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Workshop Opens Dialogue on Cancer Clinical Trials

Experts on clinical trials met last week to share ideas about how to improve a system that has served the nation well for decades but needs to be modified and updated to meet the needs of patients and its many stakeholders.

A major theme of this workshop was that the reform must be global and include regulatory agencies, third-party payers, and funding entities, such as NCI and pharmaceutical companies, noted NCI Director Dr. John Niederhuber, who delivered opening remarks.

More than 100 individuals representing government, regulatory agencies, academia, industry, and patient groups attended the Institute of Medicine's National Cancer Policy Forum event, held June 1–2 at the Keck Center of the National Academies. The focus was multicenter, final-stage clinical trials and the role of NCI's Clinical Trials Cooperative Group program.

The Cooperative Group program enrolls approximately 22,000 cancer patients each year in clinical studies at academic medical centers, cancer centers, community hospitals, and private research institutions. Congress started the program in 1955, and it has grown to include 1,700 institutions within 10 national groups.

The program has been instrumental in demonstrating the safety and effectiveness of many cancer therapies. But the current clinical trials system has not kept pace with the development of new combinations of therapies that target multiple pathways of cancer.

"The meeting generated a comprehensive and well-informed list of issues and needs that require attention," said

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Cancer Research Highlights

Androgen Deprivation No Better than Conservative Approach in Localized Prostate Cancer

Using androgen deprivation therapy alone in older men with localized prostate cancer does not improve survival outcomes when compared with a conservative management approach, according to a new analysis in the July 8 *Journal of the American Medical Association*. For localized prostate cancer, androgen deprivation therapy has become a common treatment, despite a lack of definitive evidence that it is more effective than other options, noted the study authors.

To conduct the study, the researchers, from The Cancer Institute of New Jersey, used data from NCI's

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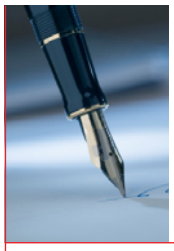

Director's Update

Enhancing the Training Experience at NCI

The importance of nurturing and developing the next generation of cancer researchers simply cannot be overstated. It is a priority that has universal support in the cancer community. The need, I believe, goes beyond replacing or maintaining the current oncology workforce; rather, there must be a very real emphasis placed on doubling this workforce over the next decade. These researchers are needed to translate and deliver on the promise of personalized oncology, working in cross-disciplinary teams and focusing on cancer as part of a biological system, rather than as a disease specific to a particular organ.

With that priority in mind, NCI is establishing the Center for Cancer Training (CCT) to coordinate the Institute's training programs, both intramural and extramural, across all areas of NCI's research. I have appointed Dr. Jonathan Wiest to lead a confederation of training programs that will work across the spectrum of trainees from high school students to researchers and clinician scientists with advanced degrees. A recognized visionary and strong leader of cancer career development programs, Dr. Wiest has, for the past 7 years, been responsible for training in NCI's Center for Cancer Research.

Working alongside NCI training officers, Dr. Wiest will be taking a critical look at scientific discovery in the 21st century, in order to anticipate the future training needs of biomedical researchers. Those requirements may very well change over time, as collaborations across diverse technologies—including mathematics, physics, and engineering—will be essential to future successes in cancer research.

> ***"[Training] collaborations across diverse technologies—including mathematics, physics, and engineering—will be essential to future successes of cancer science."***

In the near term, CCT will bring together training programs currently housed across NCI divisions, offices, and centers, in order to align programs, streamline operations, improve efficiencies, enhance communication, and identify and implement best practices across NCI's entire research portfolio. This critically important ability is an extension of some of today's successful training efforts. For example, the Joint-Fellowship Program launched by the NCI-FDA Interagency Oncology Task Force enables cancer researchers to gain greater understanding of the regulatory review process. Another important initiative, the Cancer Prevention Fellowship Program trains postdoctoral candidates in the conduct of research in cancer prevention and control.

CCT will also take advantage of NCI's intramural resources, such as career development courses and individual training plans. The goal is to create a coordinated cancer training enterprise that retains the unique missions and resources of each existing program.

