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Cancer Stem Cells May Help Brain Tumors Survive Radiation

Some brain tumors may contain small populations of cancer stem cells that are resistant to radiation therapy, and this may help explain why the disease often recurs after treatment, even when there are no detectable signs of cancer.

Researchers at Duke University Medical Center have found that cancer stem cells isolated from brain tumor tissues can survive radiation treatments. Although their DNA is damaged, these cells make repairs more efficiently than other tumor cells.

"We found that cancer stem cells could deal with DNA damage from both chemotherapy and radiation more readily than other cells and survive better," says lead investigator Dr. Jeremy Rich.

His team used a protein called CD133 to distinguish potential cancer stem cells from other cells in glioblastoma tumors, the most common form of brain cancer. The disease resists all treatments, and most patients survive only a year after diagnosis.

The new findings, published early online October 18 in *Nature*, point to a role for cancer stem cells in glioblastoma, and they add to growing evidence that these rare cells may be the critical targets for treating cancer.

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Director's Update

NCI Director's Swearing-In Remarks

Following are Dr. John E. Niederhuber's remarks made at his public swearing-in ceremony as NCI Director on October 18, 2006.

HHS Secretary Michael O. Leavitt officially swears in Dr. John E. Niederhuber as the 13th NCI Director.

Mr. Secretary, Dr. Zerhouni, fellow directors of the institutes and centers of the National Institutes of Health [NIH], honored guests, NCI colleagues, and my many friends: I am deeply indebted to all of you for being here today and for sharing with me this very special occasion in my life.

I want to express my gratitude to President Bush and to [Department of Health and Human Services/HHS] Secretary Leavitt for the privilege and distinct honor of serving as the director of the National Cancer Institute. I am profoundly humbled by your confidence in me and by the fact that you are willing to entrust me with the leadership and the distinguished his-

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(Brain Tumors continued from page 1)
Cancer stem cells were first reported in the brain in 2004. Dr. Peter Dirks of the Hospital for Sick Children in Toronto led a team that isolated brain tumor cells with some of the properties of stem cells. The cells could divide indefinitely, give rise to various types of cells, and form tumors when transplanted into mice.

The definition of a cancer stem cell has been controversial, and the Duke team did experiments to show that they were working with cancer stem cells or cells with similar properties. In one example, when a few hundred of these cells were transplanted into mice, they formed tumors that resembled the original tumors, even after being irradiated.

"This is an exciting study," says Dr. Dirks. "It's important to show that cancer stem cells are resistant to treatment because that will redouble our efforts to consider those cells as the most crucial for cancer therapy."

The study offers insights into the biology of the tumor that could be relevant to treating patients. Knowing that DNA repair was important, the researchers blocked the DNA-repair response in mice as a potential strategy for overcoming resistance.

It seemed to work—radiation treatments killed cancer stem cells in mice when drugs inhibited their "checkpoint" proteins, which regulate DNA repair.

This study provides the first evidence of a potential mechanism—enhanced DNA repair—that allows cancer stem cells in solid tumors to survive and that could be targeted by therapies, says Dr. Craig Jordan of the University of Rochester. His team has developed ways to selectively target leukemia stem cells while sparing normal cells.

"The efficacy with which the researchers could kill these cells with radiation in the presence of a checkpoint inhibitor was striking," notes Dr. Jordan. "This is proof of concept in the brain cancer field that it is possible to target malignant stem cells."

Whether the results will be clinically useful remains to be seen, but they will likely be welcomed by physicians who treat this deadly disease.

"This study is encouraging," says Dr. Paul Fisher of the Stanford Comprehensive Cancer Center. "It improves our understanding of the biology, and this is the only way we are going to move forward in treating glioblastoma." ◆

By Edward R. Winstead

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tory of this proud institution.

Never, in all the years of sitting on the edge of my patients' beds during late-evening rounds; of making the walk from the operating room to the family waiting area; of working in the lab with my students and fellows (some of whom are here today); of coming to Washington all those times to serve on committees for Vince, Sam, Rick, and, most recently, Andy—never did I picture myself standing at this podium at this time to accept the directorship of the National Cancer Institute.

And while I have been doing this job now for a year, I think it has only been in the past couple of weeks, since my official appointment, that the enormity of the responsibility of this position—the responsibility to our patients suffering with cancer—has really struck home.

On the day he formally proposed the National Cancer Act of 1971, President Nixon said, "The time has now come for us to put our money where our hopes are." But he also made it eminently clear that dollars weren't enough. "Money," Mr. Nixon continued, "can help set the stage for faster progress, but in the end it is our brainpower alone which can lead us to our goals."

