NATIONAL CANCER INSTITUTE

NCI Cancer Bulletin

Eliminating the Suffering and Death Due to Cancer

February 15, 2005
Volume 2 | Number 7

In this issue:

A Publication of the
National Cancer Institute
U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES
National Institutes of Health
NIH Publication No. 05-5498

http://www.cancer.gov

NCI Announces Senior Leadership Changes

Speaking at an "all-hands" meeting of National Cancer Institute (NCI) employees today, NCI Director Dr. Andrew C. von Eschenbach announced several changes among senior NCI leadership, including the departures of a deputy director and the director of the Center for Cancer Research (CCR).

Dr. Karen H. Antman, the deputy director for translational and clinical sciences, has accepted a job as provost of the Boston University Medical Campus and dean of the School of Medicine. And CCR Director Dr. J. Carl Barrett has taken a position with the Novartis Institutes for Biomedical Research as Global Head of Oncology Biomarkers.

"Losing these two individuals with respect to their leadership is, for us, going to be a great loss," Dr. von Eschenbach said. "But, like all great institutions, we have great people who step up." CCR Principal Deputy Director Dr. Robert Wiltrout, he announced, will become the new director of CCR.

Dr. Antman joined NCI after more than 7 years as director of the Herbert Irving Comprehensive Cancer Center at Columbia University College of Physicians and Surgeons. Dr. Antman has been instrumental in expanding NCI's interactions with cancer centers and in

(continued on page 2)

Director's Update

CTWG to Unveil Draft Proposal and Invite Continuing Input at NCAB

The Clinical Trials Working Group (CTWG), a panel of 40 clinical trialists, advocates, and government representatives established in 2004 by NCI Director Dr. Andrew C. von Eschenbach to evaluate the national cancer clinical research enterprise, will report draft recommendations to the National Cancer Advisory Board (NCAB) this week.

Dr. James H. Doroshow

As part of its transparent, inclusive approach to increasing cancer clinical trials efficiency, decreasing redundancy and administrative burdens, and better coordinating activities to enhance the development and delivery of the best therapies to people with cancer, CTWG welcomes public comment on the draft recommendations. Final CTWG recommendations, to be presented to NCAB in June, will incorporate public input.

Last year, CTWG formed subcommittees to address six key issues: coordination across different funding mechanisms, regulatory issues, core research services, patient accrual, standardization and infrastructure, and prioritization. So that

(continued on page 2)

(Leadership Changes continued from page 1)
revising the P30/P50 grant guidelines for cancer centers and Specialized Programs of Research Excellence (SPOREs).

Prior to his arrival at NCI in 2000, Dr. Barrett worked for 23 years at the National Institute of Environmental Health Sciences, the last 5 years as the Division of Intramural Research scientific director. With the merger of the NCI divisions of Basic and Clinical Sciences into the CCR, Dr. Barrett led the effort to enhance interdisciplinary and translational biomedical research within the intramural research program by promoting closer links between basic researchers and clinical investigators.

Dr. Wiltrout joined NCI in 1986 as a researcher in the Laboratory of Experimental Immunology. During his two decades at NCI, Dr. Wiltrout has established a distinguished career in cytokine-mediated immunology while taking on increasing administrative and leadership responsibilities in CCR, particularly for the NCI campus in Frederick, Md.

Finally, Dr. von Eschenbach announced that Dr. Lee Helman, currently a CCR deputy director and chief of the CCR Pediatric Oncology Branch, has been named acting scientific director for clinical research in CCR, and that Craig Reynolds will serve as the operational head of NCI-Frederick. Dr. Helman has been at NCI since 1983, beginning his career as a research fellow. In this new role in CCR, Dr. Helman will lead a renewed focus on clinical research as the process of re-engineering the intramural research program moves forward.

Highlighting some of the challenges currently facing NCI employees—from new budgetary restraints to uncertainty about the recently proposed revised NIH conflict-of-interest restrictions—Dr. von Eschenbach affirmed his commitment to ensuring that NCI continues to grow and evolve, including ongoing opportunities for NCI staff.

