THE CANCER LETTER

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Troubles of Two Landmark Cancer Drugs Likely To Shape Prevention, FDA Policy

By Paul Goldberg

Recent setbacks in the trials of Celebrex and Iressa are likely to influence the manner in which drugs for the treatment and prevention of cancer are developed and approved.

The issues at stake in the development of Celebrex and Iressa are very different, but the mechanism of approval that brought the two drugs to market is the same: accelerated approval.

Efforts to validate the endpoints on which the approvals were based resulted in trouble for the two drugs:

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In Brief:

Bush Nominates EPA Administrator, Former Utah Governor Leavitt As HHS Secretary

MICHAEL LEAVITT, head of the Environmental Protection Agency, was nominated by President George W. Bush to serve as secretary of the Department of Health and Human Services. If confirmed by the Senate, he will replace **Tommy Thompson**, who announced his resignation last month. Leavitt, a former three-term governor of Utah, served 13 months at EPA, succeeding **Christine Todd Whitman**. . . . **MICHAEL FRIEDMAN**, president and CEO of City of Hope Cancer Center, was appointed to the 27-member Independent Citizen's Oversight Committee that will govern the new California Institute for Regenerative Medicine and oversee the implementation of $3 billion stem cell research effort created by Proposition 71. "Friedman's public policy background and scientific leadership will be of enormous benefit in fulfilling the committee's critical public mission," said **Phil Angelides**, California State Treasurer. Friedman, who joined City of Hope in 2003, has served as acting commissioner of FDA and director of the NCI Cancer Therapy Evaluation Program. . . . **DAVID ABRAMS** was appointed associate director for Behavioral and Social Sciences Research and director of the Office of Behavioral and Social Sciences Research at NIH. Abrams is director of Behavioral Medicine Research at Brown University, where he also holds appointments as professor in the Department of Psychiatry and Human Behavior, director of the Miriam Hospital Centers for Behavioral and Preventive Medicine, and founding director, Brown University Centers for Behavioral and Preventive Medicine. He was chairman of the NCI Review Group Report on Cancer Control, and a member of the NCI Board of Scientific Advisors. Abrams succeeds NIH Deputy Director **Raynard Kington**. . . .

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Lawsuits, Investigations Spread To Pfizer's Celebrex

(Continued from page 1)

—After a large clinical trial found no survival advantage for Iressa, its sponsor AstraZeneca stopped all promotional activity of the agent and withdrew the application for approval in Europe. Meanwhile, FDA officials are trying to decide whether Iressa should become a landmark of a different sort: the first drug approved under the accelerated approval program to be taken off the market.

—After an NCI-sponsored clinical trial of Celebrex as a prevention of recurrence of benign polyps found an elevated risk of cardiovascular events among patients taking the COX-2 inhibitor, the polyp prevention trials have been halted, and FDA urged the Institutional Review Boards to weigh acceptability of other trials.

Whatever the ultimate outcome, Pfizer's Celebrex became the second COX-2 inhibitor to run into trouble as a result of cancer prevention trials (**The Cancer Letter**, Oct. 15 and Oct. 22, 2004). Merck's drug Vioxx was withdrawn after a similar prevention study found an elevated risk of cardiovascular events in patients taking the drug.

For Merck, the withdrawal of Vioxx meant the loss of a blockbuster drug, a drop in stock the price, an explosion of product liability suits, and investigations by two Congressional committees, the U.S. Department of Justice, and the Securities and Exchange Commission (**The Cancer Letter,** Nov. 12).

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After Pfizer announced its bad news, Congressional committees expanded their investigations to include Celebrex, and plaintiffs' attorneys started recruiting patients who may have been harmed.

Though Pfizer maintains that Celebrex is safe at approved doses and for approved indications, industry figures show that during the week ended Dec. 24, physicians wrote 54 percent fewer new prescriptions for the drug than they did the previous week.

The investigations, lawsuits, and devastating publicity have affected FDA. Congressional critics charge that the agency has grown too close to the regulated industry and has failed to protect the public. NIH, too, could potentially be affected because of its role in development of agents based on surrogate endpoints and for its role in sponsoring trials.

