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Billionaires Boost Global Fight Against Tobacco

Microsoft founder Bill Gates and New York Mayor Michael Bloomberg have pledged $500 million to fight the growing tobacco epidemic in developing countries. The investment will help governments implement proven programs and policies for reducing tobacco use. The announcement came at a press briefing in New York City on July 23.

"We are thrilled by this remarkable commitment to global tobacco control," said Dr. Robert Croyle, director of NCI's Division of Cancer Control and Population Sciences. "NCI will continue to fund research that informs the programs and policies supported by this important initiative," he noted.

The World Health Organization (WHO) has established MPOWER, a package it describes as the six most important and effective tobacco control efforts: monitor tobacco use and prevention policies; protect people from tobacco smoke; offer help to quit tobacco use; warn about the dangers of tobacco; enforce bans on tobacco advertising, promotion, and sponsorship; and raise taxes on tobacco.

The strategies are "a rigorous approach to stopping the tobacco epidemic," according to Mr. Bloomberg, whose foundation supported their development. However, despite strong evidence of effectiveness and public support, only about one in five countries has fully implemented any of the five key policies, and no country has fully implemented all six.

The billionaire philanthropists hope that will soon change. Mr. Bloomberg has pledged an additional $250 million over 4 years, on top of a

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Cancer Research Highlights

Panel Recommends Against PSA Testing in Men 75 or Older

In updated recommendations released today, the U.S. Preventive Services Task Force (USPSTF) is advising against the routine use of prostate-specific antigen (PSA) testing to screen for prostate cancer in men age 75 and older. Published in *Annals of Internal Medicine*, the recommendations state that the potential harms of PSA testing for men in this age group outweigh any benefits, and that there is "adequate evidence that the incremental benefits of treatment for prostate cancer detected by screening are small to none."

For men under 75, the panel concluded that there was inadequate evidence to say whether "treatment for

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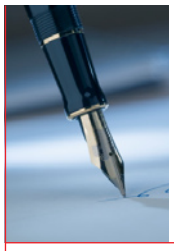

Guest

Director's Update

Personalized Medicine—BIG Health

Excitement has been building around the concept of personalized medicine for several years. The promise is a new era in which medicine is personalized, preemptive, predictive, and focused on patient participation.

Certainly, the science that is enabling a highly individualized approach has shown explosive growth. For example, just since January of this year, dozens of genes have been correlated with cancer and other diseases, any number of which may eventually be clinically validated as "biomarkers" to identify which patients will benefit from certain therapies. These novel genetic abnormalities may also serve as targets for new drugs. More and more genetically based diagnostic products or new targeted therapeutics are in development or being marketed.

In addition, an increasing number of academic medical centers and health care providers are initiating system-wide activities meant to make clinical care better tailored to individual patients. The Baylor College of Medicine, for example, is building a new hospital from the ground up with a specific focus on personalized, genetic-based medicine.

Although much progress is being made, the groups that will be essential to the success of personalized medicine too often are still operating as silos. There has been no systematic, national endeavor to connect all the requisite constituencies and capabilities together into a seamless, networked process to demonstrate the feasibility and value of this new model for health care.

With the BIG Health Consortium, I'm pleased to announce that such an endeavor is now getting started. The BIG (Biomedical Informatics Grid) Health Consortium will be a public-private partnership comprised of all the key stakeholders in health care: patient advocates, health care providers, payers, product innovators, investors, and information technologists. Conceived at NCI, its mission is to show—in real settings, in real time—how and why personalized medicine works. Through a series of demonstration projects, the BIG Health Consortium will model a new approach in which clinical care, clinical research, and scientific discovery are linked. The key enabler for this linkage is the informatics infrastructure that NCI has already developed, the cancer Biomedical Informatics Grid (caBIG).

caBIG is connecting the world of cancer research and care through the "glue" of its interoperable tools and technology. NCI's designated Cancer Centers and Community Cancer Centers—which collectively treat millions of patients—are already adopting or adapting caBIG infrastructure in order to achieve connectivity within their walls, between each other, and with the larger biomedical enterprise. That same set of tools and technology can operate inside the BIG Health Consortium to connect all the participating organizations.

