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Eliminating the Suffering and Death Due to Cancer

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Gefitinib Use Plummets Following ISEL Trial Results

More than 85 percent of clinical oncologists who treat lung cancer patients have modified their care patterns based on the results of a clinical trial that showed the targeted agent gefitinib (Iressa) failed to improve survival compared with placebo. At a meeting of the Food and Drug Administration (FDA) Oncology Drugs Advisory Committee last week, officials from the drug's manufacturer, AstraZeneca PLC, reported the data, along with additional market research on gefitinib use since the company issued a "Dear Doctor" letter on Dec. 17, 2004 and other communications describing the trial's overall survival results.

"Physicians are aware of the [trial] results and are no longer selecting Iressa as their EGFR inhibitor of choice," said Carolyn Fitzsimons, an executive director with AstraZeneca. "They are choosing erlotinib (Tarceva)."

In the Iressa Survival Evaluation in Lung cancer (ISEL) trial, gefitinib was tested as a second- or third-line therapy in nearly 1,700 patients with advanced non-small-cell lung cancer (NSCLC). AstraZeneca officials presented further data from ISEL during the advisory committee meeting, including subset analyses revealing a significant survival advantage with gefitinib in never smokers and

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Director's Update

Clinical Proteomics: Developing Standardized Tools for Cancer Research

Diagnosing cancer as early in its course as possible and developing targeted drugs for treatment result in better clinical outcomes for patients. However, the development of effective tools that enable early diagnosis and targeted therapies has been an elusive endgame. Using proteins as biomarkers has long been considered a promising clinical diagnostics approach for drug discovery and development. Some biomarkers, such as prostate-specific antigen, have been in use for many years. Many other potential biomarkers are being reported in the literature almost weekly, although few have been translated into the diagnostic arena.

In short, our progress has not been as rapid as we would like, especially given the advances in our understanding of the process by which cancer develops and becomes lethal. I believe this is about to change. This morning, in fact, during a meeting of the NCI Board of Scientific Advisors (BSA), there was rich discussion about improving both the efficiency and effectiveness of proteomic biomarker research in the United States. Specifically discussed were the need to develop animal correlates, to integrate and align existing resources such as biorepositories, and to leverage knowledge gained from

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patients of "Asian ethnicity."

These latter findings are consistent with previous studies of gefitinib, and represent a "real effect of the drug," argued AstraZeneca's Dr. Kevin Carroll. Many committee members agreed that some patients clearly benefit from gefitinib. Several others commented that the trial, while it did not meet its primary endpoint, was, as one member put it, "as close to a positive trial as you can get."

As for the subset analyses—which were not a prespecified component of the trial—a negative result in the overall population can cloud the accuracy of subsequent subset analyses, said Dr. Janet Dancey, a senior investigator in the NCI Cancer Therapy Evaluation Program. "The more subset analyses that are done, the more likely is the chance that positive results will be seen," she said. "However," she continued, "there are data from other studies which also show benefit in these subgroups, raising the probability that the beneficial effects seen in never smokers and patients with East Asian ethnicity are true."

The ISEL trial was one of several post-market trials required of AstraZeneca under the accelerated approval mechanism used by FDA to approve gefitinib in May 2003—an approval granted solely based on the agent's ability to shrink tumors in a small percentage of patients. The follow-up studies—one has been abandoned; the other, which is pitting gefitinib against docetaxel, is ongoing—were required to show whether gefitinib could extend survival. Although gefitinib fell short in ISEL, both erlotinib and pemetrexed (Alimta) have proven in clinical trials to improve survival in patients with advanced lung cancer who have previously received chemotherapy.

The committee generally agreed that AstraZeneca had done a good job of communicating the preliminary ISEL results to the oncology community, including the "Dear Doctor" letter, which advised clinicians "to consider other treatment options in the recurrent [NSCLC] patient population." According to AstraZeneca's market research, 78 percent of clinical oncologists were familiar with the letter and 86 percent said they had modified their treatment practice as a result.