President Nixon's words are even more fitting today. The momentum of our progress against cancer, and of biomedical research as a whole for all diseases, is occurring at a pace none of us could have predicted. For the very first time in more than 70 years that our country has kept statistics on cancer incidence and mortality, we have seen an actual, real decline in cancer deaths.

For every one of us here today, that is the hope—the promise—we have so desperately needed. This progress, this pace of discovery, and our nation's leadership position in biomedical research must not be taken for granted.

Today, even more so than in 1971, we face very real challenges, which test our ability to persuade the very brightest, the most visionary of our young people, to see the opportunities and the rewards of a career in biomedical research and patient care.

Our success—the ability to achieve our goals—depends on college students who see and who value the tremendous opportunities of a life immersed in scientific discovery: a life of service, of caring for those less fortunate. These young citizens need to have confidence that this great country will continue its investment in science. They need to be confident that productive careers await them.

NIH has long been the mechanism through which this great nation supports the world's premier biomedical research engine. Through its outstanding intramural laboratories and

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Cancer Research Highlights

Data on Genetic Susceptibility for Prostate Cancer Are Released

NCI recently released data from the Cancer Genetic Markers of Susceptibility (CGEMS) prostate cancer study, which could help identify genetic factors that influence the disease and affect development of new therapies.

"The immediate sharing of the database with the cancer research community will allow researchers to compare existing and developing information with CGEMS data to identify new genes associated with increased prostate cancer risk," said NCI Deputy Director for Advanced Technologies and Strategic Partnerships, Dr. Anna D. Barker.

CGEMS procured genetic samples of prostate cancer from more than 1,100 men with the disease and 1,100 men without it. The samples included over 680 million individual genotypes and 310,000 genetic variants. Finding genetic variations that differ in frequency between patient and control groups will help identify the location of multiple inherited genes that affect the risk of prostate cancer.

"CGEMS represents one of the first of a new generation of studies made possible by the Human Genome Project," added Dr. Gilles Thomas of NCI's Division of Cancer Epidemiology and Genetics and lead scientist of the project. "Through immediate data sharing, we hope to encourage other teams to make similar studies in cancer and other diseases rapidly accessible to speed progress in understanding the inherited causes of cancer."

Launched in February 2006, CGEMS is the largest comprehensive initiative to identify genetic risk factors for breast and prostate cancers, two of the most frequently diagnosed cancers in the United States. Similar data on breast cancer are now being generated and anticipated for release in early 2007.

CGEMS study data are available through NCI's cancer Biomedical Informatics Grid™ (caBIG™) at http://caIntegrator.nci.nih.gov/cgems/.

Recommended Colorectal Cancer Surgery May Be Underused

A new population-based study suggests that multivisceral resection—a surgical procedure recommended for patients with colorectal cancer that has not metastasized but that has affected organs adjacent to the colon or rectum—is drastically underused. Failure to use the procedure was associated with poorer overall survival rates, the study found.

Published in the October 18 *Journal of the National Cancer Institute (JNCI)*, the study used NCI's Surveillance, Epidemiology, and End Results (SEER) registry to review the care and outcomes of 8,400 patients who underwent surgery to remove colon or rectal tumors that had expanded into nearby organs. The study authors, led by Dr. Calvin H. L. Law of Toronto Sunnybrook Regional Cancer Center in Canada, noted that clinical guidelines recommend that such patients undergo multivisceral resection, which involves the removal of the tumor and the adjacent organs.

They found, however, that only one-third of patients included in the study—all of whom were treated between January 1998 and December 2002—underwent multivisceral resection. The remaining patients had only the tumor removed, which the authors noted is a far less complicated procedure with fewer related morbidities. Patients who underwent multivisceral resection, however, had significantly greater 5-year survival rates (35.1 percent vs. 27.7 percent), and treatment with a multivisceral resection was independently associated with improved overall survival.

Several factors were associated with a greater likelihood of receiving multivisceral resection, the authors found, including being under age 80 and being female. There was also a significant variation in the likelihood of receiving the procedure based on the region of the country in which patients were treated.

Additional studies are needed, they concluded, "to elucidate factors related to the structures and processes of care that contribute to deficiencies in surgical care and to determine future interventions to improve the quality of care delivered to this patient population."