A BIG Health Consortium roundtable, scheduled for next month, will be the first time that interested parties gather to discuss the goals of this new initiative and how they can be made operational. The roundtable will serve as a way to gather those who see the essential unity of research and care, and who wish to define specific projects that can have an impact in the near-term. Among those that have already expressed a desire to participate—NCI Cancer Centers, Community Cancer Centers, personal genomics and pharmaceutical companies, molecular diagnostic firms, health care providers, pharmaceutical companies, and advocacy organizations—there is already a new "mega-community" starting to emerge that can share information. The BIG Health infrastructure will ultimately link with electronic health records and personal health records, enabling us to achieve what some have called the "rapid learning system." Such systems draw on networks of biomedical information to acquire knowledge and process it into practice much more quickly than is currently possible.

NCI leadership is very excited about this new initiative, BIG Health, and our hope is to have the broadest participation possible. NCI is inviting academic, advocacy, government, and commercial organizations to participate in the BIG Health Consortium. For more information, please contact me at mail@bighealthconsortium.org. ◆

Dr. Ken Buetow
NCI Associate Director for Bioinformatics and Information Technology

Cancer Research Highlights

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prostate cancer detected by screening improves health outcomes compared with treatment after clinical detection." In its report, the panel added that there is "convincing evidence that treatment for prostate cancer detected by screening causes moderate-to-substantial harms, such as erectile dysfunction, urinary incontinence, bowel dysfunction, and death. These harms are especially important because some men with prostate cancer who are treated would never have developed symptoms related to cancer during their lifetime."

The USPSTF is a panel of independent experts convened by the U.S. Agency for Healthcare Research and Quality. Opinions on this issue among urologists and prostate cancer researchers run the gamut, with some arguing that PSA testing in men 75 and older does indeed save lives.

Dr. Howard Parnes, chief of the Prostate and Urologic Cancer Research Group in NCI's Division of Cancer Prevention, notes that the potential harms of screening are well documented, while there is no evidence of a mortality benefit from routine PSA screening in men 75 or older, or in any age group.

The available evidence, he notes, "indicates that the benefit from treatment of a PSA-detected cancer is not likely to be seen for 10 to 15 years. But the potential harms of being treated now are immediate."

Even so, Dr. Parnes stresses, the recommendation is not an absolute. Clinicians and their patients may decide that PSA testing is the best course of action. "Every physician should still individualize care and shouldn't discriminate on the basis of age," he says.

Lapatinib Limits Growth of Breast Cancer Brain Metastases in Mice

Investigators from NCI's Laboratory of Molecular Pharmacology report that in a mouse model of breast cancer, the small-molecule inhibitor lapatinib (Tykerb) can cross the blood-brain barrier and prevent approximately 50 percent of large HER2-positive brain metastases. Their study appeared online July 29 in the *Journal of the National Cancer Institute*.

The drug trastuzumab (Herceptin) targets cancer cells that overexpress the protein HER2. These cells have shown a greater potential to spread (metastasize) to the brain, but trastuzumab, a large antibody molecule, cannot cross the blood-brain barrier to reach these metastatic cells.

Lapatinib, which is approved for the treatment of metastatic breast cancer, is a much smaller molecule that is capable of permeating the blood-brain barrier. Its effectiveness in clinical trials treating large secondary tumors in the brain has been limited, so the researchers wanted to see if it might be better at preventing the growth of these tumors when they are still small.

They injected mice with a breast-cancer cell line engineered to overexpress HER2. The mice received a low or a high dose of lapatinib, or a control solution, twice daily for 24 days. Those that received lapatinib in either dose developed half as many large metastases as those that received the control solution.

"What our model system shows is that lapatinib might prevent micrometastases from growing into life-threatening macrometastases," explained Dr. Patricia Steeg, senior author of the study. In the future, stated the authors, preventative therapy to suppress the growth of micrometastases could possibly be combined with standard treatments for large brain metastases, such as neurosurgery or radiation therapy.

Eliminating a Common Bacterium Reduces Risk of Second Gastric Cancer

Researchers in Japan have shown that when the bacterium *Helicobacter pylori* is eliminated in patients who are treated for early stage gastric cancer, the risk of developing a second gastric cancer decreases by two-thirds. Their report appeared August 2 in *The Lancet*.

H. pylori infects the stomachs of approximately half the people in the world and has been clearly linked to stomach problems, including peptic ulcers and cancer. Previous studies in animals have shown a preventive effect when the bacterium is eliminated, but results in human studies have been inconclusive.