I am confident that coordinating intramural and extramural training through the CCT will synergize existing programs and help us foster a dedicated cancer research workforce for the future. ◆

Dr. John E. Niederhuber
Director, National Cancer Institute

For related information, please visit the resources page from our special issue on NCI training.

Also In the News

On July 2, the Centers for Medicare and Medicaid Services (CMS) announced it will add chemotherapy treatments from Elsevier Gold Standard's *Clinical Pharmacology* compendium to the list of Food and Drug Administration-approved drugs it uses to determine which treatments may be covered under Medicare Part B. ◆

(Workshop continued from page 1)

Dr. Niederhuber. "It also produced some excellent ideas for positive change. These suggestions will certainly inform NCI's plan of action in the weeks ahead, as we continue our work to enhance this crucial—and rapidly evolving—clinical research enterprise."

Other topics discussed included the recruitment of patients and physicians; costs and payments; and regulatory issues such as data collection standards to establish safety and efficacy.

There seemed to be general agreement on some basic issues, including the need to prioritize the most important trials. Doing fewer trials could allow planners to shift precious resources from poorly accruing trials to other studies.

The annual funding for the Cooperative Groups is approximately $145 million, which is administered by the Cancer Therapy Evaluation Program of NCI's Division of Cancer Treatment and Diagnosis. In 1997, an independent review panel said that the Cooperative Group program needed to be properly funded, and since then the costs of running trials have risen without similar budget increases.

"We must confront not only the crucial scientific questions, but also address funding issues and long-range inefficiencies in the clinical trials system," said Dr. Niederhuber.

Dr. John Mendelsohn, president of the University of Texas M.D. Anderson Cancer Center, chaired the workshop planning committee. He predicted that Cooperative Groups are increasingly going to turn to industry for financial support. These groups are attractive to companies because they offer a greater diversity of patients than many companies can recruit. Another asset is that some groups have tissue banks, and some can look at the expression of genes and molecular targets in real time.

"As we're moving into more personalized medicines, these groups can carry out the kinds of trials we are all interested in," Dr. Mendelsohn said.

During a panel discussion about the collection of data on safety and efficacy, Dr. Richard Pazdur of the Food and Drug Administration (FDA) suggested that the topic could be explored in a future workshop or public forum, as has been done previously with the American Society of Clinical Oncology (ASCO).

The president of ASCO, Dr. Richard Schilsky, responded to the offer immediately by saying his organization would be "delighted" to work with the FDA and other stakeholders to discuss developing data sets required for regulatory approval.

Dr. Harold Moses, director emeritus of the Vanderbilt-Ingram Cancer Center and chair of the National Cancer Policy Forum, noted that previous reviews of NCI Cooperative Groups did not lead to action and said that this time would be different.

A workshop summary will discuss areas of broad agreement, and this could be the basis for an Institute of Medicine study committee. Such a group could form and make recommendations, potentially by next spring.

"Everyone here is interested in action," said Dr. Mendelsohn. ◆

By Edward R. Winstead

Legislative Update

FY08 Supplement Signed; FY09 Appropriations Bill Still Pending

On June 30, President George W. Bush signed H.R. 2642, the Supplemental Appropriations Act of 2008, into law (P.L. 110-252). The bill provides funding for another year of military operations in Iraq and Afghanistan but also provides $24.7 billion for domestic programs, including $150 million for NIH. Of that, NCI will receive $25 million.

Both the U.S. House of Representatives and the U.S. Senate have introduced fiscal year (FY) 2009 appropriations bills for the Departments of Labor, Health and Human Services, and Education that exceed President Bush's budget request. The Labor-HHS-Education appropriations bill, approved by the Senate Appropriations Committee on June 26, would provide $153.1 billion in discretionary spending—$8 billion more than in FY2008 and $7.7 billion more than the President requested for the agencies it covers. President Bush has threatened to veto any spending bill that exceeds his budget. The House version of the Labor-HHS-Education appropriations was scheduled to be marked-up on June 26 but was postponed until after the July 4 recess.