"This will always remain one of my highest priorities: the mentorship, the nurturing, and the development of our 'human capital,'" he said. "Nothing is more important than the people who make up this institution." ◆

(Director's Update continued from page 1)
the community at large could convey suggestions about the future of cancer clinical trials, CTWG posted 27 questions pertaining to these areas on its Web site. Thousands of clinical trial stakeholders, including academic clinical investigators; community medical oncologists; patient advocates; and representatives from government agencies, industry, and professional groups, were invited to provide input and submitted over 2,200 replies.

These replies informed the activities of the CTWG subcommittees who were simultaneously formulating draft recommendations. Among the recommendations refined by public input is a proposal for NCI to establish a correlative science budget to be accessed on a protocol-by-protocol basis. Web responses noted the lack of funding for correlative studies as a barrier to robust clinical trials. Web responses also overwhelmingly agreed that standardizing many elements of clinical trials would improve the quality of studies. Similarly, a draft CTWG recommendation is that NCI establish standards, in concurrence with the Food and Drug Administration (FDA), for appropriate data collection. Another important initiative identified by both public responders and CTWG is a Web-based informational tool on all federally funded cancer clinical trials.

Although I chair CTWG, the group's recommendations represent the consensus of the extramural research community—a diverse group of researchers making up the majority of CTWG members—along with NCI staff. Thus, the subcommittee chairs, representing various clinical trial stakeholder groups, will present the draft recommendations on February 17, at 8:30 a.m. Eastern Time (available at http://videocast.nih.gov).

The subcommittee chairs and co-chairs are Drs. David Johnson, president, American Society of Clinical Oncology; David Alberts, director, University of Arizona Cancer Center; Richard Schilsky, chair, Cancer and Leukemia Group B national cooperative group; Fred Appelbaum, director, Clinical Research Division, Fred Hutchinson Cancer Research Center; David Parkinson, vice president, Amgen; Peter Adamson, chief, Clinical Pharmacology, Children's Hospital of Philadelphia; James Abbruzzese, director of the NCI-sponsored pancreatic SPORE at the University of Texas M.D. Anderson Cancer Center; Mark Ratain, Cancer Research Center, University of Chicago; Richard Pazdur, director, FDA Division of Oncology Drug Products; and Steven Averbuch, executive director, Merck Research Laboratories.

In addition to comments from NCAB, CTWG will continue to seek community input on the recommendations. Instructions on how to comment on the draft proposal will be posted on the CTWG Web site (http://integratedtrials.nci.nih.gov) following the NCAB presentation. I know CTWG members look forward to continued interactions in defining a new cancer clinical trials infrastructure that will lead us to accelerating the translation of novel cancer therapies into the clinical oncology community. ◆

Dr. James H. Doroshow
Director, NCI Division of Cancer Treatment and Diagnosis

Special Report

Smoking Cessation Program Improves Overall and Lung Cancer Survival

Intensive smoking cessation programs not only can help people stop smoking, but, for those who do quit, they also can significantly improve long-term survival, according to new results from the Lung Health Study (LHS) released today. Among the LHS participants randomly assigned to an intensive smoking cessation program, there was a 15 percent lower death rate at more than 14 years of follow-up. The finding, the study authors stressed, is striking because the intervention only led to cessation at 5 years in less than one-quarter of participants. However, of the 22 percent of participants who were able to stop smoking for 5 years, 90 percent continued to abstain at 11 years, compared with just 5 percent of those randomly assigned to usual care.

In addition to the overall survival findings, lead author Dr. Nicholas Anthonisen from the University of Manitoba and colleagues reported death rates from lung cancer were also lower in the special intervention group than the usual care group. This is the first time, the authors noted, that such data have been reported "in the context of a clinical trial." The data, they continued, "are consistent with those of previous cohort and case control studies that showed that measurable effects of cessation on lung cancer are usually not evident in the first 5 years, and that lung cancer risk is probably still elevated after 15 years of cessation."

Dr. Scott Leischow, chief of the NCI Tobacco Control Research Branch, called the reduction in lung cancer incidence "one of the study's most critical findings." It also demonstrates again, he continued, "that after smoking prevention, smoking cessation is the single most effective method to prevent lung cancer; the study showed that lung cancer deaths were decreased more than 50 percent within 15 years of complete smoking cessation."