Top NCI officials and many scientists have advocated development of cancer prevention agents based on their impact on surrogate endpoints, and chemoprevention appears to be a component of the plan by NCI Director Andrew von Eschenbach to end "suffering and death due to cancer" by the year 2015.

Two years ago, NCI, the American Association for Cancer Research, and C-Change developed detailed plans to attract pharmaceutical companies to the emerging area of development of cancer preventions based on surrogate endpoints.

One such plan called for reliance on the NCI Surveillance, Epidemiology, and End Results program to monitor toxicity. The plan, floated by NCI, also called for reform of tort laws, changes in protection for intellectual property, and fundamental reform of FDA's approach to evaluation of compounds used for cancer prevention (**The Cancer Letter**, May 30, 2003).

Celebrex: A Milestone in Cancer Prevention

In 1999, Celebrex was approved as a pharmacologic adjunct to usual care for familial adenomatous polyposis, a rare condition that invariably leads to the development of colon cancer.

The drug was approved based on its ability to reduce the number and size of lesions in FAP patients, and it is yet to receive regular FDA approval by demonstrating benefit to patients.

While FAP is rare, scientists used the approval as the basis for developing a larger indication: reduction of sporadic tumors, in effect proposing to use COX-2 inhibitors as an alternative to colonoscopy in patients with a history of benign polyps.

"[FAP] was a springboard," said Bernard Levin, vice president for cancer prevention and population

sciences at M.D. Anderson Cancer Center and co-principal investigator of the Pfizer-sponsored study of Celebrex. "It led to the possibility that celecoxib alone could be used in a much more common condition, namely sporadic polyps, and then, if it were safe and it were effective, it could be used in combination."

Suddenly, it seemed that prevention of cancer was on the verge of moving toward rational drug design.

"The rationale for a drug like Celebrex or Iressa was stronger than the rationale for some of the natural compounds, because there was evidence that those pathways were up-regulated or were turned on in cancer progression," said Fadlo Khuri, Blomeyer Professor of Hematology and Oncology at Emory University Winship Cancer Institute, who was involved in planning a chemoprevention trial with Iressa.

When bad news on the toxicity of Vioxx first surfaced last October, researchers held out hope that the "class effect" wouldn't engulf Celebrex. The two agents are different, as Vioxx is more specific to COX-2, experts said.

On Dec. 17, NCI reported that its prevention trial showed a significant increase in cardiovascular risk on the Celebrex arm, where patients were taking 400mg (200mg twice daily) and 800mg (400mg twice daily) doses of the drug. The common arthritis dose is 200mg per day.

A separate trial by Pfizer reported no difference in cardiovascular risk between 400mg once daily of Celebrex and placebo. The company trial and the NCI trial were analyzed in an identical fashion, Levin said.

Three days later, an NIH Alzheimer's prevention study that compared the 400mg dose of Celebrex with the over-the-counter dose of naproxen (440mg per day) and placebo found an apparent increase in risk for patients on naproxen, compared to placebo. The Alzheimer's study found no significant increase in cardiovascular risk on the Celebrex arm, but found.

On. Dec. 23, FDA issued a "public health advisory" on non-steroidal anti-inflammatory drugs, including COX-2 inhibitors and urged the IRBs to reevaluate these studies in view of the new findings.

The Celebrex polyp prevention trials were put on hold by formal action of the Data and Safety Monitoring Boards. Levin agrees with the rationale for putting a hold on the trials and having the IRBs and NCI examine each trial individually.

"What was done was right," he said. "The reaction was, don't assume any risk. Public safety is on the line. Stop the trial to be sure of what you are exposing people to. Now comes a more in-depth analysis of what accounts for differences in side-effect profiles between the various studies."

Levin said he favors prompt resumption of the FAP trials, which he says are appropriate, given the high risk of colorectal cancer in that population.

The fundamental rules of cancer prevention haven't changed, Levin said. Acceptability of a prevention strategy is determined by a correlation of risks and benefits.

"If you are talking about someone who has a substantial risk of developing a cancer that's not going to be handled well by conventional means, then chemoprevention is very justifiable," Levin said. "If you are talking about a condition that could be handled by more conventional means, then you don't want to incur risks."

Richard Pazdur, director of the FDA Division of Oncology Drug Products, agrees.