Both the House and the Senate versions of the Labor-HHS-Education bill emphasize funding for NIH. The Senate bill provides NIH about $30 billion, a $1 billion increase. The House bill would provide $30.1 billion. ◆

Cancer Research Highlights

(continued from page 1)

Surveillance, Epidemiology, and End Results (SEER) program and linked Medicare files to compare the outcomes in men aged 66 and older, who were diagnosed with localized prostate cancer between 1992 and 2002 and had not undergone surgery. Of these men, nearly 8,000 received androgen deprivation therapy and approximately 11,400 were treated with conservative management, often called "watchful waiting."

Patients treated with androgen deprivation therapy—half of whom were treated for more than 30 months—had a lower 10-year, cancer-specific survival rate than those who underwent conservative management (80.1 percent vs. 82.6 percent) and equivalent 10-year overall survival rates. Androgen deprivation therapy did slightly improve cancer-specific survival at 10 years in men with poorly differentiated cancer, the authors noted, but there was no significant difference in overall survival in that patient subset.

"There have been more reports of health risks such as fractures, diabetes, heart disease, and other adverse effects associated with chronic use of this therapy," said the study's lead author, Dr. Grace L. Lu-Yao. "Therefore, it is imperative that more exploration is done on the appropriate application of this treatment."

Testing SNPs Improves Breast Cancer Risk Tool Modestly

In recent years, at least seven common genetic variants—single nucleotide polymorphisms, or SNPs—have been definitively linked to breast cancer. Researchers have begun to ask whether this knowledge can improve current tools for assessing breast cancer risk. The answer is yes, but only modestly, according to an analysis by Dr. Mitchell Gail of NCI's Division of Cancer Epidemiology and Genetics in today's *Journal of the National Cancer Institute*.

Dr. Gail led the team that developed NCI's Breast Cancer Risk Assessment Tool (BCRAT), which is based on questions about a woman's family and reproductive histories. The tool has helped women make decisions such as whether to take a drug to prevent breast cancer.

The new study found that a panel of seven SNPs was not as informative as the BCRAT in assessing a woman's breast cancer risk and therefore should not replace it as a screening tool. When the SNPs were combined with the BCRAT, they modestly improved the "discriminatory accuracy" of the BCRAT, which is the ability to distinguish women who will develop breast cancer from women who will not.

"These SNPs can improve the discriminatory accuracy of the BCRAT, but it is a small incremental change," Dr. Gail notes. "One would do better by asking women the questions [about their health and family histories] than by looking at these SNPs alone."

The SNPs, reported by two genome-wide association studies and a study of candidate genes, are located in *FGFR2, TNRC9, MAP3K1, LSP1, CASP8*, chromosomal region 8q, and chromosomal region 2q35.

Dr. Gail estimates that if many additional risk SNPs are identified, it could improve the risk prediction models substantially, but this will need to be evaluated once the true scope of genetic susceptibility factors for breast cancer are known.

Noninvasive Approach to Monitoring NSCLC Shows Promise

In a small study involving patients with metastatic non-small-cell lung cancer (NSCLC), researchers have shown that rare, circulating tumor cells (CTCs) in the blood can be molecularly analyzed before and after treatment to identify mutations that can affect treatment outcomes and influence decision making.

To conduct the study, published online June 2 in the *New England Journal of Medicine* (*NEJM*), researchers from Massachusetts General Hospital used an investigational CTC-chip device to capture the CTCs. They then used the Scorpion Amplification Refractory Mutation System (SARMS) assay to analyze the cells for mutations in the *epidermal growth factor receptor* (*EGFR*) gene that have been associated with response and eventual resistance to EGFR-targeted agents.

"Together with the CTC-chip, the SARMS assay may allow for noninvasive genotyping in patients with [NSCLC], which could then be repeated at therapeutic decision-making points during a patient's course of therapy," wrote study leader Dr. Shyamala Maheswaran and colleagues.

Using the CTC-chip, the researchers

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isolated CTCs in all 27 patients in the study in sufficient quantities and with sufficient purity for molecular analyses. So-called "activating" mutations in the *EGFR* gene were detected in the CTCs from all patients; a specific mutation that is associated with resistance to EGFR-targeted agents was detected in 55 percent of the 20 patients who had CTC and/or tumor and plasma specimens available for molecular analysis.

Reductions or increases in CTCs were associated with response to treatment and progression of disease, respectively, the authors wrote.