The study—sponsored by the National Heart, Lung, and Blood Institute and published in the February 15 *Annals of Internal Medicine*—was launched in 1986 and followed nearly 5,900 middle-aged smokers who had mild to moderately abnormal lung function but were otherwise healthy at enrollment. Participants were assigned to either a 10-week intensive smoking cessation program (see sidebar) or to usual care. There were 731 deaths: 33 percent due to lung cancer (240 cases), 22 percent due to cardiovascular disease (163 cases), and 21 percent (154) due to cancers other than lung.

Participants 45 and younger saw the biggest survival benefit from the specialized intervention, which, the authors argued, demonstrated that smoking cessation was "most effective in preventing truly premature death."

LHS Smoking Cessation Program

- Strong physician message
- Twelve 2-hour group counseling sessions
- Behavior modification and nicotine gum
- Quitters entered a maintenance program that stressed coping skills

Approximately 75 percent of original participants were followed continuously for the subsequent 10 years by biannual phone contact and one clinic visit 11 to 12 years after randomization.

Dr. Leischow agreed, adding that it also offers a critical public health message. "This argues for a continued emphasis on encouraging teens and young adults not to start smoking," he said. "But if a person is smoking, we need to get them to quit at the earliest possible age. It's critical that all health care providers be aggressive in helping smokers to quit, and to follow up and do what they can to help them maintain abstinence."

When the 5-year LHS results were published, the smoking cessation program was associated with a lower rate of lung function decline, but there were no differences between morbidity or mortality among treatment groups. But the results seen nearly a decade later, wrote Dr. Jonathan M. Samet of the Johns Hopkins School of Public Health in a related editorial, place a stamp of urgency on current antismoking efforts.

"If we are to begin to control the rising number of smoking-related deaths soon," Dr. Samet wrote, "we must increase rates of smoking cessation now, since we won't see the benefits for decades." ◆

Cancer Research Highlights

APC Trial Safety Data Published: Increased Risk of Serious Cardiovascular Events Shown

Participants in a large colorectal cancer prevention study had an increased risk of serious cardiovascular events—cardiovascular death, heart attack, stroke, or heart failure—if they took the arthritis drug celecoxib (Celebrex) daily for an average of almost 3 years, according to an analysis released online by the *New England Journal of Medicine* on February 15. Celecoxib is one of several compounds that preferentially block one of two cycloxygenase (COX) enzymes that are produced in response to inflammation and by precancerous tissues. It was approved by the FDA for the treatment of osteoarthritis and adult rheumatoid arthritis in December 1998.

The participants in the Adenoma Prevention with Celecoxib (APC) Trial taking 200 mg of celecoxib twice a day had more than 2 times the risk of cardiovascular events, and those taking 400 mg of celecoxib twice a day had more than 3 times the risk of cardiovascular events compared with those taking a placebo twice daily. These results led to the December 2004 suspension of the drug within the trial, which was cosponsored by NCI and Pfizer, Inc., celecoxib's manufacturer. The APC Trial included more than 2,000 people with a history of precancerous colon polyps. It began in late 1999 and is scheduled to be completed this spring.

The effectiveness of celecoxib in preventing the recurrence of colon adenomas in APC participants is being analyzed. "The ability of celecoxib, or another agent that inhibits COX-2, to prevent colorectal cancer is an important question that remains to be answered," said Dr. Ernie Hawk, director of NCI's Office of Centers, Training, and Resources and project officer on the APC Trial. "The cardiovascular events seen in the trial were serious, but the total number of events was relatively small. The potential benefit of celecoxib to prevent cancer or to relieve pain must be weighed against this risk."

Zinc Deficiency in Humans Increases Risk of Esophageal Cancer

Using X-ray fluorescence spectroscopy, NCI researchers have found an inverse relationship between tissue zinc concentration and subsequent risk of developing esophageal squamous cell carcinoma. This study, appearing in the February 16 *Journal of the National Cancer Institute*, provides some of the first human evidence of an association between zinc deficiency and esophageal cancer, and also demonstrates a novel approach to studying mineral concentrations in a variety of tissues.