Viral Protein Promotes Kaposi's Sarcoma Lesion Formation

Researchers at the University of North Carolina (UNC) at Chapel Hill have discovered that Kaposi's sarcoma-associated herpesvirus (KSHV) may promote the development of malignant lesions in Kaposi's sarcoma (KS)

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patients by extending the lifespan of virally infected endothelial cells.

In KS lesions, expression levels of a KSHV protein, K1, vary widely. In order to determine the contribution of K1 to KS tumor progression, the investigators expressed K1 in primary human umbilical vein endothelial cells. They found that the K1-expressing cells survived for more than 200 days in culture, whereas cells expressing a control protein stopped dividing after about 130 days.

Lengthier endothelial cell survival was attributed to a fourfold increase in the secretion of vascular endothelial growth factor (VEGF) following K1-induced activation of gene transcription. VEGF stimulates proliferation of infected endothelial cells, as well as healthy neighboring cells, and fuels the growth of new blood vessels.

Two cell-signaling pathways, VEGF/VEGFR-2 and PI3K/Akt, which enhance cell survival by promoting growth and inhibiting apoptosis, were also highly activated in K1-expressing endothelial cells. In mouse models, the researchers observed that K1 enhances epithelial tumor vasculature and size.

Protein expression changes that affect cell growth control or the ability of cells to invade deeper tissues, such as those provoked by K1, can lead to the development of cancer.

"Understanding how K1 functions may help us understand the pathogenesis of KSHV-associated malignancies and how KSHV functions as a tumor virus in the human population," noted Dr. Blossom Damania, who presented the findings October 16 at the NCI-sponsored 10th International Conference on Malignancies in AIDS and Other Acquired Immunodeficiencies, held in Bethesda, Md.

Radiotherapy Threatens Babies Born to Childhood Cancer Survivors

Radiation exposure has been linked with the occurrence of some childhood cancers, and radiotherapy treatments for children with certain cancers may also cause a second primary malignancy. New findings published in the October 18 *JNCI* suggest that women who were exposed to radiotherapy during treatment for childhood cancer—especially pelvic radiation—are more likely to deliver infants who are born prematurely (defined as less than 37 weeks gestation) and who have a low birthweight (less than 5.5 pounds).

The data resulted from a new analysis of the ongoing, long-term Childhood Cancer Survivors Study, an NCI-funded longitudinal cohort study of some 20,000 survivors of childhood cancer, with more than 4,000 of their siblings used as controls. Dr. Lisa B. Signorello of the International Epidemiology Institute of Rockville, Md., and colleagues looked at the live children born to 1,264 survivors and 601 controls between 1972 and 2002.

When the cumulative radiation their mothers had received exceeded 500 centigrays (cGY), babies were 3.5 times more likely to be born preterm than were babies born to women who received no radiation. Irrespective of treatment, survivors' risk of giving birth preterm was 21 percent, 1.9 times that for controls. Kidney cancer was the original disease most likely to be associated with preterm birth. There was little or no risk associated with chemotherapy.

While conceding that "the etiology of preterm birth is largely unknown… [and] the mechanism is likely multifactorial," the authors concluded that "the adverse association between uterine irradiation and the risk of future preterm birth might be especially important for girls who receive such treatment before menarche."

In an accompanying editorial, Dr. Leslie R. Schover of the University of Texas M.D. Anderson Cancer Center added that "we should design professional education materials that map out the paths to making informed decisions." ◆

FDA Update

FDA Approves Vorinostat for Cutaneous T-Cell Lymphoma

The Food and Drug Administration (FDA) has approved vorinostat (Zolinza) capsules for the treatment of cutaneous T-cell lymphoma (CTCL), a type of non-Hodgkin's lymphoma. The disease is a cancer of T cells, which are part of the lymph system. In CTCL, which affects an estimated 20,000 Americans each year, malignant T cells migrate to the skin and may be deposited there.

Vorinostat was approved for patients who have tried and failed other therapies. The drug is to be used when the disease persists, gets worse, or recurs during or after treatment with other medicines, according to the FDA.

Approval was based on two clinical trials involving 107 CTCL patients who received vorinostat after their disease had recurred following treatment. About 30 percent of patients responded to the drug, defined by measurable improvement in skin lesions; the response lasted 168 days on average.

Vorinostat is manufactured by Pantheon, Inc., of Mississauga, Ontario, for Merck. ◆

Spotlight

Translational Breast Cancer Research Gets Personal

In recent decades, revolutionary advances in our knowledge of the molecular and cellular biology of cancer have emerged from the laboratory. The resulting challenge has been how to turn these advances in knowledge into advances in the clinic as rapidly and practically as possible.