In the CTCs from several patients, they also identified the emergence of additional *EGFR*-activating mutations during treatment, which "we therefore presume… represents the emergence of different tumor clones," they wrote.

In a related *NEJM* commentary, Dr. Joan Schiller from the Harold C. Simmons Comprehensive Cancer Center in Texas said the study represents a proof of principle. "The ease with which this approach can be used by others remains to be determined," she wrote.

Glioblastoma Stem Cell Signature Identified

Researchers from the University of Lausanne have identified a "stem-cell like" gene signature associated with poorer survival outcomes in patients with glioblastoma treated with radiation therapy and temozolomide.

The researchers analyzed 80 tumors taken from patients in two other prospective clinical trials investigating glioblastoma (one phase II and one phase III trial), they reported in the June 20 *Journal of Clinical Oncology*. Patients whose tumors expressed a signature dominated by *homeobox* (*HOX*) genes, which play an important role in development, had outcomes nearly three times worse than patients without that signature.

The researchers suggest that the *HOX* signature belongs to a stem-cell-like phenotype that responds poorly to the temozolomide-radiotherapy regimen that has shown some success in treating glioblastoma. The results support the idea that tumors with the signature may include mutated self-renewing progenitor cells which give rise to malignant gliomas that are resistant to radiotherapy and chemotherapy, compared with other glioblastoma cells.

This work underlines "the need for multimodality treatments" aimed at the factors that determine outcomes in glioblastoma, the researchers suggest. Their data also show that tumors overexpressing the *epidermal growth factor receptor* gene conferred a comparably poor outcome, though this effect was independent of the *HOX* association.

"These findings provide the first clinical evidence to our knowledge for the relevance of a stem-like cell phenotype in treatment resistance of glioblastoma," the researchers write. The signature, they note, "is evocative of a self-renewal signature recently described for leukemia."

Yeast-Based Vaccine Triggers Immune Response in Mouse Models of Cancers

Researchers in NCI's Center for Cancer Research have tested a new approach for developing cancer immunotherapy; genetically engineering a harmless strain of yeast to produce a tumor protein called carcinoembryonic antigen (CEA) that triggers an immune response against certain types of cancer but not against healthy tissue. Their study results appeared July 1 in *Clinical Cancer Research*.

The scientists, led by Dr. Jeffrey Schlom, genetically engineered *Saccharomyces cerevisiae*, a strain of yeast that causes no disease in humans and has been used safely in other clinical trials, to express CEA, a surface protein that is normally expressed in the blood during fetal development but rarely appears again in healthy individuals. In patients with some carcinomas, however, CEA is overexpressed. Using mouse models for colon and pancreatic cancer types that were also engineered to express CEA, the researchers injected either the CEA-yeast vaccine or a control vaccine, a non-genetically engineered form of the yeast that was heat-killed prior to injection.

In mice that received the CEA-yeast vaccine, CD4+ and CD8+ T-cells responded to the stimulus and began to attack the tumors. Giving the vaccine as a series of injections (up to four times) increased the T-cell response. Higher vaccine doses and multiple injection sites also increased the response, which resulted in tumor shrinkage and increased overall survival. These results were also seen in a CEA-mouse-model in which tumors had metastasized to the lung. In all cases, the mice that received the CEA-yeast vaccine showed no toxicity or autoimmune disease.

S. cerevisiae is easy to genetically engineer and culture, it triggers a strong immune response, and it is safe. "All of these qualities make [it] an attractive vehicle for cancer immunotherapy," the authors conclude. ◆

Spotlight

Some Exercise a Day May Keep Cancer at Bay

The observations were compelling, to say the least. First it was breast cancer, then colorectal cancer: 40 to 50 percent reductions in the risk of cancer-related death and cancer recurrence.

The apparent cause was not a new targeted agent or a novel combination therapy, but rather, frequent trips back and forth in heavily chlorinated water, regular bouts with yard mulch and garden weeds, striding through the neighborhood for 30 minutes every morning. In other words, old-fashioned exercise.

Five large observational studies have now linked reports of regular post-treatment physical activity with superior outcomes compared with patients who remained sedentary after treatment. And now the first prospective, randomized clinical trial is nearly set to test whether physical activity can indeed influence cancer's course after treatment.