The latest report, published by the Japan Gast Study Group, comes from an open-label study that included 544 patients aged 20-79 who were either newly diagnosed with gastric cancer and planning to undergo endoscopic surgery, or who had recently undergone surgery for gastric cancer. All patients had confirmed *H. pylori* infection.

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Those randomized into the test group received a combination of the antibiotics lansoprazole, amoxicillin, and clarithromycin twice a day for a week to prevent cancer recurrence, while those in the control group received standard care but no antibiotics.

The bacterium was eliminated from approximately 75 percent of patients who received the antibiotic regimen, and approximately 5 percent of patients from the control group. The only adverse effects of the antibiotic group with notable occurrence were soft stools and diarrhea. After 3 years of endoscopic monitoring, second gastric cancers occurred in 9 patients from the treated group and 24 patients from the control group.

An accompanying editorial discusses the benefits and drawbacks of widespread *H. pylori* screening and treatment, concluding, "Worldwide, gastric cancer kills more people [than colorectal cancer], and there is better evidence that *H. pylori* eradication can prevent mortality than there is for colonoscopy screening. Preventing gastric cancer by eradicating *H. pylori* in high-risk regions should be a priority."

Metastatic Process Disrupted by Targeting Tumor Cells' Cytoskeleton

Some tumor cells that travel to distant sites in the body and lay dormant for long periods require help from factors in their immediate environment to eventually develop into metastases, researchers reported in the August 1 *Cancer Research*. This conversion from hibernation to active growth, they found, is initiated by a reorganization of the dormant cells' interior cytoskeletal architecture, induced by signaling molecules immediately outside the cell in the extracellular matrix (ECM), and could be disrupted by targeting a molecular pathway that regulates the cytoskeleton

Led by Dr. Dalit Barkan from NCI 's Laboratory of Cancer Biology and Genetics, the study used mouse models and a three-dimensional (3-D) culture system, in which signaling factors typically found in the tumor microenvironment could be introduced.

"We show that the switch from quiescence to proliferative metastatic growth is strongly influenced by interactions with the ECM," they wrote. The ECM surrounds cells and contains proteins, often signaling molecules, that other cells secrete.

Using cellular imaging techniques, the researchers showed that one protein component of the ECM, fibronectin, initiated reorganization of the dormant cells' interior cytoskeleton. This reorganization set the stage for the switch from quiescence to metastatic growth and was mediated by an enzyme called MLC kinase. In both the mouse models and the 3-D culture system, metastatic growth could be tamped down by interfering with MLC kinase activity.

"Our results suggest that targeting pathways affecting the cytoskeleton… may provide an important means of inhibiting the switch from tumor cell dormancy to clinical metastatic disease," the authors concluded. "This approach, perhaps in combination with immunotherapeutic strategies, may reduce the incidence of tumor recurrence from disseminated, dormant tumor cells."

Agent Safe, Active in Hormone-Refractory Prostate Cancer

An investigative agent that blocks the production of testosterone in tissue is a safe treatment for men with hormone-refractory prostate cancer and shows promising signs of clinical activity, British researchers report.

Published online July 21 in the *Journal of Clinical Oncology*, results from a 21-patient phase I trial involving the drug abiraterone acetate showed that it was safe and led to reductions in prostate-specific antigen (PSA) levels by as much as 90 percent in some patients. A majority of patients given the drug also had reductions in tumor size, both in the primary tumor and in metastatic tumors.

The trial, led by Dr. Johann de Bono from the Institute of Cancer Research, where the drug was developed, involved men with advanced, hormone-refractory (also called castrate-resistant) prostate cancer.

Some study participants have been taking the drug for as long as 2.5 years, "and with continued use of abiraterone they were able to control their disease with few side effects," Dr. de Bono explained in a news release. "A number of patients were able to stop taking morphine for the relief of bone pain."

Abiraterone—which has been licensed to the company that funded the trial, Los Angeles-based Cougar Biotechnologies—works by blocking the activity of CYP17, a key enzyme that helps cells produce androgen and estrogen. It's being tested in phase II and III studies of this same patient population.

While the findings have received a significant amount of media attention, particularly in the British press, some U.S. researchers urge caution. "A PSA decline or tumor shrinkage are only evidence of activity, and activity

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only means there's a need for a good randomized trial," said American Cancer Society Chief Medical Officer Dr. Otis Brawley. "The bottom line for patients and the public is we need a randomized trial showing longer survival time or improved quality of life as the endpoint."