The idea of using translational research teams—multidisciplinary groups of investigators who work together to move an idea from "bench to bedside"—to achieve this goal has been gaining momentum. In 1992, NCI funded the first eight Specialized Programs of Research Excellence (SPOREs) translational research grants awarded to institutions and designed to promote such interactions between basic, clinical, and applied scientists. Since then, the program has expanded to include 59 grants focusing on 14 cancer types.

The success of this program is evident in the output, explained Dr. Jorge Gomez, chief of NCI's Organ Systems Branch, which oversees the SPORE grants. "Back in 1998, there were maybe 15 to 17 clinical trials in the SPORE program. As of 2005, we had 255 clinical studies, all based on molecular pathways of cancer. The SPORE program has created an environment that is very conducive to translational research, whether the clinical application is in the area of detection, diagnosis, treatment, or prevention."

One area of research that has proven particularly amenable to the translational approach is applying the knowledge of differential gene expression within a specific cancer type to customize treatment for different patients, with the ultimate goal of "personalized medicine"—treatment selected to match the unique molecular characteristics of each patient's tumor.

In a promising recent example in this field, work from the breast cancer SPORE at UNC-Chapel Hill has shown that several experimental gene-expression-based predictors for breast cancer outcome show strong concordance in their predictions, even though there was little overlap in the gene sets used to create the different predictive models.

The UNC SPORE paper, published in the August 10 *New England Journal of Medicine*, provides an important step in validating these models for future clinical use, explained Dr. Charles M. Perou, assistant professor of Genetics and Pathology at UNC. "There are a dizzying number of prognostic and predictive profiles for breast cancer," said Dr. Perou. "We kept saying to ourselves, 'They can't all be saying different things,' and they're not. They do tend to point to the same results."

Two of the models used in the North Carolina study are currently being tested in large-scale clinical trials: the European Organization for Research and Treatment of Cancer's Microarray in Node-Negative Disease May Avoid Chemotherapy (MINDACT) trial and the Eastern Cooperative Oncology Group's Trial Assigning Individualized Options for Treatment (TAILORx) study. These trials will test if these predictive models can be used prospectively to determine which women will benefit from adjuvant chemotherapy and which can be spared unnecessary treatment.

The SPORE investigators examined a total of five well-known gene-expression-based models, all based on different sets of genes and developed in different laboratories. The 5 models were each tested in tissue samples taken from 295 women with breast cancer and known relapse-free and overall survival times.

Patients were classified using each model, and the assignments of good or bad prognosis, or low or high recurrence probability were compared. The investigators also performed analyses that included the models and variables currently used to make treatment decisions in the clinic, such as estrogen-receptor status, tumor grade, and whether or not tumor cells had spread to the lymph nodes.

For all 295 patients, 4 out of 5 models "were significant predictors of relapse-free survival and overall survival," and "added new and important prognostic information beyond that provided by the standard clinical predictors," stated the authors, led by Cheng Fan and Dr. Daniel Oh of UNC. In addition, they explained, three of the models—including those being tested in the MINDACT and TAILORx trials—were more predictive of outcome than traditional pathological data, such as tumor size and grade.

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the support of an unmatched cadre of extramural scientists, we have been blessed with success after success.

There is no other NIH. There is no other place like NCI anywhere in the world. It is imperative that we tell our story, and that we work with the leaders of our country to ensure that the United States continues to lead the world, that we continue to serve the world.

Elias, my friend, I could not be more proud, nor can I think of any greater honor, than to be asked to join my colleagues on the NIH team. To my fellow institute and center directors, I extend a hand of friendship, of collegiality, and—perhaps most important—of collaboration.

While we at NCI are dedicated to lessening the burden of cancer, we also recognize that cancer has been, and will continue to be, a research model for many diseases. An article in the *Journal of the National Cancer Institute* provides a timely reminder of our importance as a community of scientists. "Progress," the author wrote, "has been most rapid in scientific research when imaginative, talented, technically curious, and, above all, sincerely interested investigators are encouraged to search for new facts, beyond the curtains that limit our knowledge and to pool their specialized resources and skills on a basis of mutual interest and respect."

That's a message we can—and do—embrace. But it is even more profound when you consider that the quote I just read comes from an article written nearly half a century ago, in 1957, by G. Burroughs Mider, NCI's associate director in charge of research. His words remind us that the need for scientific collaboration across disciplines is not a new idea.