Results from the observational studies "are certainly compelling enough to warrant a randomized trial of physical activity," says Dr. Kerry Courneya, of the University of Alberta, who will lead the trial in patients who have been treated for colon cancer.

The trial represents a shift of sorts, because most cancer-related physical activity research to this point has not focused on recurrence or survival.

"There is extensive evidence [from prospective studies] that post-treatment activity improves cancer patient-reported outcomes such as quality of life or fatigue," explains

Dr. Rachel Ballard-Barbash, associate director of the Applied Research Program in NCI's Division of Cancer Control and Population Sciences. Although there isn't much evidence to indicate which specific types of activities might be most beneficial from a recurrence or survival standpoint, Dr. Ballard-Barbash continues, "We do have good evidence on how to get cancer patients physically active."

The level of activity required for a measurable benefit varied, but the cancer mortality risk reductions reported from the large observational studies of physical activity—two of which came from the long-running Nurses' Health Study—have been fairly consistent. (See side bar on page 8.)

"It's certainly intriguing data," says Dr. Wendy Demark-Wahnefried, from the Department of Behavioral Science at the University of Texas M.D. Anderson Cancer Center, who has been studying the impact of diet and exercise on long-term cancer survivors for more than a decade. "One of the questions now is whether the clinical trials [of physical activity] can be done, because I think there is tremendous interest."

NCI sponsored a workshop 2 years ago on how best to design such trials, notes Dr. Ballard-Barbash, and NCI has been fielding proposals to conduct them.

Dr. Lee W. Jones, director of the Tug McGraw Research Center at the Duke University Medical Center, says data to help inform optimal trial design (e.g., type of activity, intervention delivery strategies, etc.) is coming, as well as data on the potential biological mechanisms by which exercise may inhibit tumor growth.

Researchers, Dr. Jones says, have speculated that physical activity might influence post-treatment outcomes in breast cancer patients by dampening levels of estrogen or insulin, elevated levels of which are associated with poor outcomes. Several studies involving breast cancer patients, for instance, have consistently found a threefold increased risk of death among women with the highest insulin levels.

Meanwhile, studies involving patients with a range of problems, including diabetes and heart disease, have shown that physical activity can reduce insulin levels. Last year, researchers from Dana-Farber Cancer Institute (DFCI), led by Dr. Jennifer Ligibel, showed that a regimen of cardiovascular and strength training lowered insulin levels in sedentary

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(Spotlight continued from page 6)

women who had completed adjuvant therapy for early stage breast cancer.

"We're very interested in what happens biologically with physical activity," explains Dr. Ligibel, from DFCI's Breast Cancer Program. "We think it has to be modification of hormone levels.…And the data suggest that estrogen is not the whole story."

The data, however, are far from consistent.

"In our preclinical studies, we've found that the hypoxia/angiogenic pathways are really upregulated with exercise, but that insulin doesn't change much," says Dr. Jones. (This does not necessarily mean that exercise doesn't alter insulin signaling in the tumor, he cautions.) And in one animal model study of prostate cancer, Dr. Jones adds, voluntary exercise actually accelerated tumor growth.

The trial Dr. Courneya is leading, dubbed CHALLENGE, is set to launch by the end of this year in Canada, and will investigate whether increased physical activity can improve disease-free survival (DFS) in patients treated for high-risk stage II and III colon cancer. (Another Canadian clinical trial that is already underway, called LISA, is testing whether a dietary and physical activity regimen focused on weight loss can improve DFS in overweight or obese women who have been treated for early stage breast cancer.)

The physical activity intervention in the trial follows from a similar—and highly successful—trial, the Diabetes Prevention Program.

"The activity in this trial will be a mix," Dr. Courneya explains. "The literature doesn't point to a specific type of exercise that has the most benefit. So we're going to promote aerobic exercise, assuming that most participants will walk, but expecting that others will do things like biking or swimming."

The physical activity component will include in-person or phone-based meetings with exercise consultants

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FDA Update

FDA Still Considering Gardasil Use in Older Women

The HPV vaccine Gardasil is not yet approved for women aged 27 to 45, according to a "complete response" letter to the vaccine's manufacturer, Merck & Co., from the Food and Drug Administration (FDA). The FDA wrote that its review of the company's supplemental biologics license application (sBLA) to add women 27 to 45 as an approved indication is complete, but that the vaccine will not be approved within the 6-month "priority review" period due to issues with the submission.

