberg; and "When Cancer Returns," by Louise Cunningham, Lori Keesey, Susan Spangler, Rhonda DeJoice, and Melinda Moyer.

Excellent Awards went to: "NCI Office of Communications Orientation Resources," by Robyn Bason, Cheryl Burg, Ilene Burstyn, Kevin Broun, Nina Ghanem, Tanisha Gregory, Cindy Lollar, Sahil Malik, Henry Ostapiej, Nicole Saiontz, and Valerie Secker; and "Understanding Cancer," by Donna Kerrigan, Miguel Monroy, and Jeanne Kelly. Seven other NCI projects received Honorable Mention awards. ◆

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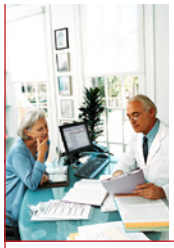
determine if they have activity against new molecular targets.

NCI's Cancer Therapy Evaluation Program (CTEP), meanwhile, has had great success working with industry to test combinations of targeted agents. While targeted agents are powerful in their own right, the research community and industry agrees that combining targeted agents will greatly increase their efficacy, and in fact may be essential. To date, CTEP has begun some 100 clinical trials featuring combinations of targeted agents, most of which have been started in the past 2 years.

Finally, through partnerships with extramural investigators, industry, and other private entities in the areas of screening, imaging, and preclinical pharmacology, we are moving to formalize a cancer therapeutics development consortium. Through this partnership we will conduct the so-called phase 0 studies to facilitate rapid screening of new targeted agents in humans before taking them into more full-scale development. The program also will launch a new national clinical target validation lab to find new ways to analyze the effects of small-molecule anticancer drugs.

NCI has made a major commitment to supporting the development of genomic and molecular assays to identify the patients most likely to benefit from a particular therapy regimen. As cancer researchers become more adept at developing molecular profiles of individual patients' tumors, we will ensure that many more patients receive a treatment with the best chances of success. This is the true promise of molecularly targeted therapies. ◆

Dr. John E. Niederhuber
NCI Deputy Director and Deputy Director for Translational and Clinical Sciences



CCOP Profile

Southeast Cancer Control Consortium, Inc., CCOP

Principal Investigator: Dr. James N. Atkins • Administrator: Susan Tuttle, RN, CCRP • SCCC Operations Office, 2150 Country Club Road, Suite 200, Winston-Salem, NC 27104 • Phone: 366-777-3036 • Web site: http://www.southeastcancercontrol.org

Background

In 1986, Dr. Charles L. Spurr, a medical oncologist with Bowman Gray School of Medicine, developed the concept for the Southeast Cancer Control Consortium (SCCC). The consortium received NCI funding as a Community Clinical Oncology Program (CCOP) in 1987 and is designed to treat adult oncology patients as well as deliver community-based cancer prevention and control programs. In 1993, Dr. Spurr handed over leadership to Dr. James N. Atkins, a medical oncologist affiliated with Wayne Memorial Hospital in Goldsboro, N.C., and a clinical associate professor of internal medicine and oncology at Wake Forest University Health Sciences in Winston-Salem.

SCCC includes 122 physicians, among them oncologists, surgeons, urologists, and radiation oncologists. Its operations office is located in Winston-Salem and is staffed by five employees who oversee the daily functions of the program.

SCCC's mission is to offer clinical trials aimed at cancer prevention and control in the communities it serves, thus improving the quality of cancer treatment, reducing incidence through education, and reducing morbidity and mortality through early diagnosis.

Community Characteristics

In the beginning, 11 charter communities participated in SCCC. Now participation has grown to include 17 communities and 21 institutions within a 5-state area: Georgia, North Carolina, South Carolina, Tennessee, and Virginia. Each community has a designated community leader who is responsible for local coordination of participation in clinical trials and cancer prevention and control programs, and a study coordinator who assists the community leader in implementing CCOP activities in their community. The affiliation with local institutions provides patients with access to state-of-the-art clinical research trials in rural and medically underserved areas, where minority populations are as high as 45 percent.

Recruitment and Outreach Activities

Since 1987, SCCC has enrolled 9,501 participants in clinical trials. The population of SCCC's referral area exceeds 9 million people, with an average of 20.4 percent who are African American.

Accrual to clinical trials for minority populations is challenging, but on average, SCCC achieves a 15-percent minority enrollment for its trials. Minority nurse recruiters have been used in several communities to provide cancer education and promote clinical trial research.

In addition to its funding as an NCI CCOP, SCCC collaborates with eight NCI-funded clinical trial cooperative group research bases, including the National Surgical Adjuvant Breast and Bowel Project, for which it is the highest accruing CCOP for treatment studies; the Cancer and Leukemia Group B, for which it is the second-highest accruing CCOP overall; and the Southwest Oncology Group, in which SCCC recruits patients for cancer-treatment and cancer-control studies. Other research affiliations are with the Radiation Therapy Oncology Group, the Cancer Trials Support Unit, the University of Rochester Cancer Center, the University of Michigan Cancer Center, and the Comprehensive Cancer Center of Wake Forest University. SCCC receives its clinical trial protocols and processes the resulting data through the eight research bases; patients are recruited to clinical trials through the CCOP itself.

Other Key Facts

SCCC was the number-one accruing CCOP for the Breast Cancer Prevention Trial and the Study of Tamoxifen and Raloxifene Trial. It was the number-two accruing CCOP for the Prostate Cancer Prevention Trial and the Selenium and Vitamin E Cancer Prevention Trial.

This year, Dr. Atkins was recognized for his outstanding contribution as a community investigator by the Association for Community Cancer Centers, and in March, he received the NCI Harry Hynes Award for outstanding dedication and commitment in bringing clinic trials to the community. ◆

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. Contact the *NCI Cancer Bulletin* staff at ncicancerbulletin@mail.nih.gov.