Gene Signatures May Help Predict Lung Cancer Survival

A new study provides perhaps the strongest evidence yet that profiling the activity of genes in lung tumors yields information that can help physicians and patients make treatment decisions. Yet the researchers caution that lung tumors are genetically diverse and it may be difficult to develop a single gene signature that could reliably classify all patients. The findings appeared online in *Nature Medicine* July 20.

The NCI Director's Challenge Consortium for the Molecular Classification of Lung Adenocarcinoma analyzed 442 lung tumors from patients with known health outcomes. Previous research suggested that lung tumor signatures may provide information such as whether patients may benefit from aggressive treatments, but the signatures and the results often varied from study to study.

The Consortium developed new gene signatures, and their prediction models produced risk scores that correlated with the actual outcomes of patients. Most models performed better with clinical data, leading the researchers to conclude that prognostic models for early stage lung cancer should include both molecular and clinical information, as has been done in prostate and breast cancers.

Drs. David Beer of the University of Michigan Comprehensive Cancer Center and James Jacobson of NCI's Cancer Diagnosis Program led the study, which included a blinded validation step to assess the performance of new gene signatures.

"We put the Consortium together and initiated the study both to explore the challenges involved in carrying out these large confirmation studies for molecular signatures and to identify strategies that could be used to overcome these challenges," said Dr. Jacobson. "I think this work will be a reference point for how these studies should be carried out."

In addition to NCI and the University of Michigan, the Consortium includes researchers from the H. Lee Moffitt Cancer Center, Memorial Sloan-Kettering Cancer Center, Dana-Farber Cancer Institute, and the Ontario Cancer Institute. ◆

(Fight Against Tobacco continued from page 1)

$125 million-commitment made in 2005. The Bill and Melinda Gates Foundation will invest $125 million over 5 years, including a $24 million grant to the Bloomberg Initiative.

"Our commitments will help governments confront the tobacco epidemic by implementing the proven MPOWER package," said Mr. Bloomberg in a statement. "This means [ensuring] well-staffed tobacco control programs, raising tobacco taxes, running hard-hitting public information campaigns, creating comprehensive smoke-free public places, and banning tobacco advertising."

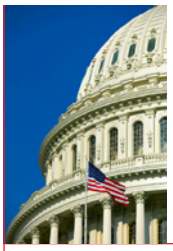
There are one billion smokers in the world. In recent years, the epidemic of tobacco use has shifted from high-income nations, where tobacco use is generally decreasing, to low- and middle-income nations. By 2030, global tobacco deaths will reach 8 million per year, with 80 percent occurring in developing nations. WHO warns that unless urgent action is taken, more than one billion people could be killed by tobacco during the 21st century.

The Bill and Melinda Gates Foundation funds will be used to build economic evidence to support tobacco control and to educate the public about the harmful effects of tobacco. Gates Foundation funds will also support efforts to prevent the epidemic from taking hold in sub-Saharan Africa, where smoking rates have traditionally been low.

"Tobacco-caused diseases have emerged as one of the greatest health challenges facing developing countries," said Mr. Gates in a press release. "The good news is we know what it takes to save millions of lives, and where efforts exist, they are working." Tobacco control is a new focus for the Gates Foundation, but the organization has considerable experience working with governments and civic organizations on diseases such as malaria.

In their announcement, both Mr. Bloomberg and Mr. Gates called on government and business leaders to make the fight against tobacco a higher priority by increasing resources for tobacco control and implementing proven policies to reduce tobacco use.

"The Bloomberg and Gates effort will not only save millions of lives but will also serve as a series of natural experiments to determine the impact of new policies that could be utilized in the United States, especially if the Food and Drug Administration is granted the authority to regulate tobacco," said Dr. Croyle. ◆



Legislative Update

Senators Seek Additional Funds for NIH and NCI

At a July 16 hearing to consider the NIH appropriation for fiscal year 2009—held by the Senate Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies—the panel Chairman Senator Tom Harkin (D-IA) and Ranking Minority Member Arlen Specter (R-PA) announced plans to introduce supplemental spending bills to add $5.2 billion to the NIH budget, which is currently about $29 billion.

Their aim is to restore the purchasing power that NIH and its Institutes have lost during the past 5 years of flat or lower-than-inflation budget increases approved by Congress. The proposed increase will include an additional $1.2 billion for NCI, in line with the Institute's recommendations in its annual bypass budget request.