Merck expects to submit its responses this month, the company noted in a statement. Gardasil is already approved for use in females aged 9 to 26 for the prevention of HPV 6, 11, 16, and 18 infection.

The sBLA was based on data from a study of 3,800 women aged 24 to 45, who were free from infection by at least one of the four HPV types covered by the vaccine. Gardasil prevented 91 percent of persistent HPV infections, low-grade cervical abnormalities, and precancers caused by one of those four HPV types compared with women given placebo. The prevention rate for those endpoints was 83 percent when the analysis was limited to HPV types 16 and 18, which are responsible for approximately 70 percent of cervical cancer cases.

The FDA issued a second complete response letter to Merck regarding an sBLA to market Gardasil as "cross-protection" against HPV types not specifically covered by the vaccine.

"According to the FDA, the data submitted do not support extending the indication for Gardasil to include nonvaccine HPV types," Merck said.

HER2 Test for Breast Cancer Approved

A genetic test that can help identify women with breast cancer who are candidates for the drug trastuzumab (Herceptin) was approved by the FDA today. The test measures the number of copies of the gene *HER2* in tumor tissue; women with extra copies of this gene may benefit from trastuzumab.

The SPOT-Light HER2 CISH kit involves staining a small sample of tumor tissue. The stain causes tissue with extra copies of *HER2* to change color. "The color change can be visualized under a standard microscope, eliminating the need for the more expensive and complex fluorescent microscope," according to a statement by the FDA.

Unlike existing tests, the SPOT-Light, which is manufactured by Invitrogen Corp., allows labs to store the tissue for future reference, the FDA said. ◆

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for 3 years, with more frequent meetings for the first year.

"This isn't like taking a drug," Dr. Courneya acknowledges. "These types of lifestyle interventions are difficult and have to be delivered over a longer period of time."

Dr. Ligibel agrees that delivery of the intervention is a challenge.

"The data suggest there is better compliance with dietary modifications than physical activity modifications," she says.

Even so, small studies and trials of the influence of exercise on cancer outcomes are multiplying and expanding to other cancer types. Dr. Jones' group at Duke, for example, has been conducting studies in patients before and after lung cancer surgery, as well as in patients with primary brain tumors.

"I'm very confident that anybody, regardless of where they are in the cancer survivorship continuum, can exercise," Dr. Jones says. "It's just a matter of what type of exercise, the frequency, and the intensity." ◆

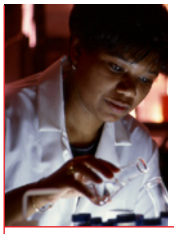
By Carmen Phillips

Studies That Got the Ball Rolling

Physical activity and survival after colorectal cancer diagnosis—Meyerhardt et al., *Journal of Clinical Oncology*, August 2006

Impact of physical activity on cancer recurrence and survival in patients with stage III colon cancer—Meyerhardt et al., *Journal of Clinical Oncology*, August 2006

Physical activity and survival after breast cancer diagnosis—Holmes et al., *JAMA*, May 2005 ◆



Featured Clinical Trial

New Drugs for Multiple Myeloma Consolidation Therapy

Name of the Trial
Phase III Randomized Study of Consolidation Therapy Comprising Bortezomib and Dexamethasone with Versus without Lenalidomide in Patients with Symptomatic Multiple Myeloma Who Have Completed a Dexamethasone-Based Induction Regimen (ECOG-E1A05). See the protocol summary at http://cancer.gov/clinicaltrials/ECOG-E1A05.

Principal Investigators
Dr. Rafael Fonseca and Dr. S. Vincent Rajkumar, Eastern Cooperative Oncology Group

Why This Trial Is Important
Multiple myeloma is a type of cancer that begins in plasma cells, white blood cells that are part of the immune system. In this disease, malignant plasma cells (myeloma cells) multiply and form small lesions in the bone marrow and the solid parts of bone. Although multiple myeloma is usually not curable, advances in drug treatment and the use of stem cell transplantation have substantially increased the average survival time of patients with this disease.