Dr. Richard Pazdur, director of FDA's Division of Oncology Drug Products, said the agency will not make a decision on gefitinib's fate in the marketplace until the final ISEL data are reviewed. The final trial data, including an analysis of survival in relation to EGFR expression and mutation status—potential indicators of patient response to the drug—will be available by June, AstraZeneca officials said. ◆

(Director's Update continued from page 1)
work with tumors where the biology is known and apply this to the complex proteomics of serum and other body fluids.

Over the past 2 years, we have conducted an extensive planning process, analyzing U.S. and international proteomics programs, resources, and capabilities; conducting symposia with thought leaders; and seeking other disease models as possible guides for future NCI activities.

What has emerged is a consensus that, while proteins are critical to future progress in cancer biology, we will not realize clinical applications unless we take action. There is clearly the opportunity to apply biomarkers to support a host of clinical tools and capabilities, from early detection to molecular imaging probe and sensor development, to drug discovery, to rationally developed and conducted clinical trials.

As many researchers have pointed out, the field has been handicapped by barriers related to technology, reagents, bioinformatics, and systems. In particular, there is a lack of standard protocols and internal standards for current technologies to enable reproducibility of researchers' work. We also are faced with the enormous biological diversity, range, and dynamic nature of the proteins that we are attempting to measure. Other issues, like the insufficient supply of biospecimens specifically collected for protein analysis and variable approaches for data capture, analysis, and management also have slowed progress. Overall, we have heard repeatedly that what's needed is a coordinated system that no single academic or commercial entity is in a position to develop and operate.

Today, the BSA deferred action in order to further refine and develop the proposal. NCI is committed to removing barriers to success. We will continue to develop and integrate our proteomic initiatives. We plan to develop a coordinated proteomics technology development system that will provide the cancer research community with the technologies, reagents, standards, bioinformatics platforms, databases, and other resources necessary to systematically discover cancer biomarkers—in effect, to build the "base of a pyramid" that will be the foundation of the clinical development of biomarkers for early detection and diagnosis. This system will be managed with specific program milestones to ensure the best use of resources and progress.

This has been a true team effort, coupling the work of NCI staff and some of the cancer's community most eminent researchers. We look forward to continued discussions with experts and advisors around the country as we further develop this vision. ◆

Dr. Andrew C. von Eschenbach
Director, National Cancer Institute

Spotlight

Rapid Advances in Overcoming Drug Resistance to Molecularly Targeted Therapies

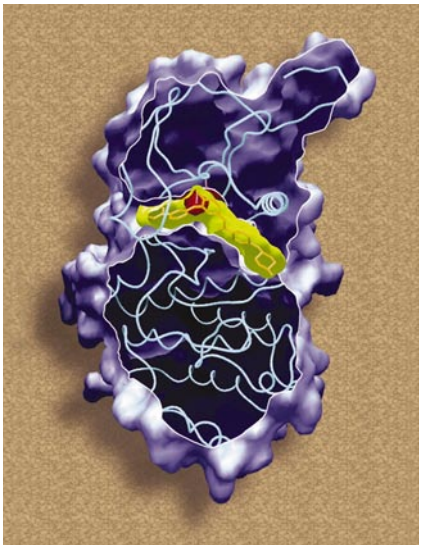
Virtually every oncologist has been faced with a patient who developed resistance to a chemotherapy treatment that had been working—this is called acquired drug resistance. Targeted therapies are not immune to this phenomenon, including the most successful targeted agent, imatinib (Gleevec).

The FDA's approval of imatinib for the treatment of chronic myeloid leukemia (CML) in 2001 launched the era of targeted therapy for cancer treatment. The drug directly inhibits an abnormal protein tyrosine kinase on white blood cells called BCR-ABL that, instead of regulating cell growth, remains continually active, fueling uncontrolled cancer cell growth in this form of leukemia.

"Many patients who initially respond well to imatinib therapy are at risk of developing resistance to the drug and suffering relapse—even those whose disease may appear to be in complete remission," explains Dr. R. Allan Mufson, chief of the Cancer Immunology and Hematology Branch in NCI's Division of Cancer Biology. Resistance comes on, Dr. Mufson adds, as the leukemia cells begin to derive mutations in BCR-ABL that prevent the drug from binding, rendering it impotent.