Dr. Christian Abnet of NCI's Cancer Prevention Studies Branch and colleagues obtained esophageal tissue samples from a cohort in Linzhou, China. They measured zinc, copper, iron, nickel, and sulfur levels in samples from 60 subjects who developed esophageal squamous cell carcinoma and from 72 subjects who did not develop the disease. The team detected these levels of key elements by bombarding the samples with high-intensity X-rays, causing each element to glow with its characteristic energy signature.

"This technique has many advantages," said Dr. Abnet. "You can apply it to most elements, you only need a tiny tissue sample, and it doesn't damage the tissue, so you can make multiple measurements on one sample."

The average tissue zinc concentration was significantly lower in subjects who developed esophageal cancer than in control subjects. Subjects in the highest quartile of zinc concentration had a 5-fold lower risk of developing esophageal cancer than those in the lowest quartile. Overall, 90 percent of subjects in the highest quartile were alive and cancer-free after 16 years, compared with 65 percent of the subjects in the lowest quartile. There were no consistent associations with cancer risk for any of the other elements studied.

Two Studies Find Cause of Pediatric Brain Cancer; One Identifies Possible Treatment

A gene that helps guide prenatal brain development, orthodenticle homologue 2 (OTX2), is normally shut off after babies are born. But in the case of medulloblastoma, the most frequent pediatric malignant brain tumor, sometimes there are too many copies of OTX2 and the copies have been turned back on, according to two studies published in the February 1 *Cancer Research*.

In the first study, researchers at Johns Hopkins University School of Medicine cut DNA from medulloblastoma tumors into pieces and measured the quantity of each section to identify genomic duplications

(continued on page 5)

(Research Highlights continued from page 4)
and deletions. Two portions of DNA, both of which came from chromosome 14, appeared more frequently than expected; only one gene in these sequences, however, had high transcription levels: OTX2. The researchers analyzed copies of OTX2 in 42 other medulloblastoma samples and found the gene was amplified in 19 percent of these, with anywhere from 8 to 56 copies present. By comparison, OTX2 was expressed only rarely in samples from normal adult tissue and from other tumor types.

The second study, led by researchers at Duke University Medical Center and collaborators at Johns Hopkins and the University of Utah Medical Center, also identified multiple copies—as many as 10-fold—of OTX2 in medulloblastomas, with high transcription levels in 93 percent of cases. They then tested the effect of a known OTX2 blocker, all-trans retinoic acid (ATRA), and found that it decreased gene expression and increased apoptosis in the tumors. They concluded, "Our studies of ATRA in medulloblastoma, in conjunction with the studies of others, lay the conceptual framework for clinical trials of retinoids in the treatment of a commonly lethal pediatric brain tumor."

Circadian Rhythms' Effect on Immune Cells Influences Chemo Toxicity

The body's internal or circadian clock may influence chemotherapy toxicity through its effect on immune system B cells, researchers reported last week in a *Proceedings of the National Academy of Sciences* early online release. It has been long known that the time of day when chemotherapy is delivered can influence toxicity in animal studies. Researchers from the Cleveland Clinic and Northwestern University tested the chemotherapy agent cyclophosphamide (CY) in mice with mutations in genes that control circadian rhythms: the Clock, Bmal1, and Cryptochrome (Cry) genes.

According to the researchers, led by Dr. Marina Antoch, a cell biologist at the Cleveland Clinic Foundation, and Dr. Joseph Takahashi, a Howard Hughes Medical Institute (HHMI) investigator at Northwestern, the Clock and Bmal1 genes are major activators of the molecular circadian clock, and mutations in these genes slow or stop the clock at the low point of its cycle. However, defects in Cry genes, which are activated by Clock and Bmal1, lock up the clock at its most active point. Treatment with CY, the team found, was significantly toxic to mice with Clock or Bmal1 mutations at any time of day. Mice that lacked the Cry genes, on the other hand, were more resistant to toxicity, again, regardless of the time of day.