Patients with multiple myeloma are often treated first with chemotherapy drugs and the steroid dexamethasone to induce remission (induction therapy). This is often followed by "consolidation therapy" with high-dose chemotherapy and stem cell transplantation. Although consolidation therapy has produced longer survival, the side effects associated with it can be severe and may dramatically affect quality of life. Doctors want to study new consolidation therapy options, using recently developed drugs, to see if they can achieve the same or better outcomes without as much risk to the patient.

In this trial, newly diagnosed patients who have undergone induction therapy will be treated with consolidation therapy consisting of dexamethasone and the drug bortezomib. Some patients will also be randomly assigned to receive a third drug called lenalidomide. Both bortezomib and lenalidomide have been approved by the FDA to treat patients with relapsed multiple myeloma, and they have shown promise in early clinical trials involving patients with newly diagnosed disease.

"One of the biggest questions in the minds of patients in this era of new drugs is, 'Do we still need to have a transplant?'" said Dr. Rajkumar. "Autologous transplants are associated with significant morbidity and can be life changing. Both of these regimens hold the promise of high response rates that may rival what we can achieve with stem cell transplantation while being easier on patients."

For More Information
See the list of entry criteria and trial contact information at http://cancer.gov/clinicaltrials/ECOG-E1A05 or call the NCI Cancer Information Service at 1-800-4-CANCER (1-800-422-6237). The toll-free call is confidential. ◆

Notes

DCTD's Sheila Taube Retires

Dr. Sheila Taube, of NCI's Division of Cancer Treatment and Diagnosis, retired on June 30 after serving as associate director of the Cancer Diagnosis Program (CDP) since 1997. During her nearly 25-year tenure at NCI, Dr. Taube helped advance personalized medicine approaches and technologies for detecting molecular markers for cancer.

Under Dr. Taube's guidance, CDP created the Program for the Assessment of Clinical Cancer Tests (PACCT) to translate new knowledge and technology related to cancer diagnosis into clinical practice. As part of PACCT, the first prospective trial using a molecular signature for risk of recurrence to guide treatment decisions in early stage breast cancer, the Trial Assigning IndividuaLized Options for Treatment (TAILORx), opened in 2006.

Dr. James Jacobson will act as the CDP associate director. Dr. Jacobson is chief of the Diagnostic Biomarkers and Technology Branch in CDP.

caBIG Annual Meeting Widely Attended

On June 23–25, nearly 1,500 researchers attended the fifth caBIG annual meeting in Washington, DC. Attendees learned about trends in molecular medicine and how to adopt and adapt caBIG tools and infrastructure to reach research goals.

The meeting program, materials from the plenary presentations, and a meeting summary are available at https://cabig.nci.nih.gov.

BSA Meeting Held

NCI's Board of Scientific Advisors (BSA) met June 23–24 on the NIH campus in Bethesda, MD. The public portions of the meeting can be viewed at http://videocast.nih.gov/PastEvents.asp.

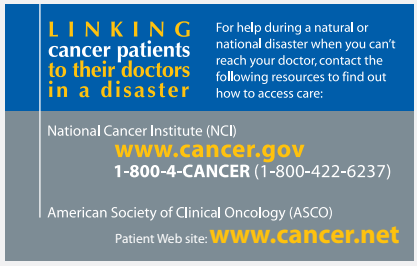
Community Cancer Centers Program Begins Year 2 with National Meeting

Nearly 175 oncologists, principal investigators, nurses, key administrative and support personnel, and NCI staff involved with the NCI Community Cancer Centers Program (NCCCP) met June 26–27 in Arlington, VA, one year after the 3-year pilot program was launched. NCCCP links 16 community hospitals in an effort to bring high-quality cancer care to more Americans. Attendees discussed the progress and the challenges as the pilot moves into its second year. Key goals are to expand clinical trials recruitment, reduce cancer health disparities, expand the collection and use of biospecimens, and explore the utility of a national database of electronic health records. ◆

Wallet Card Helps Doctors and Patients Stay Connected During Hurricane Season

NCI and the American Society of Clinical Oncology (ASCO) continue to pilot test a wallet card developed to help reconnect displaced patients and doctors in the Gulf Coast states after a natural disaster, like the devastating hurricanes of 2005. In such an emergency, the card guides cancer patients to ASCO's patient information Web site, Cancer.gov, NCI's Cancer Information Service (CIS) national toll-free number (1-800-4-CANCER), *LiveHelp* instant messaging service, and e-mail service available at www.cancer.gov/help.