"It's just a scandalous situation to have seen NIH cut in recent years," said Senator Specter, who had just finished treatment for a recurrence of Hodgkin lymphoma. Despite the current constraints on federal domestic spending, "We have to do something about it," he said.

Chairman Harkin noted that the President recently signed an earlier supplemental appropriations bill which included an additional $150 million for NIH ($25.5 million for NCI) in the current fiscal year.

NIH Director Dr. Elias Zerhouni, NCI Director Dr. John Niederhuber, and several other NIH institute directors testified at the hearing. Senator Specter asked about NCI's response to a previous request by the subcommittee for a best estimate of the cost for a "major frontal assault" towards curing cancer, to which Dr. Niederhuber replied, "We've felt that if we could add $2 billion a year [to the NCI budget], each year, for the next 5 years, that would go a long way toward helping us build capacity within our country in terms of attracting young people, and attracting disciplines that haven't previously worked on cancer." ◆

FDA Update

FDA Orders New Restrictions on ESA Use

The Food and Drug Administration (FDA) is requiring changes to the labels of three anti-anemia drugs—Aranesp (darbepoetin alfa), Procrit (epoetin alfa), and Epogen (epoetin alfa)—to revise their indications for cancer patients.

In a "complete response and safety labeling order" issued on July 30 to the drugs' manufacturer, Amgen, the FDA said the revised labeling must state that the medications should not be used in patients "when the anticipated outcome is cure." The FDA ordered the changes using new authorities granted to the agency last year that allow it to directly require labeling changes to address emerging safety issues.

The revised labels must also state that the drugs, called erythropoiesis-stimulating agents (ESAs), should not be used unless a patient's hemoglobin level dips below 10 g/dL; and the revision removes language indicating the drug can be safely used until patients' hemoglobin reaches 12 g/dL.

Amgen has 5 days to appeal the order or 15 days to submit a biologics license application supplement to the FDA with the revised labeling. The change was "consistent with our expectations," Amgen noted in a brief statement, adding, "We will soon be communicating the revised product labeling for ESAs to both physicians and patients."

The FDA did not require barring the drugs in patients with breast cancer or head and neck cancer, for which available data suggest the risk of serious adverse events may be greatest. At its March 2008 meeting, the FDA Oncologic Drugs Advisory Committee recommended instituting such a restriction. That meeting came on the heels of a meta-analysis of 51 phase III clinical trials, which found a 57 percent increased risk of venous thromboembolism (VTE), or blood clots, and a 10 percent increased mortality risk in cancer patients who were treated with ESAs. ◆

Profiles in Cancer Research

Dr. Chad Mirkin

Professor of Chemistry, Director of the International Institute for Nanotechnology, and Principal Investigator at the Center for Cancer Nanotechnology Excellence, Northwestern University

To say that Dr. Chad Mirkin is a high achiever would be an understatement. But beyond his many awards, honors, and prizes; beyond the fact that he is among the most commonly cited chemists in the world or that he has more than 70 patents in the field of nanotechnology, Dr. Mirkin seems happiest when he's talking about the science itself, and the impact he foresees for nanotechnology in medicine.

"Nano is game-changing," he says, "when you realize that *anything* you're dealing with will have different unique properties when you shrink it down to nanoscale."

A colleague of his in the Chemistry Department at Northwestern University, Dr. Fraser Stoddart, agrees. "Nanotechnology will ultimately change the culture as much as the Internet," he says. And on Dr. Mirkin's role in this revolution, he adds, "The creative life is not so easy to live, the more so in science. And yet, Chad has managed to live his with such passion, curiosity, and practical wisdom that he has invented large swathes of nanotechnology single-handedly."

Dr. Mirkin prefers to think of it as being in the right place at the right time.

The earliest years of his life were spent traveling in Asia, living with his parents and three older brothers in Korea and Malaysia.

"My dad was looking for something I don't think he ever found," mused Dr. Mirkin. "His own father had come from Russia, and I think he wanted us kids to become independent, self-reliant people, atypical of the parental programming kids typically experience in a suburban cocoon in America."