The cause of these time-of-treatment differences has traditionally been thought to be due to circadian differences in drug metabolism. What researchers found, however, was that severe reductions in B cells (immune system cells targeted by CY) were more pronounced in mice with Clock mutations. "Thus, this paper gives us specific mechanistic insight into the role of circadian rhythms in sensitivity to [chemotherapy] drugs," Dr. Takahashi said in an HHMI news release. "This is not some vague metabolic difference between night and day. This is a tangible difference in the immune system that influences sensitivity."

Neoadjuvant Therapy Should Not Replace Surgery in Breast Cancer Treatment

Neoadjuvant systemic therapy—delivery of hormone or chemotherapy before surgery or radiation—has been recognized as a promising option for nonmetastatic breast cancer patients because it controls local disease progression and can minimize surgery. But, as researchers from the University of Ioannina School of Medicine in Greece have shown, timing of treatment makes no difference in terms of mortality, disease progression, or disease recurrence, and treatment beforehand may actually have adverse consequences. Their findings were published in the February 2 *Journal of the National Cancer Institute*.

For their analysis, the researchers reviewed 9 randomized trials with collective data from 3,861 patients in which neoadjuvant therapy was compared with adjuvant therapy. In addition to showing that there was no difference between the two arms in terms of survival, disease progression, and recurrence, the data showed a 22-percent higher risk for local disease recurrence in women who received neoadjuvant therapy, likely because those who showed a positive response forewent surgery. "Consequently," the authors wrote, "despite gross clinical response, the tumor bed may not be free of malignant cells, and tumor cell foci may be present in the majority of patients, increasing the risk for subsequent loco-regional disease recurrence." They concluded that, for patients who show a positive response to neoadjuvant therapy, surgery should not be replaced by radiation.

In an editorial, researchers at the Johns Hopkins Kimmel Cancer Center and Fox Chase Cancer Center agreed with this conclusion, and added, "We should strive to move beyond this limited understanding by formulating a uniform definition of a pathologic complete response and delineation of its molecular and imaging predictors." ◆

Featured Clinical Trial

Treating Kidney Tumors in Patients With Von Hippel-Lindau Disease

Name of the Trial
Phase II Study of 17-N-Allylamino-17-Demethoxygeldanamycin in Patients With Von Hippel-Lindau Disease and Renal Tumors (NCI-04-C-0238). See the protocol summary at http://cancer.gov/clinicaltrials/NCI-04-C-0238.

Principal Investigators
Dr. W. Marston Linehan and Dr. Ramaprasad Srinivasan (Protocol Chair), NCI Center for Cancer Research

Dr. W. Marston Linehan
Principal Investigator

Why Is This Trial Important?
Von Hippel-Lindau (VHL) disease is a rare inherited disorder characterized by the abnormal growth of tumors and/or cysts in the kidneys, eyes, brain, spinal cord, adrenal glands, and other parts of the body. While many of the tumors are benign (noncancerous), some—especially those of the kidney—may be malignant (cancerous). In fact, renal cell carcinomas are the major form of cancer in VHL disease and are seen in up to 45 percent of patients. The current standard treatment is surgical removal.

In this phase II trial, researchers are investigating whether treatment with 17AAG (17-N-Allylamino-17-Demethoxygeldanamycin) can effectively shrink kidney tumors in patients with VHL disease. Past research has shown that 17AAG can help cells eliminate proteins that play a role in cancer development and growth.

Patients in this study will receive three cycles of therapy over a 3-month period. Patients whose tumors shrink with 17AAG treatment may continue to receive the drug for another 12 weeks. Those whose tumors do not shrink or that grow after 12 weeks will be asked to undergo surgery to remove their kidney tumors.

"If this drug is well-tolerated, it has the potential to reduce or eliminate the need for multiple surgeries in patients with VHL," said Dr. Linehan.

Who Can Join This Trial?
Researchers seek to enroll 16–25 patients aged 18 and over, diagnosed with VHL disease, who have one or more kidney tumors that pose a risk of spreading and for which surgical removal would be considered the standard approach. See the full list of eligibility criteria for this trial at http://cancer.gov/clinicaltrials/NCI-04-C-0238.

Where Is This Trial Taking Place?
This study is taking place at the NIH Clinical Center in Bethesda, Maryland.