"The chemoprevention trials are about 'risk reduction,'" he said. "One cannot quantify risk without adequately knowing the risk of developing cancer, the implications once cancer is detected, and long term safety issues of the drug being tested. Risk reduction must be considered a balance—reducing the risk of cancer on one hand—and safety issues on the other."

It is unclear whether the surrogate endpoint on which the COX-2 inhibitor studies were based would be conclusively tested, Khuri said.

"These were surrogate endpoints and they weren't validated yet," Khuri said. "We hoped to validate them through the trials, but there is a big question as to how many companies, if any, are going to be willing to take the risk of losing a multibillion-dollar drug for what is now a much smaller market?"

If Merck's and Pfizer's experience make other companies reluctant to test their drugs in patients at a relatively low risk of developing cancer, researchers would have to return to working with nutraceuticals, Khuri said.

"We will be looking at nutraceuticals for cancer prevention, and the likelihood is that they are not going to be as effective as the coxibs and other agents we have," Khuri said. "This is a huge step back."

Levin agrees that the future of chemoprevention doesn't look as bright as it did five years ago.

"Celecoxib opened up new vistas for potential for chemoprevention," he said. "Those windows are no longer as open, but you can't say the that the whole field is dead. There are other promising pharmacological leads, e.g. statins, that need to be explored.

"I think it means that we have to understand

molecular action, we have to understand risk better. It needs more refinement. You need better science. There are no shortcuts.

"Nature guards its secrets jealously."

The Iressa Challenge

From the outset, Iressa tested the boundaries of FDA's accelerated approval regulations.

The drug was approved on the thinnest of evidence, a small, single-arm trial that demonstrated a 10 percent response in third-line lung cancer.

Though the response rate scraped the bottom of the lower bound of the confidence interval, testimonials from patients who claimed to have experienced a dramatic benefit from the drug appeared to have swayed the vote Oncologic Drugs Advisory Committee (**The Cancer Letter**, Sept 27, 2002, May 9, 2003).

"The agency realized an inherent risk in approving drugs under accelerated approval," Pazdur said. "The uncertainty is reflected in the regulations stating that the surrogate endpoint must be 'reasonably likely' to predict clinical benefit—an improvement in survival or disease-related symptoms. The endpoint for accelerated approval is not necessarily an established surrogate for clinical benefit.

"This risk is balanced by the need to avail drugs that are better than available therapies to Americans who face serious and life-threatening diseases," Pazdur said. "The post-approval confirmatory trials to document clinical benefit take an added importance in accelerated approval. We have been adamant that these the initial accelerated approval trials be part of a comprehensive drug development plan with the confirmatory trials preferentially being started prior to drug's commercial availability."

On Dec. 17, Zeneca announced that its Iressa Survival Evaluation in Lung cancer (ISEL) trial with 1,692 patients showed that the agent failed to significantly prolong survival in comparison to placebo in the overall population (HR 0.89, p=0.11, Median 5.6 vs. 5.1 months), or in patients with adenocarcinoma (HR 0.83, p=0.07, Median 6.3 vs. 5.4 months).

The trial demonstrated a statistically significant improvement in tumor shrinkage. According to the company, "prospective subgroup analyses suggested survival benefits in patients of Oriental origin and in patients who never smoked."

Separately from the trial, two teams of researchers from Massachusetts General Hospital and Dana-Farber Cancer Institute found somatic mutations of the epidermal growth receptor gene that correlate with response to Iressa (**The Cancer Letter**, April 30, 2004).

After Iressa received and accelerated approval based on the surrogate endpoint of response, another, similar drug, Genentech's Tarceva (erlotinib), received full approval for the same indication. This makes Iressa's position more precarious: if the drug is pulled off the market, patients would still have a treatment option, Tarceva.

The FDA statement on the Iressa trials demonstrates that the agency is considering withdrawal:

"After the approval of Iressa in 2003, AstraZeneca conducted a study… to determine whether the drug would in fact prolong survival in comparison to patients taking placebo," the agency said in a statement dated Dec. 17. "The results… indicate that the drug did not prolong survival.

"Under FDA's accelerated approval program, the agency has the authority to remove a drug from the market if a post-marketing clinical study fails to verify clinical benefit. After FDA has evaluated the recent study results, FDA will determine whether Iressa should be withdrawn from the market or if other regulatory actions are appropriate."