When he was 7 years old, the family returned to the United States and eventually moved to southwestern Pennsylvania, where he went to a one-room school for fourth grade, was interested primarily in basketball throughout high school, and didn't think much about chemistry. In graduate school at Penn State everything changed, however, thanks to a mentor in the Chemistry Department, Dr. Greg Geoffrey. "He ignited a real curiosity about chemistry and gave me the creative license to do what I wanted to," says Dr. Mirkin.

Dr. Geoffrey sent his prize student to the Massachusetts Institute of Technology to work with Dr. Mark Wrighton, a friend and colleague from graduate school at Caltech. "Dr. Wrighton was the major force in the early interdisciplinary research," recalls Dr. Mirkin. "He paved the path for many people by getting the chemistry community to begin to think about the consequences of miniaturization," which was the term that preceded nanotechnology in the 1990s.

Dr. Mirkin accepted a job, formally as an inorganic chemist, in Northwestern University's Chemistry Department, one of the best in the country. It was here, in 1996, that his lab began a journey of discovery that led to the heart of a new field.

"I'm a great proponent of tinkering," explains Dr. Mirkin. A nanoparticle is anything between 1 and 100 nanometers. One nanometer is a billionth of a meter, or roughly the size of a water molecule. Colloidal metals such as gold were at that time being used to build nanostructures, using chemical approaches that were hard to control and impossible to reverse at that scale. His group also is adept at popularizing these ideas. (See a tutorial on the university Web site.)

"We wondered what might happen if we could exploit the unique recognition features of specific strands of DNA," recalls Dr. Mirkin. To use DNA as an assembler, he explains, "You just attach the material you want to assemble, such as gold spheres, to a DNA strand that's been cut where you want, and then let it find its own base pair partner." It gets a bit more complicated, but the process "actually lets us manipulate nanoscale building blocks into the structures with the physical and chemical properties we are after—theoretically any structure—and build materials from the bottom up."

They published a letter in *Nature*, which would eventually be cited by some 2,000 subsequent papers and launch Dr. Mirkin's meteoric career. "We didn't foresee at the time all of the biological applications," he

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explained, "but I did have a 'holy smokes' moment when I realized this could lead to a whole new arsenal of diagnostic systems." His group's latest paper, published earlier this year in *Nature*, illustrates how the original idea has matured into an important sub-industry of materials synthesis: diagnostic and therapeutic applications.

Dr. Mirkin is gratified his work has had a catalytic effect on biology and engineering in such a revolutionary way. But when he tells his story, he is always the lucky guy whose enthusiasm and joy of the hunt infects everyone around him.

In 2004, he harnessed that energy to establish the world's first federally funded institute for nanotechnology research and education at Northwestern, one of the factors that earned him the NIH Director's Pioneer Award in its first year. "That was significant," he recalls gratefully, explaining that the half-million dollar annual prize for 5 years helped his group establish a strong presence in the biomedical field, and enabled them to develop high-risk ideas that would have been difficult to get funded by more conventional mechanisms.

When his father was diagnosed with cancer in 2002, Dr. Mirkin saw it as "slash and burn, with heavy doses of poison to follow," until his father's death. While Dr. Mirkin was in Bethesda accepting the Pioneer Award 2004, he began to talk to NCI about diagnostic applications of his technology. His laboratory at Northwestern is one of eight Centers of Cancer Nanotechnology Excellence funded under NCI's Alliance for Nanotechnology in Cancer.

He has high hopes that nanotechnologies like his own FDA-approved Verigene System—which uses nanoparticle probes to detect nucleic acid targets and proteins—will be instrumental in studying and, eventually, treating and curing cancer.

"We are now close to nanoparticle diagnostic systems that can be applied away from a centralized lab at the point of care, with rapid results," he says. "These are the things we should be talking about in nanotechnology—pragmatic applications we can accomplish in a real time frame. The real nanotech pioneers aren't those with just grand ideas, but rather those who make them happen." ◆

By Addison Greenwood

Notes

DCTD Leadership Appointments Announced

NCI recently announced two appointments to top leadership positions within the Division of Cancer Treatment and Diagnosis (DCTD). Dr. Jeffrey Abrams was selected as associate director of the DCTD Cancer Therapy Evaluation Program (CTEP) and Dr. James Tatum was chosen as the associate director of the DCTD Cancer Imaging Program (CIP).

Dr. Jeffrey Abrams

Dr. James Tatum

Dr. Abrams, who served as CTEP's acting associate director for the past year, joined DCTD in 1993 as a clinical research scientist to oversee the breast cancer treatment trials portfolio and conduct clinical trials at the NIH Clinical Center and the National Naval Medical Center.