Contact Information
For more information, call the NCI Clinical Studies Support Center (CSSC) toll free at 1-888-NCI-1937 or call the protocol coordinator, Sarah Fowler, R.N., in the Urologic Oncology Branch at 301-435-6255. The call is confidential. ◆

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

Funding Opportunities

The following are newly-released NCI research funding opportunities:

Research on Sleep and Sleep Disorders

PA-05-046
Application Receipt Dates: May 10 and Sept. 10, 2005; Jan. 10, May 10, and Sept. 10, 2006; Jan. 10, May 10, and Sept. 10, 2007; Jan. 10 and May 10, 2008

This funding opportunity will use the NIH R01 and R21 award mechanisms. For more information see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=2560. Inquiries: Dr. Ann O'Mara, R.N.—ao45s@nih.gov.

Protein Biomarkers of Infection-Associated Cancers

PA-05-048
Application Receipt Dates: May 10 and Sept. 10, 2005; Jan. 10, May 10, and Sept. 10, 2006; Jan. 10, May 10, and Sept. 10, 2007; Jan. 10, 2008

This funding opportunity will use the R01 and R21 award mechanisms. For more information see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=2562. Inquiries: Dr. Karl Krueger—kruegerk@mail.nih.gov.

Units for HIV/AIDS Clinical Trials Networks

RFA-AI-05-002
Letter of Intent Receipt Date: Jun. 10, 2005.
Application Receipt Date: Jul. 11, 2005.

This funding opportunity will use the U01 award mechanisms. For more information see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=2561. Inquiries: Office of the Director—FY06UNITRFA@niaid.nih.gov.

For comprehensive information about NCI funding priorities and opportunities, go to http://www.cancer.gov/researchandfunding.

(continued on page 7)

(Funding Opportunities continued from page 6)

The NIH Roadmap for Medical Research Funding *provides a framework of the priorities NIH must address to optimize its research portfolio. It identifies the most compelling opportunities in three main areas: new pathways to discovery, research teams of the future, and re-engineering the clinical research enterprise. Newly released Roadmap funding opportunities are listed below. For information on additional Roadmap funding opportunities, go to http://nihroadmap.nih.gov.*

Predoctoral Clinical Research Training Programs

RFA-RM-05-015
Letter of Intent Receipt Date: Feb. 25, 2005.
Application Receipt Date: Mar. 25, 2005.

For more information on predoctoral clinical research programs see http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-05-015.html. Application materials for this process are posted at http://grants.nih.gov/grants/funding/phs398/phs398.html.

Multidisciplinary Clinical Research Career Development Programs

RFA-RM-04-00

Applications for this RFA must be prepared using the PHS 398 forms, available online at http://grants.nih.gov/grants/funding/phs398/phs398.html. ◆

NCI Director's Gold Star Awards

At a Feb. 15 NCI All-Hands meeting, director Andrew C. von Eschenbach presented the NCI Director's Gold Star Award in recognition of special accomplishments. Award recipients were Drs. Michelle Christian, Cancer Therapy Evaluation Program; Gregory J. Downing, Office of Technology and Industrial Relations; Daniel Gallahan, Division of Cancer Biology; Jon F. Kerner, Division of Cancer Control and Population Sciences; and Sanya Springfield, Comprehensive Minority Biomedical Branch. ◆

Notes

NCI Releases Software for Sharing Microarray Data

NCI recently released a new software tool, caArray, that will help medical researchers share and analyze microarray data. This technology can be used by cancer researchers to identify new genes associated with certain cancers, classify tumors, and predict patient outcomes. Researchers in fields other than cancer are expected to find equally valuable applications for caArray.

The tool's open-source, open-access software was developed by NCI's Center for Bioinformatics (NCICB) and can be used to create public repositories of microarray data, linking scientists across the country and around the world. Built on international standards of MAGE and MIAME, caArray promotes the sharing of high-quality, well-annotated microarray data within the research community while ensuring secure sharing of sensitive data. The software is compatible with the cancer Biomedical Informatics Grid (caBIG), so data can be integrated for further analysis.

Researchers can download the software at http://ncicb.nci.nih.gov/download. For more information, contact Mervi Heiskanen at heiskame@mail.nih.gov or Sue Dubman at dubmans@mail.nih.gov.