"We now know of over 30 different mutations that can cause BCR-ABL to become resistant to imatinib," says Dr. Charles Sawyers of UCLA's Jonsson Cancer Center. "In patients with newly diagnosed disease, we are seeing resistance to imatinib in about 4 percent of patients per year. The further the disease has progressed before initiating imatinib treatment, the greater the chances are that resistance will arise."

In many cases, practicing oncologists whose patients become resistant to chemotherapy have few, if any, options to combat the problem. But that's beginning to change. Recent advances in understanding the molecular basis of many cancers are allowing researchers to reverse engineer therapeutics by identifying the source of resistance and developing agents to combat it. The rapid development and testing of several second-generation therapies aimed at overcoming imatinib resistance is a case in point.



Courtesy of: Lore Leighton, Laboratory of John Kuriyan, HHMI.

Imatinib (orange) shuts down the overactive BCR-ABL protein (purple). Mutations, however, can alter the shape of the protein's active site, preventing imatinib from binding tightly and reducing its effectiveness.

Studies on two new compounds—BMS354825 and AMN107—have generated excitement. Like imatinib, both agents inhibit the aberrant function of the BCR-ABL kinase. Bristol-Myers Squibb (BMS) was already developing BMS354825 to inhibit a closely related kinase in solid tumors. Following Dr. Sawyers' presentation at a scientific conference on potential methods to combat imatinib resistance, BMS officials contacted him to see if their agent might fit the bill. AMN107, on the other hand, was specifically designed by Novartis to overcome imatinib resistance based on their studies of the molecular interactions between BCR-ABL and imatinib. Both new drugs are less specific than imatinib, which allows them to bind and inhibit many imatinib-resistant mutants. They are also more potent than imatinib, meaning less of the drug is needed to cause the same biological effect.

"Preclinical studies show BMS354825 is about 300 times more potent than imatinib, and AMN107 is about 20 times more potent than imatinib," says Dr. Sawyers.

Last summer, Dr. Sawyers and colleagues published a report in *Science* on their preclinical studies with BMS354825. The drug, they reported, was effective against 14 of the 15 different imatinib-resistant mutations tested, and significantly prolonged the survival of mice with CML.

Based on these studies, BMS began a phase I clinical trial in conjunction with Dr. Sawyers and Dr. Moshe Talpaz at M.D. Anderson Cancer Center. Preliminary trial results, reported in December 2004 at the American Society of Hematology

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Cancer Research Highlights

Adjuvant Chemo Works Equally Well in Older Women

Women over the age of 65 who have lymph node-positive breast cancer but are otherwise in good health can benefit from adjuvant chemotherapy just as much as younger women, according to a study published in the March 2 *Journal of the American Medical Association*.

The research team reviewed data from 4 clinical trials that collectively enrolled more than 6,000 women. They found that women over age 65 had more lymph nodes positive for cancer and a higher rate of treatment-related mortality than did younger women, but that age had no relationship to the positive effects of chemotherapy and tamoxifen on disease-free and overall survival.

The authors stress that elderly cancer patients may experience age discrimination from health care providers and family members who fear that they are too frail for the toxic effects of chemotherapy. This is underscored by the fact that only 8 percent of patients enrolled in the 4 studies analyzed were aged 65 or older, though about half of new breast cancer diagnoses occur in women in this age group.

The authors caution that not all older patients are good candidates for chemotherapy, and cite www.adjuvantonline.com as a model for healthcare providers to use in estimating the benefit of adjuvant chemotherapy for these women.

High Blood Levels of Vitamin E Linked to a Lower Prostate Cancer Risk

Men with higher levels of vitamin E in their blood were found to have a lower risk of developing prostate cancer, according to a report in the March 2 *Journal of the National Cancer Institute*.

The study was led by Drs. Stephanie J. Weinstein and Demetrius Albanes of NCI's Division of Cancer Epidemiology and Genetics. They conducted a case-control analysis of 300 men from the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) trial of nearly 30,000 Finnish participants. The ATBC trial had previously shown that men who took vitamin E supplements had a 32 percent lower incidence of prostate cancer than those who did not.