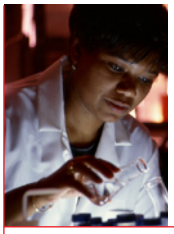
Dr. Tatum joined CIP in 1998 as a special assistant to the associate director. In 2006, Dr. Tatum assumed leadership of CIP's Molecular Imaging Branch. Since July 2007, he has used his expertise in the areas of molecular imaging and imaging drug development to guide CIP as its acting associate director.

DCCPS Report Highlights 10 Years of Progress

NCI's Division of Cancer Control and Population Sciences (DCCPS) recently posted online *2007 Overview and Highlights*, a report describing the institute's return on 10 years of investment in DCCPS since its creation in 1997.

The report highlights progress in research areas including epidemiology and genetics; cancer prevention and control; detection and diagnosis; tobacco control; diet, weight and physical activity; health communication; risk factor monitoring and prediction; quality of care and health services outcome; health disparities; cancer survivorship; surveillance; and research dissemination.

To order a free copy of the report, go to www.cancer.gov/publications or call NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237). ◆



Featured Clinical Trial

Refining Treatment for Gastrointestinal Stromal Tumors

Name of the Trial
Phase III Randomized Study of Imatinib Mesylate with Versus without Bevacizumab in Patients with Metastatic or Unresectable Gastrointestinal Stromal Tumor (SWOG-S0502). See the protocol summary at http://cancer.gov/clinicaltrials/SWOG-S0502.

Principal Investigators
Dr. Charles Blanke and Dr. Margaret von Mehren, Southwest Oncology Group; Dr. George Demetri, Cancer and Leukemia Group B; Dr. Vivien Bramwell, NCIC-Clinical Trials Group

Why This Trial Is Important
Gastrointestinal stromal tumors (GIST) are a type of sarcoma that usually forms in the stomach or small intestine, but it can arise anywhere in the gastrointestinal tract. About 5,000 new cases of GIST are diagnosed in the U.S. each year.

The Food and Drug Administration's approval of the drug imatinib (Gleevec) for the treatment of GIST in 2002 dramatically improved the outlook for patients with tumors that cannot be surgically removed (unresectable) or that have spread (metastatic). In previous clinical trials, imatinib helped block tumor growth in more than 80 percent of patients with advanced GIST. Unfortunately, however, patients frequently develop resistance to imatinib after an average of about 24 months.

Recent studies suggest that blocking the growth of new blood vessels (angiogenesis) may help prolong the time during which GISTs don't grow and thus prolong progression-free survival. The biological agent bevacizumab (Avastin) blocks the activity of a protein called VEGF that promotes angiogenesis. High levels of VEGF in GIST usually indicate that the cancer is more aggressive.

In this randomized trial, patients with unresectable or metastatic GIST will receive imatinib therapy with or without the addition of bevacizumab. Researchers hope that the combination of imatinib and bevacizumab will extend progression-free survival by 6 or more months.

"Imatinib works extremely well for most patients with advanced GIST, but we're trying to make it better by extending the time to imatinib resistance," said Dr. Blanke. "Additionally, we're trying to modify the imaging techniques we use to see whether the tumors are responding so that we can better determine the success of treatment for patients with GIST."

For More Information
See the lists of entry criteria and trial contact information at http://cancer.gov/clinicaltrials/SWOG-S0502 or call the NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237). The toll-free call is confidential.

This trial is eligible for special Medicare coverage. See Clinical Trials Covered Under the Medicare Anti-Cancer Drug National Coverage Decision. ◆

Funding Opportunities

For a complete listing of current NCI funding opportunities, please go to the HTML version of today's *NCI Cancer Bulletin* at http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_080508/page9. ◆

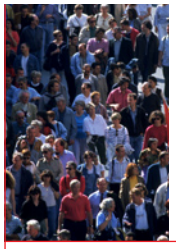
Special Issue on Personalized Drug Development

Don't miss our August 19 special issue of the *NCI Cancer Bulletin*, which will focus on how the process of drug development is changing to accommodate new research about targets for cancer therapy, as well as the advent of personalized medicine.