The ongoing pilot study will continue during the 2008 hurricane season, and an evaluation of the pilot will help determine whether the program is expanded to cover other geographic areas or other potential disasters. The card lists the patient's name, diagnosis, current treatment, and doctor's contact information.



NCI and ASCO encourage oncologists to discuss with their patients what to do in the event of a natural disaster. Oncology practices in the Gulf States can order copies of the card by calling the CIS at 1-800-4-CANCER (1-800-422-6237). ◆

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_070808/page10. ◆

Profiles in Cancer Research

Dr. Tom Misteli

Senior Investigator, Center for Cancer Research, NCI

Dr. Tom Misteli had no intentions of becoming a scientist when he grew up in a small town near Berne, Switzerland.

"I wasn't one of those kids running around saying, 'I'm going to be a doctor.' I was interested in lots of different things," he explains. "After high school I was torn between studying literature and biology. Then, one day, I was on a train trip, and I bought a copy of *Scientific American* for whatever reason—it was a special issue on molecular biology—and it absolutely captured my attention. That's how I decided I was going to be a biologist.

"I remember my father asking me 'Are you sure about this?' And I said, 'Not at all, but I'm going to see whether I like it,'" he laughs.

Today, Dr. Misteli remains a committed cell biologist, heading the Cell Biology of Genomes Group in the Laboratory of Receptor Biology and Gene Expression in NCI's Center for Cancer Research, where he focuses on an unusual niche in molecular research: How the spatial organization of the genome within a cell's nucleus contributes to cell functioning and to the origins of disease.

After earning his Ph.D. from the University of London and the Imperial Cancer Research Fund, London, Dr. Misteli worked as a postdoctoral fellow at Cold Spring Harbor Laboratory in New York, where he became interested in genome organization.

"This is an area of research that 5 or 6 years ago, literally nobody in the United States worked on because it was extremely high risk," says Dr. Misteli. That is, few other researchers had explored this area of cell biology, leaving a gap in the scientific literature that made it difficult to justify a project on the neglected subject. "I came to NCI because it provided a lot of freedom to do high-risk research, which is increasingly more difficult in the outside [research] world."

Dr. Misteli's lab uses molecular techniques including polymerase chain reaction and microarrays to measure gene expression, in addition to time-lapse microscopic techniques that visualize the movement of gene loci in single living cells.

In a recent paper published in the *Journal of Cell Biology*, he and a colleague from his laboratory visualized major genome reorganization during early tumorigenesis in a 3D cell culture model of early breast cancer, using fluorescent microscopy.

All but one of the genes they observed undergoing repositioning during early tumor differentiation also moved during normal differentiation, but several additional genes—including genes known to drive cancer development—also changed their location within the nucleus in the tumor model. Dr. Misteli's group is now exploring these positional changes of tumor genes for diagnostic purposes.

Other recent work from the lab has shown how the proteins that repair damaged DNA physically interact with the chromosomes, and how the mutant protein responsible for Hutchinson-Gilford Progeria Syndrome—a premature aging disease—interferes with the functioning of stem cells that produce the bones, blood vessels, connective tissues, and other vital structures of the body. The next step in this field with regards to cancer, explains Dr. Misteli, is to discover the mechanisms by which higher order genome organization helps drive the process of tumorigenesis.

"We're at a point where we now understand the fundamental concepts, the fundamental principles by which genomes are organized in the nucleus, and I would argue, even the principles by which genomes function," he says. "So the next step is to link some of these morphological observations to function, to physiology, and to disease." ◆

The work of Dr. Misteli and his colleagues is featured in the current edition of *CCR connections*, the news magazine of NCI's Center for Cancer Research. Please click here to read the online version of the *CCR connections* article: http://home.ccr.cancer.gov/connections/features.asp ◆