Listening to Iressa

"If you go by the letter of the law, if the follow-up phase III study fails to show patient benefit, then the drug shouldn't be on the market any longer," said Brian Druker, JELD-WEN professor of Leukemia Research at the Oregon Health & Science University Cancer Institute and a developer of the targeted drug Gleevec.

"But in the meantime, there have been advances in the science and the understanding of what patient population the drug would work for that I think supersede the phase III trial results," he said.

According to MGH and Dana-Farber studies, no more than 15 percent of lung cancer patients have the EGF receptor mutations that predict response to Iressa, a fact that makes it less of a surprise that a trial in a general population of patients showed no survival advantage, Druker said.

Also, the technology for selecting likely responders has been developed and is available. "They should do a quick trial in patients with the mutation, show that it has a high response rate, and be done with it," Druker said. "But I wouldn't pull it from the market while the trial is being done."

There are other subtleties in the Iressa story, Druker said. First, it is unclear whether some patients who don't have the EGF mutations stand to benefit from

the drug, and it is unknown why Tarceva, a drug similar to Iressa, demonstrated a survival advantage.

"It needs to be sorted out why one would have a survival advantage and the other wouldn't, when by all indications they look to be very similar drugs," Druker said.

Pazdur said FDA is encouraging AstraZeneca to conduct trials in a subset of patients likely to benefit from the drug.

"We have more information about the EGFR drugs than when Iressa was initially approved," Pazdur said. "The agency detailed in Tarceva's product label an exploratory survival analysis of subgroups based on immunohistochemistry staining for EGFR status.

"We are not talking about EGFR mutations where the science is evolving, performed only in academic labs," he said. "We are talking about a simple, commercially available test.

"Could a similar subgroup analysis based on EGFR status that we provided in the Tarceva label salvage Iressa? The answer would be driven by the results of such an analysis, and we are encouraging AstraZeneca to rapidly proceed in this direction."

NCI Programs

NCI To Award 15 Contracts For Cancer Information Service

NCI has selected 15 organizations for five-year contracts to operate its Cancer Information Service.

These regional CIS offices will work with local organizations through the CIS Partnership Program to disseminate cancer information. Four awardees will operate CIS Contact Centers, providing information through a toll-free telephone service (1-800-4-CANCER), and instant messaging on NCI's Web site, www.cancer.gov.

Previously, 14 offices operated a Partnership Program and a Contact Center. "I am pleased to say that we have been successful in streamlining the program, enabling us to retain key regional partnerships with organizations that work to address cancer health disparities and to consolidate the Contact Center functions while containing costs," NCI Director Andrew von Eschenbach said.

Following are the awardees:

New England Region (Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont): Yale University Cancer Center, Vincent DeVita Jr.

New York Region (New York): Memorial Sloan-Kettering Cancer Center (Contact Center award), Thomas Fahey Jr.

Atlantic Region (Delaware, New Jersey, Pennsylvania): Fox Chase Cancer Center, Paul Engstrom.

Mid-Atlantic Region (District of Columbia, Maryland, Virginia, West Virginia): West Virginia University/Mary Babb Randolph Cancer Center, Pamela Brown.

Southeast Region (Georgia, North Carolina, South Carolina): Duke University Cancer Center, Isaac Lipkus Reiner.

Mid-South Region (Alabama, Arkansas, Kentucky, Louisiana, Mississippi, Tennessee): University of Kentucky/ Markey Cancer Center, Steven Wyatt.

Coastal Region (Florida, Puerto Rico, US Virgin Islands): University of Miami (Contact Center award) Sylvester Comprehensive Cancer Center, Clyde McCoy.

Mid-West Region (Indiana, Michigan, Ohio): Wayne State University/Karmanos Cancer Center, Terrence Albrecht.

Heartland Region (Illinois, Kansas, Missouri, Nebraska): University of Kansas Medical Center (Contact Center award), Gary Doolittle.

North Central Region (Iowa, Minnesota, North Dakota, South Dakota, Wisconsin): University of Wisconsin Cancer Center, Patrick Remington.

South Central Region (Oklahoma, Texas): M. D. Anderson Cancer Center, Stephen Stuyck.