For the current report, the scientists measured for the two principal forms of vitamin E—alpha-tocopherol and gamma-tocopherol—in the baseline serum before the men took vitamin E pills. Men with the highest baseline levels of alpha-tocopherol had a 53 percent reduction in risk and those with the highest levels of gamma-tocopherol had a 39 percent reduction in risk.

"These data reinforce the protective relationship seen in the ATBC trial for alpha-tocopherol," said Dr. Weinstein. "They also suggest that the other major form of vitamin E—gamma-tocopherol—may also inhibit prostate carcinogenesis."

Dr. Albanes noted that the findings "should be reassuring" for the SELECT trial, which is testing the effects of alpha-tocopherol and selenium supplements in prostate cancer prevention, because "we saw stronger inverse associations between prostate cancer and serum concentrations of both tocopherols in the men who were receiving the trial alpha-tocopherol supplements."

Gene Mutations Associated with Lung Cancer in Nonsmokers

A new study confirms previous reports that mutations in the EGFR (epidermal growth factor receptor) gene, which are associated with responsiveness to the lung cancer drug gefitinib (Iressa), occur preferentially in four subsets of patients: women, patients who have never smoked, Asians, and patients with adenocarcinoma.

The reason the mutations appear among these groups is not clear, but they can lead to the development of non-small-cell lung cancer, according to research in the March 2 *Journal of the National Cancer Institute*. In the largest such study to date, researchers profiled more than 600 lung tumors from patients in Japan, Taiwan, the United States, and Australia.

EGFR mutations were more common in females than males (42 percent vs. 14 percent), in never-smokers than in smokers (51 percent vs. 10 percent), in adenocarcinomas than in other types of lung cancer (40 percent vs. 3 percent), and in patients of East Asian ancestry than in other ethnicities (30 percent vs. 8 percent).

EGFR mutations are the first known to occur in nonsmokers with lung cancer, according to Dr. Adi F. Gazdar of the University of Texas Southwestern Medical Center at Dallas, who led the study. "We always believed that lung cancer in nonsmokers was due to exposure to second-hand smoke, but here we're seeing very different changes at the molecular level in nonsmokers and smokers," said Dr. Gazdar. "The implication is that there may well be factors that lead to cancer in nonsmokers other than second-hand smoke."

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(Research Highlights continued from page 4)

Intervention for Rural Residents Improves Dietary Behavior

The first physician-endorsed, low-intensity dietary intervention to target a rural, low-income population made up of poorly educated, minority individuals demonstrated the feasibility of effectively changing dietary behavior in rural residents. Results of the NCI-funded Rural Physician Cancer Prevention Project, published in the February *American Journal of Preventive Medicine*, demonstrate significant improvement in dietary fat and fiber consumption in this population.

Dr. Elizabeth Fries, of Virginia Commonwealth University, and her colleagues enrolled patients from three physician practices in rural Virginia and randomly assigned them to an intervention (tailored feedback on eating habits, brief counseling, and dietary self-help booklets) or control group. Intervention materials were written at or below a sixth-grade reading level and mailed along with letters from participants' physicians. Investigators conducted follow-up phone interviews 1, 6, and 12 months after the intervention. Individuals in the intervention group significantly reduced their dietary fat intake, increased dietary fiber consumption, and expressed an intention to reduce dietary fat and eat more fiber, fruits, and vegetables.

Efforts to improve health in rural areas may be compromised due to reduced access to health care and lack of appropriate nutrition education. The authors note that rural primary care providers may be viewed by community members as the only legitimate source of health information; however, many are overburdened with a large patient load. This study shows that a low-intensity dietary intervention can net significant changes without increasing time constraints on physicians. ◆

Funding Opportunities

The following are newly-released NCI research funding opportunities:

In Utero Exposure to Bioactive Food Components and Mammary Cancer Risk

PA-05-059
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 NIH investigator-initiated research project grants (R01) and Exploratory/Developmental (R21) award mechanism(s). For more information see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=2620. Inquiries: Dr. Cindy D. Davis—davisci@mail.nih.gov.