It is my great hope that through my leadership at NCI and through the talented NCI scientific community, we can continue, and even fortify, the tradition Dr. Mider so eloquently described.

To the staff of NCI: I am honored and proud to work in your service. Institutions—university or government, private or public—that do great work and make a true difference in this world are always infused with people of enormous talent, commitment, and drive.

The importance of what we do at NCI—on behalf of every man, woman, or child who knows or fears cancer—cannot be underestimated. And, as a cancer research community, we are certainly not exempt from the disease we dedicate our careers to fight. Indeed, for a great many of our colleagues at NCI, cancer is a personal, as well as a professional, issue, because they—or perhaps I should say we—are survivors, patients, caregivers, or loved ones of cancer patients.

Sometimes, in the course of our lives, we talk about being in the right place at the right time. Sometimes we may speak of destiny or fate or direction. However we choose to interpret them, I believe that these important crossroads in life are about recognizing and grasping opportunities, and making all you can of them.

As I said earlier, the rapidity with which we are gaining new knowledge, coupled with the emergence of constantly advancing technologies, is creating greater opportunity to accelerate progress against cancer than any of us dared to dream at the time I began my career. Cancer, we know today, is a disease of alterations in genes, which accumulate over a lifetime. Each day, it seems, our insights grow deeper. We come to a greater understanding of the genetic changes that render a cell malignant. We learn more about the complex interactions of the cancer cell with its microenvironment and host. We learn more about the drivers of metastasis.

In today's post-genomic scientific environment, we are rapidly entering an entirely new era of risk determination, disease prevention, diagnosis, and highly targeted therapies. It is the era of genomically and proteomically characterized disease. As we move into this new era of personalized medicine, ideas, tactics, and techniques are coming from many sectors of science. The physical sciences and engineering are being applied to optimize the discovery, development, and, ultimately, the delivery of interventions to the patient. The once-futuristic tool of nanotechnology is being used to perform molecular classification of tumors to enable high-throughput screening and to predict therapeutic efficacy. Imaging is becoming a tool to ascertain just how much of a small molecule is reaching a targeted receptor and whether the therapeutic molecule changes cellular function. Computational biology—systems biology, if you will—is addressing issues such as information scale, modeling, simulations, and data interpretation.

For certain, new technologies will continue to blossom and multiply.

I know that our time together at NCI will hold moments of great success. I look forward to every exciting advance and discovery.

I also know our time together will bring many challenges. We are in a fiscal period in which management of NCI will involve the careful stewardship of finite resources.
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Notes

Greenwald Promoted Within PHS

The Commissioned Corps of the U.S. Public Health Service (PHS) recently promoted Dr. Peter Greenwald, director of NCI's Division of Cancer Prevention, to Rear Admiral (Upper Half, designating two stars), Assistant Surgeon General. While he will continue to work in the field of cancer prevention, his promotion will provide opportunities to advance the common goals of PHS and NIH.

Looking Ahead: NCI's Plan and Budget for FY 2008

The Nation's Investment in Cancer Research: A Plan and Budget Proposal for Fiscal Year 2008 describes NCI's strategies and progress to reduce the impact of cancer on the lives of all Americans. The budget request represents the institute's professional judgment about FY 2008 resources needed to maintain the present level of operations and provide for minimal growth, as well as expand carefully considered existing initiatives to advance the speed of reaching our goal.

NCI is mandated by legislation to prepare and submit an annual budget estimate directly to the President for review and transmittal to Congress. The actual FY 2008 budget will be determined by Congress during the spring and fall of 2007.

This document can be found at http://plan.cancer.gov. Hard copies can be ordered via e-mail at cisocc@pop.nci.nih.gov, phone at 1-800-4-CANCER, fax at 301-339-7968, or online at www.cancer.gov.

Deadline for Comments on Translational Research

NCI's Translational Research Working Group (TRWG), a 63-person panel established in 2005, was charged with evaluating the current status of the institute's investments in translational research and charting a vision for its future.

TRWG is currently seeking public input to improve translational research at NCI and is welcoming comments on the proposed initiatives and their associated implementation concepts. This input will be considered as TRWG develops final recommendations, which will be offered to the National Cancer Advisory Board in early 2007.

To comment, visit http://www.cancer.gov/trwg. The deadline for feedback is November 3.