Rocky Mountain Region (Arizona, Colorado, Montana, New Mexico, Utah, Wyoming): Penrose-St. Francis Health Systems, Donna Bertram.

Northwest Region (Alaska, Hawaii, Idaho, Nevada, Oregon, Washington): Fred Hutchinson Cancer Research Center (Contact Center), Lee Hartwell.

California Region (California)**:** Northern California Cancer Center, Dee West.

Pacific Region (Hawaii and U.S. Associated Pacific Territories): University of Hawaii, Brian Issell.

Letter to the Editor:

American Legacy Foundation Fighting For Survival In Court

To the Editor:

Re "As Legacy Foundation Seeks New Money, Critics Fear Symbiosis With Big Tobacco," Oct. 29.

The article completely ignored the fact that the foundation is fighting for its very life in the courts of Delaware. Because of our tough and effective youth prevention campaigns, the foundation is being sued by Lorillard Tobacco Co. The court recently recognized that the more effective our campaigns are, the more likely it is that our organization will be sued. Lorillard has asked the court to order that all of the funds paid to the foundation on behalf of the states under the MSA be returned, not just to Lorillard but to all the signatories of the MSA. None of the other tobacco manufacturers has stepped forward to distance themselves from this claim.

This is hardly a "symbiotic relationship."

We are particularly concerned about the suggestion that we are solely concerned with our own institutional survival even if it means accepting funds from the tobacco industry. Nothing could be further from the truth. Our funding is not a "windfall," but an integral part of a historic settlement agreement resolving the states' multi-billion dollar claims against the tobacco industry. The foundation is charged by the Master Settlement Agreement to counter-market tobacco to the nation. While the payments seem sizable, they are miniscule in comparison to the funds spent by the tobacco industry marketing its products. According to the Federal Trade Commission's Cigarette Report for 2002, the tobacco industry spent $12.5 billion in 2002 alone—an increase of $1.25 billion over 2001. The foundation's budget for the year was about $145 million.

The imbalance is made even more lopsided by a flaw in the MSA which allows the participating manufacturers to end their payments to the Public Education Fund after five years if their aggregate domestic market share drops below 99.05% of the total cigarette market. Their current share is in the neighborhood of 94%. Because of this clause, the foundation's ability to continue meeting its responsibilities will be severely compromised. As noted in the article, this provision in the MSA is now widely recognized by the public health community as having been a serious mistake.

To remedy this error, the foundation is seeking to build on the MSA by achieving a legally-binding amendment to obviate the 99.05 % provision. No one involved in this effort is soliciting donations from the tobacco companies.

There is ample precedent for using the MSA structure to execute a binding, legally-mediated agreement. One such agreement was reached with R.J. Reynolds Tobacco Co. that settled complaints brought by attorneys general in three states against the company's KOOL Mixx cigarette promotion targeting inner-city African American youth. As part of the agreement, funds will be made available to several organizations in tobacco control.

To ignore our funding crisis would be irresponsible. Our foundation's national "truth" campaign has been proven to significantly decrease youth smoking prevalence, as an upcoming article in the American Journal of Public Health will demonstrate. If we can no longer do this life-saving work, we may likely see youth smoking rates fail to decline further—as they have in Florida following the demise of the statewide truth campaign there—or very possibly increase.

In Minnesota, youth smoking declined following a successful tobacco prevention campaign, which was later eliminated due to budget cuts. Following the campaign's termination, surveys found a statistically significant increase in Minnesota's youth being "open to smoking."

There is no question that we meet with tobacco industry executives. We are required to do so. We have met with tobacco companies, with our lawyers, when they have lodged complaints against the foundation. We also meet with representatives of the tobacco industry publicly, as we did in February of 2002 at the Society of Research on Nicotine and Tobacco in New Orleans, at the MSA's Triennial Conference in 2001, and recently in Vermont. We use these meetings to openly challenge the industry—for example, on products about which we believe they are making false claims or to stop them from making direct grants, made in secret, that undermine the public health.

To clarify other items:

—The funding for the Citizen's Commission to Protect the truth is not derived from our resources. The American Legacy Foundation did not provide NAAG with the funding for the Commission. In fact, precisely the opposite occurred. NAAG provided the funds to the foundation, which in turn passed them on to the Citizen's Commission.