NCI Workshop Identifies Strategies and Priorities for Biomarker Discovery

NCI has recently funded two consortia that will create public informatics and data resources to help evaluate profiles of serum and tissue proteins associated with mouse models of human cancer. These resources will integrate with NCICB's caBIG and ultimately extend beyond mouse models to support cooperative clinical cancer biomarker discovery efforts. Last week, consortia representatives met in Seattle with proteomics informatics experts, potential resource users, and NCICB staff to prioritize development needs and outline a plan to accomplish consortia goals. Representatives discussed consortia designs and the current state of supporting informatics, data, and specimen annotation resources. Workshop attendees identified priorities and strategies to optimize resource use and discussed the issues and needs for extending the informatics resources to meet emerging needs in clinical cancer biomarker research. More information about the mouse model consortia and NCI clinical proteomic technologies initiatives will be available online this spring.

Langer to Present at NCI Nanotechnology Seminar Series

Dr. Robert S. Langer, Kenneth J. Germeshausen Professor of Chemical and Biomedical Engineering at the Massachusetts Institute of Technology, is the next featured speaker in NCI's Nanotechnology Seminar Series. The series features innovative perspectives on current research and development efforts in nanotechnology applied to cancer diagnosis, treatment, and prevention. Dr. Langer's lecture, "Novel Drug Delivery Systems for Cancer," will take place February 24 from 2:00 to 3:00 p.m. at the NIH campus in Bethesda, Md., in the Clinical Center's Lipsett Amphitheater.

This presentation will be webcast at http://videocast.nih.gov. Sign language interpreters will be provided. For more information on the lecture, visit http://nano.cancer.gov/events_nanotech_seminar_series.asp. ◆

Community Update

NCI, FDA Sponsor Biomarker Meeting

NCI and FDA jointly sponsored a meeting February 2-4 at M.D. Anderson Cancer Center in Houston to develop new strategies for integrating biomarkers into cancer clinical trials. Participants focused on how best to speed discovery of biomarkers and translate their use into clinical practice.

NCI Director Dr. Andrew C. von Eschenbach noted that the oncology field is poised for a quantum leap that may change the outcome of the cancer process, in which normal cells become malignant ones.

Biomarkers are characteristics that are measured and evaluated as indicators of normal and disease processes or responses to therapy. For example, prostate-specific antigen and CA-125 are biomarkers for prostate and ovarian cancer, respectively.

As researchers learn more about cancer at the molecular level, biomarkers could be used to:

- Define homogeneous disease subgroups at the molecular level
- Understand specific disease pathways
- Select patients based on identification of drug target
- Demonstrate drug efficacy that might otherwise have been missed in a study population
- Conduct clinical trials more efficiently
- Expedite FDA approval of drugs that benefit patients in a cost-effective manner

The sequencing of the human genome and emergence of proteomics has spurred the search for biomarkers, but the field has not developed as quickly as expected, according to Dr. Leland Hartwell, president, Fred Hutchinson Cancer Research Center, especially with regard to the discovery of protein biomarkers.

Dr. Hartwell noted that broad-based initiatives with teams of scientists supported by large-scale information technologies will be needed to successfully meet the biomarker discovery challenge in proteomics.

The speakers described the current technical challenges in the field, particularly the need to identify and quantify the many proteins affected in cancer. Many of the speakers also called for standardized methods, new technologies, and common reagents to identify and validate potential biomarkers to ensure comparability across laboratories.

Collecting, archiving, and annotating human blood, serum, and tumor tissue samples is a current challenge. Wide variability in collection techniques and annotation methods is a major obstacle. Participants agreed that common databases are needed to enable the best use of available data.

Dr. Anna Barker, NCI deputy director for Advanced Technologies and Strategic Partnerships, ended the meeting, noting that, "The development of biomarkers for integration into clinical trials is both a scientific and regulatory challenge. Therefore, it is gratifying that the FDA has participated so fully in this meeting, as advances in science can inform biomarker development through FDA's Critical Path Initiative." ◆

Featured Meetings and Events

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

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

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

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