Two More TCGA Pilot Project Components Are Announced

NCI and the National Human Genome Research Institute (NHGRI) announced two more components of The Cancer Genome Atlas (TCGA) Pilot Project, a 3-year, $100 million collaboration to test the feasibility of using large-scale genome analysis technologies to identify important genetic changes involved in lung, brain, and ovarian cancers.

Awards have been made to seven institutions in five states to establish Cancer Genome Characterization Centers (CGCCs). CGCCs will work as a network, with each center using advanced genome analysis technologies to identify major changes in the genomes of the cancers chosen for the TCGA Pilot Project. NCI awarded a total of $11.7 million per year to support the CGCCs.

Additionally, a Data Coordinating Center (DCC) for the TCGA Pilot Project will be developed. The DCC will track data produced by components of TCGA and make TCGA data publicly accessible through databases supported by NCI's caBIG™ and the National Library of Medicine's National Center for Biotechnology Information.

Scientists to Compete for 2007 NIH Director's Pioneer Awards

The 2007 NIH Director's Pioneer Award competition was launched on October 12. The program, which is part of the NIH Roadmap for Medical Research, supports scientists who take innovative approaches to major challenges in biomedical research. Each Pioneer Award provides $2.5 million in direct costs over 5 years.

"We hope this opportunity stimulates even more investigators to send us their boldest, most imaginative concepts," said NIH Director Dr. Elias A. Zerhouni.

Scientists from all career levels and research disciplines may apply for the Pioneer Award with the provision that they are interested in exploring biomedical issues. The application period is December 1, 2006, to January 16, 2007.

More information on the Pioneer Awards, including application instructions, can be found at http://nihroadmap.nih.gov/pioneer. ◆

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I will do my best to provide you with an open door and a listening ear, with strong leadership skills honed in the operating room and the laboratory, to captain this team in difficult times. It will be up to the leaders of NCI to find and allocate the resources necessary to maintain our scientific momentum.

To this end, NCI will need to consider new partnerships in order to leverage resources and knowledge. We will need to carefully consider each new research program and scientific proposal. We will need to examine all existing programs, to search for ways to be leaner, but at the same time even better, in achieving our mission. Our responsibility is to continue conducting quality research, offering solutions to our challenges. As Albert Einstein said, "In the middle of every difficulty lies opportunity."

It is critical in these times that we communicate effectively across our various constituencies. As a cancer community, we must strive to speak with a more unified voice in order to call others to action on behalf of cancer research.

I believe we must work to find the best ways to bring the latest science to patients in the communities where they live—through our NCI-supported cancer centers, which are always referred to as the "crown jewels" of NCI—and by the building of a new rim of community-based cancer care.

We must make our science, our medical advances, available to all of our citizens, especially those who may lack the financial means, the language capacity, the education, or simply the physical strength to seek out the best care. We must bring our science—our technology—to the patients where they live.

I share the view of my friend and colleague John Seffrin, chief executive officer of the American Cancer Society, who so effectively states his belief that, in the next decade, patient access to our accomplishments—our science—will become a greater determinant of cancer mortality than any currently recognized cause.

In one of the most-quoted lines of American politics, the late Vice President Hubert Humphrey said the moral test of government is how it treats "those who are in the dawn of life, the children; those who are in the twilight of life, the elderly; and those who are in the shadows of life, the sick, the needy, and the handicapped."

It is, after all, our responsibility to continually earn, and always merit, the public's trust. We maintain that bond by being good financial stewards, by letting the best science be our guide, by clearly and plainly communicating what we learn about cancer, and by honestly saying what we have yet to learn. We should convey hope, but always be grounded in facts.

And so it is with an unshakable commitment—to every cancer patient, every survivor, advocate, friend, father, mother, son, daughter, and caregiver—that I sincerely thank you for the opportunity to serve this great institution and this great country, and solemnly pledge to do my very best. May God bless America, and give us the knowledge and wisdom to serve our patients. ◆

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A greater understanding of the molecular subtypes of breast cancer may lead not only to more targeted use of available treatments, explained Dr. Perou, but also to the development of new therapies specifically aimed at certain subtypes.

"I think one of the exciting things about identifying these subtypes is that it's not just prognostic information," said Dr. Perou. "Going along with the subtypes are all these potential therapeutic targets, present in some tumors and absent in others. We know the importance of [the] ER and HER2 [proteins], but there are others embedded in our profiles."

The investigators are further using their translational research relationships and have initiated an inter-SPORE clinical trial to test a targeted therapy against the protein HER1, which was found to be overexpressed in the basal-like breast cancer subtype. ◆

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_102406/page8. ◆

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.