—The American Legacy Foundation provided C-Change with a restricted, $3 million dollar grant over a three-year period to ensure they were funding key components of the new 501(c)(3) and meeting the 7-Point Plan. Over a three-year period, our grant was not "twice as large as of other public and private sector contributors." The breakdown is as follows: half of the funds are intended for programs and half for general support. In fact, $150,000 was earmarked for the Tobacco Control Committee and $350,000 was directed for Early Detection and Prevention. The foundation's restrictions were intended to encourage C-Change to more strongly embrace tobacco as a top priority, given its ranking as the No. 1 cause of preventable death in the U.S. and the leading cause of cancer (a fact not reflected in NCI's current funding priorities).

—C-Change's public relations firm, Edelman, dropped the overseas account in question before they had been informed of the foundation's policy that they not take tobacco money. Moreover, Edelman is no longer working for C-Change. The "model policy" to not accept tobacco funding has to encourage all the diverse organizations that are members of C-Change to follow suit. C-Change itself may not accept tobacco industry

funding and retain our grant.

—Regarding grantees accepting tobacco industry funding, the foundation proudly adheres to the toughest conflict of interest policy of all, declining to fund researchers within university schools (e.g. schools of public health, medical schools and departments of government) where other researchers or programs accept money from tobacco companies.

—The Ethics Workshop in New Orleans was planned over the period of a year, and sponsored in cooperation with NCI and the California Tobacco-Related Disease Research Program. The meeting was planned by a team of tobacco control leaders, including: Francisco Buchting (California Tobacco-Related Disease Research Program), Co-Chair; Lyndon Haviland (American Legacy Foundation), Co-Chair; Mark Parascandola (NCI), Co-Chair; Lisa Bero (University of California at San Francisco); Brion Fox (University of Wisconsin); Tom Glynn (American Cancer Society); Jack Henningfield (Pinney Associates); John Hughes (University of Vermont); Ken Warner (University of Michigan); and Mitch Zeller (Pinney Associates).

While many leaders from the tobacco control community were present, there were just eight representatives from the industry. The conference was an effort to improve on the current very negative climate in regards to researchers accepting tobacco industry funding. The workshop was not established to reach consensus on this complex issue, rather, it was a chance to air concerns and share ideas and perspectives.

—The article quoted Cheryl Healton, Legacy president and CEO, as saying, "Post-MSA, there is much more appreciation for taking their money and laughing all the way to the bank." We felt it was important to reiterate that when she made that statement, she was actually referring to the current scenarios involving the flow of money—lacking the benefits of scrutiny—between researchers whose work is funded by the tobacco industry.

Julia Cartwright
Vice President, Communications
American Legacy Foundation

Funding Opportunities:

DoD To Provide $26 Million For Two Awards Programs

DoD Concept Awards ($10 million). Deadline: Feb. 1. Concept Awards are intended to fund an initial concept or theory that could give rise to a testable hypothesis within breast cancer research. The awards can be requested for $75,000 in direct costs over a 12-month performance period, plus indirect costs as appropriate.

DoD Era of Hope Scholar Awards ($16 million). Deadline: Feb. 10. These awards are intended for early-career scientists who have shown a strong potential for leadership in the breast cancer research community as well as a vision for the eradication of breast cancer. Unlike the previous Era of Hope Scholar Awards offering, eligible researchers may be 0-6 years from their last mentored training experience and the application does not require nominations. The awards can be requested for up to $2.5 million in direct costs plus indirect costs as appropriate for up to a 5-year performance period.

Inquires: http://cdmrp.army.mil.

RFAs Available

RFA-CA-05-002: Innovative Technologies for Molecular Analysis of Cancer

Letter of Intent Receipt Dates: Jan. 17, May 17, Sept. 18. Application Receipt Dates: Feb. 17, June 17, Oct. 18.

NCI invites applications for research projects to evaluate the usefulness of emerging technologies that are ready for initial application to clinical or biological questions in cancer research. Technologies solicited include, but are not limited to, those that are suitable for the detection of alterations and instabilities of genomic DNA; measurement of the expression of genes and gene products, including proteins; analysis and detection of gene and/or cellular products, including post-translational modification and function of proteins; identification and characterization of exogenous infectious agents in cancer; and assaying the function of major signal transduction networks involved in cancer. The RFA is available at http://grants.nih.gov/grants/guide/rfa-files/rfa-ca-06-002.html.