Continued Development and Maintenance of Software

PAR-05-057
Application Receipt Dates: May 17 and Sept. 13, 2005; May 17 and Sept. 13, 2006; May 17 and Sept. 13, 2007

This funding opportunity will use the R01 award mechanism as well as competitive supplements to existing R01, R33, P01, P41, P50, and P60 grants that have already been awarded by one of the participating Institutes or Centers. For more information see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=2600. Inquiries: Dr. Jennifer A. Couch—couchj@mail.nih.gov.

Correlative Studies with Specimens from Multi-Site Trials

PA-05-062
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 NIH investigator-initiated research project grant (R01) and the NIH exploratory/developmental grant (R21) award mechanisms. For more information see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=2640. Inquiries: Dr. Heng Xie—xieh@mail.nih.gov.

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

***The NIH Roadmap for Medical Research Funding** provides a framework of the priorities NIH must address to optimize its research portfolio. For information on Roadmap funding opportunities, go to http://nihroadmap.nih.gov.* ◆

CCR Grand Rounds

March 15: Dr. Cynthia Dunbar, Head, Molecular Hematopoiesis Section, Hematology Branch, NHLBI, and Dr. Neal G. Copeland, Director, Mouse Cancer Genetics Program, CCR, NCI-Frederick
"Of Mice and Monkeys: Stem Cell Immortalization Genes Unmasked"

March 22: Dr. Kenneth C. Anderson, Kraft Family Professor of Medicine, Harvard Medical School; Chief, Division of Hematologic Neoplasia; Director, Jerome Lipper Multiple Myeloma Center, Department of Medical Oncology, Dana-Farber Cancer Institute
"Targeting the Myeloma Cell in its Microenvironment"

CCR Grand Rounds are held 8:30 to 9:30 a.m. at the NIH campus in Bethesda, Md., in the Clinical Center's Lipsett Amphitheater. ◆

(Spotlight continued from page 3)
Annual Meeting, showed that BMS354825 overcame imatinib resistance in 31 of 36 patients.

"We have seen outstanding responses with no side effects in patients with all phases of the disease," comments Dr. Hagop Kantarjian, another clinician involved in the clinical trial and principal investigator of the leukemia-focused NCI Specialized Program of Research Excellence at M.D. Anderson.

While the phase I trial with BMS354825 is almost complete, Dr. Sawyers explains, "Our results to date are so promising that we have already begun the phase II portion."

Preliminary results from the phase I trial testing AMN107 in patients with imatinib-resistant disease show no adverse effects in any of the 95 patients treated, says Dr. Kantarjian, who also is involved in trials developing that agent. "Most of our patients are in later stages of the disease, and we are getting an early response rate of about 50-60 percent." Currently researchers are correlating responses with particular BCR-ABL mutations and trying to determine the optimal dose for the phase II portion of the study.

"Both BMS354825 and AMN 107 seem to have similar clinical potency. These new drugs pave the way for designer cancer treatments that could be used as second-line therapies for those who develop resistance to imatinib," says Dr. Kantarjian. "Alternatively, these drugs could be administered as an initial kinase inhibitor cocktail to prevent the development of resistance to any of the particular drugs—akin to how protease inhibitor cocktails are used to treat HIV." ◆

Featured Clinical Trial

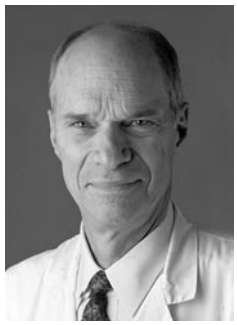
Comparing Treatment for Women with DCIS

Name of the Trial

Phase III Randomized Study of Anastrazole Versus Tamoxifen in Postmenopausal Women with Ductal Carcinoma *in Situ* of the Breast Undergoing Lumpectomy and Radiotherapy (NSABP-B-35). See the protocol abstract at http://cancer.gov/clinicaltrials/NSABP-B-35.

Principal Investigators

Dr. Richard Margolese, National Surgical Adjuvant Breast and Bowel Project; Dr. Betty Mincey, North Central Cancer Treatment Group; Dr. Kathy Albain, Southwest Oncology Group; Dr. Pat W. Whitworth, American College of Surgeons Oncology Group.