NCI Cancer Bulletin special issues are some of the most popular among our readership. Past special issues have focused on cancer prevention, NCI-Frederick, and childhood cancer. ◆

NCI Cancer Bulletin *Publication Break*

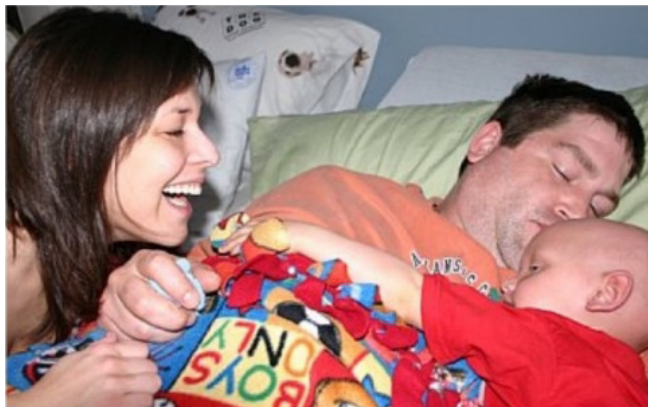
The *NCI Cancer Bulletin* will not be published on September 2. We will resume our usual twice-monthly publication schedule on September 9. ◆



Community Update

Lessons Learned from Katrina

The upside to mayhem and devastation caused by a natural disaster is that the rebirth of affected communities usually makes them stronger. This is what is happening to the oncology groups that participate in NCI's Community Clinical Oncology Program (CCOP) in the Gulf Coast region, which was devastated by Hurricane Katrina late in 2005.



Lake and his parents at the hospital in Little Rock, where they were able to continue his cancer treatment after Hurricane Katrina.

"We were not prepared for Katrina," admits Eric Anderson, the clinical trials coordinator and CCOP administrator at Ochsner Cancer Institute in New Orleans, one of three CCOPs affected by the storm that caught so many off guard.

Despite a lack of preparation, patients who were enrolled in clinical trials were able to continue their treatment at other hospitals, even as far away as Seattle, because of CCOP connections around the country.

"If a Katrina patient had come to us, it would have been easy to care for them," says Dr. Loren Tschetter, principal investigator at the Sioux Community Cancer Consortium in Sioux Falls, SD. "The mechanism of a national CCOP program ensures that these patients can be taken care of in an efficient and careful manner by experienced staff."

This was the case for Hewan Gebrehiwot, whose daughter, Wintana Solomon, was 5-years-old at the time and in treatment for acute lymphoblastic leukemia with the Louisiana State University Minority-based CCOP (LSU MB-CCOP) at Children's Hospital in New Orleans.

"I was so worried," recalls Mrs. Gebrehiwot. When the order came to evacuate, she drove her family to Atlanta to stay with friends, and checked in with the hospital at Emory University. "I showed them Wintana's paperwork, and they had no problem at all. They started the correct medicine right away."

Another Louisiana resident, Chantel Kiger, fled to Little Rock, AR, with her toddler son, Lake, who had been diagnosed with medulloblastoma earlier in the year and was just finishing his first month of chemotherapy after surgery to remove the tumor.

"The hurricane wasn't nearly as scary as learning that Lake's cancer had come back," she recalls.

With her son's medical records in hand, the hospital staff in Little Rock was able to notify the boy's New Orleans oncologist of his location and continue his course of treatment. "They did a phenomenal job of helping us to get the care that my son needed," says Ms. Kiger.

Three years later, there's good news to report. Both Wintana and Lake are in remission and have returned home with their families.

The CCOPs are also back to business, with emergency measures in place, including patient ID cards developed by or similar to the ones developed by ASCO, and other methods to track patients and recover medical records, should they need to evacuate again.

"Out of the Katrina catastrophe, a model program has evolved in which public and state institutions and community doctors who weren't previously engaged in clinical research are working together," says NCI's Dr. Worta McCaskill-Stevens, who helps to oversee the CCOP program in the Division of Cancer Prevention. She notes that the LSU MB-CCOP has enrolled more than 150 new cancer patients since the hurricane.

Mr. Anderson reports that the Ochsner CCOP has caught up with where it was before the storm, in terms of protocols and patients enrolled in trials.

"We have a lot of institutional pride and commitment to the CCOP mission," he says. "As we recovered from the storm, we looked back at the time when our CCOP had been hugely successful, and it felt like a quest to see how we could make it good again, in the face of this great adversity." ◆

By Brittany Moya del Pino