Dr. Richard Margolese
Principal Investigator

Why Is This Trial Important?

Ductal carcinoma *in situ* (DCIS) of the breast is a noninvasive condition in which a small mass of cells has formed within a milk duct but has not spread outside the duct. Some but not all DCIS will become invasive breast cancer. Breast-conserving surgery (lumpectomy) combined with radiation therapy and total mastectomy are standard treatments for DCIS. Post-surgical treatment with the drug tamoxifen may further reduce the chance of DCIS recurrence or invasive breast cancer development.

Recent studies indicate that anastrazole, which belongs to a class of drugs called aromatase inhibitors, is more effective than tamoxifen in preventing breast cancer recurrence in postmenopausal women treated with surgery for invasive breast cancer. In this trial, researchers are investigating whether anastrazole is more effective than tamoxifen in preventing DCIS recurrence and invasive breast cancer development in postmenopausal women treated with lumpectomy and radiation therapy for DCIS.

"Anastrazole has shown significant improvements over tamoxifen in terms of safety and efficacy," said Dr. Margolese. "We believe it has the potential to be an important treatment option for women with DCIS."

Who Can Join This Trial?

Researchers seek to enroll 3,000 postmenopausal women with a confirmed diagnosis of DCIS who have had their tumors surgically removed. See the list of eligibility criteria at http://cancer.gov/clinicaltrials/NSABP-B-35.

Where Is This Trial Taking Place?

Multiple study sites in the United States and Canada are recruiting patients for this trial. See the list of study sites at http://cancer.gov/clinicaltrials/NSABP-B-35.

Contact Information

See the list of study contacts at http://cancer.gov/clinicaltrials/NSABP-B-35 or call the NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237). The call is toll free and completely confidential. ◆

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

Notes

Los Angeles Science Writers Seminar

The NCI Press Office conducted two special events in Los Angeles last month. On February 23, NCI sponsored its first Science Writers' Seminar outside of the D.C. area, partnering with local Comprehensive Cancer Centers in presenting a seminar on cancer and genetics. Dr. Steve Libutti of the CCR Surgery Branch of NCI and researchers from UCLA's Jonsson Cancer Center, USC/Norris Cancer Center, and City of Hope presented information to reporters from National Public Radio, the *L.A. Times*, *N.Y. Times*, *Pasadena Star-News*, *Santa Monica Daily Breeze*, and a number of major publications that target Hispanic and Asian populations in the L.A. basin. The archived webcast of the seminar can be viewed at http://videocast.nih.gov/PastEvents.asp?c=4.

On February 24, Dr. Libutti joined staff from the Centers for Disease Control and Prevention (CDC) in visiting head writers and producers from such TV shows as *Medical Investigations*, *ER*, and *Grey's Anatomy* to discuss potential stories related to cancer and how NCI and CDC can assist them in developing factual and informative dramas. That evening Dr. Libutti, along with five other prominent spokespersons, addressed a well-attended symposium at the Writers Guild of America on areas of interest and concern in genetic testing for cancer and other diseases.

Correction

In the March 1 Note about Dr. Keith Wailoo's National Library of Medicine (NLM) lecture on "Race, Science, and Cancer," the *NCI Cancer Bulletin* incorrectly stated that videotapes were available for purchase. Tapes are not available for purchase but the lecture may be viewed at the NLM's History of Medicine Reading Room or borrowed via interlibrary loan. For more information, please contact Dr. Stephen J. Greenberg, Coordinator of Public Services, History of Medicine Division, National Library of Medicine, at 301-435-4995 or greenbes@mail.nih.gov. We regret the error. ◆

Roberts Wins Leopold Griffuel Prize

Dr. Anita Roberts of CCR's Laboratory of Cell Regulation and Carcinogenesis, has won the 2005 Leopold Griffuel Prize, awarded by the French Association for Cancer Research. The prize of 100,000 euros goes to an individual or group whose research has led to a major discovery in the field of cancer.

Dr. Roberts was recognized for her seminal work in the purification, characterization, and further analysis of transforming growth factor-β (TGF-β), which she began almost 20 years ago in the NCI laboratory of Dr. Michael Sporn. TGF-β is a protein with properties and functions common to many growth factors. TGF-β has emerged as a growth factor with unique signaling paradigms and plays key roles in wound healing, as well as in autoimmune disease, fibrosis, and cancer.

Past winners of the Leopold Griffuel Prize include Drs. C. Everett Koop, Samuel Broder, Steven Rosenberg, Robert Gallo, and Vincent DeVita. The award ceremony will take place in Paris on October 15.

Prostate Cancer Endpoints Discussed at FDA Advisory Meeting

Endpoints for prostate cancer clinical trials was the topic of discussion at the FDA's quarterly meeting of the Oncologic Drugs Advisory Committee on March 3. An endpoint is an event or outcome that can be measured objectively to determine whether the intervention being studied is beneficial.

The discussion focused primarily on the utility of endpoints based on prostate-specific antigen (PSA) levels and other indicators such as quality-of-life measures. No clear consensus emerged about endpoints, but part of the discussion focused on a proposal to use a reduction in PSA by 50 to 75 percent over 3 months as the primary indicator of efficacy in a prospective clinical trial for advanced prostate cancer.

Liotta to Leave NCI

Dr. Lance Liotta of the Section of Tumor Invasion and Metastases in NCI's CCR announced that he will leave NCI in May to become co-director of the Center for Proteomics and Molecular Medicine at George Mason University in Fairfax, Va., with Dr. Emanuel Petricoin, of FDA's Center for Biologics Evaluation and Research. The new center will work with the university's resources in mathematics, engineering, life sciences, and nanotechnology to accelerate the translation of basic science discoveries in the world of proteomics to innovative clinical research and patient-tailored medicine. ◆

Community Update

How Will New Ethics Guidelines Affect NCI's Relationships with the Cancer Community?

The release last month of new conflict-of-interest guidelines for NIH researchers and staff has generated questions throughout the cancer community about how relationships with NCI intramural scientists may change. NCI Director Dr. Andrew C. von Eschenbach emphasized that NCI scientists will be able "to continue to pursue these critical relationships and, in fact, find new avenues for partnerships, collaboration, and cooperation as official duty activities."

"As a dynamic research institution, we will continue the tradition of supporting and encouraging collaborative research," commented Dr. Robert Wiltrout, director of NCI's Center for Cancer Research (CCR). "Although there have been new policies relating to conflict-of-interest review, CCR is committed to using all of the available official duty mechanisms to ensure that our researchers maintain their traditional research interactions with industry and academia.

"Our researchers remain ready to fully participate in collaborations through a variety of well-established collaborative mechanisms such as Cooperative Research and Development Agreements (CRADAs), Clinical Trial Agreements (CTAs), and Material Transfer Agreements, while continuing to look for additional mechanisms to facilitate research interactions," Dr. Wiltrout continued. "The new rules and regulations retained most of the existing flexibility in regard to maintaining and engaging in official duty activities outlined in the February 22 *NIH Catalyst*. CCR will continue to use these mechanisms to ensure future collaborative research successes."

The partnerships NCI pursues as official duty activities are designed to take the comparatively early findings coming out of NCI, help them mature, move forward, and eventually become commercial treatments and products that benefit the public health. As long as an activity is consistent with their official duties, NIH researchers can continue to participate in collaborations with pharmaceutical and biotech companies and academic research centers. With the appropriate clearances, NIH researchers will also be able to maintain memberships on committees and boards of professional associations.

In addition, as part of official duties, NIH researchers will still be able to:

- Present research at scientific conferences and through publication
- Lecture or conduct a workshop on their research at appropriate venues
- Exchange research materials
- Edit publications
- Hold a patent and receive royalties from an invention arising from NIH work

A tighter standard applies to some activities—such as writing or editing a peer-reviewed scientific publication and teaching Continuing Medical Education courses—for which scientists can still be paid to perform in a personal capacity, subject to funding source.

"Clearly these regulations are bringing about some significant changes at NCI and NIH," acknowledged Dr. Wiltrout. "But as far as our researchers' official interactions with others who are affected by what we do here, NCI researchers will continue to be active collaborators and participants." ◆

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.