Inquiries: Gregory Downing, Office of Technology and Industrial Relations, phone 301-496-1550; fax 301-496-7807; e-mail downingg@mail.nih.gov.

RFA-CA-05-003: Application of Emerging Technologies for Cancer Research

NCI invites applications for research projects to evaluate the usefulness of emerging technologies that are ready for initial application to clinical or biological questions in cancer research. The RFA would support studies that start with an unproven technology, adapt or refine the technology slightly as needed, and begin to generate biological data to assess the relative robustness of the technology in the chosen biological or clinical context. The RFA is available at http://grants.nih.gov/grants/guide/rfa-files/rfa-ca-06-003.html.

Inquiries: See preceding RFA.

RFA-CA-05-024: Centers of Cancer Nanotechnology Excellence

Letter of Intent Receipt Date: Feb. 25. Application Receipt Date: March 25.

The intent of this RFA is to establish interdisciplinary research teams with expertise to identify approaches, and to validate and translate nanotechnology for a variety of cancer

applications, up to and including pre-clinical testing. The over-arching goals of the CCNE initiative are to design and test nanomaterials and nanodevices and to translate their use into clinical research, resulting ultimately in the introduction of novel diagnostic tools and techniques to modulate and overcome cancer processes. The RFA will use the NIH U54 cooperative agreement mechanism. The RFA is available at http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-05-024.html.

Inquiries: Gregory Downing, director, Office of Technology and Industrial Relations, NCI, phone 301-496-1550; fax 301-496-7807; e-mail downingg@mail.nih.gov.

RFA-CA-05-025: Multidisciplinary Career Development in Cancer Nanotechnology Research

Application Receipt Date: March 25

The RFA supports the career development of individuals from the basic, biomedical, clinical, and information sciences and engineering who are pursuing research that applies nanotechnology development and application for the prevention, detection, diagnosis, or treatment of cancer. The RFA will support individual postdoctoral fellowships F32 and senior fellowships F33. The RFA is available at http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-05-025.html.

Inquiries: See preceding RFA

Program Announcement

PA-05-029: Social and Cultural Dimensions of Health

The PA encourages the development of health research that integrates knowledge from the biomedical and social sciences to (a) elucidate basic social and cultural constructs and processes used in health research, (b) clarify social and cultural factors in the etiology and consequences of health and illness, (c) link basic research to practice for improving prevention, treatment, health services, and dissemination, and (d) explore ethical issues in social and cultural research related to health. The PA is available at http://grants.nih.gov/grants/guide/pa-files/PA-05-029.html.

Inquiries: For NCI--Sabra Woolley, phone 301-435-4589; fax 301-480-2087; e-mail woolleys@mail.nih.gov.

In Brief:

Hait Named Editor-In-Chief, Clinical Cancer Research

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WILLIAM HAIT, director of the Cancer Center of New Jersey, was named editor-in-chief of the AACR journal, Clinical Cancer Research. Hait, who has been co-deputy editor of the journal for five years, succeeds **John Mendelsohn**, president of M.D. Anderson Cancer Center, who served as editor-in-chief for 10 years. . . **STEVEN SHERMAN** was appointed chairman of the Department of Endocrine Neoplasia and Hormonal Disorders at M. D. Anderson Cancer Center. Sherman served as interim chairman of the department for the past four years. He also is chairman of the Thyroid Cancer Panel for the National Comprehensive Cancer Network Guidelines Program and director of the National Thyroid Cancer Treatment Cooperative Study Group. . . . **EDWARD SNYDER** was appointed associate director for shared resources at Yale Cancer Center, said **Richard Edelson**, director of the Yale Cancer Center. Snyder is professor of laboratory medicine at Yale School of Medicine and is director of the Blood Bank/Apheresis Service at Yale-New Haven Hospital and director of the Richard Frisbee Hematopoietic Cell Processing Laboratory at Yale Medical Center. . . . **AMERICAN SOCIETY OF CLINICAL ONCOLOGY** has formed a survivorship task force to address the long-term physical, emotional, and practical needs of cancer survivors. The task force will revise the ASCO oncology training curriculum, develop clinical practice guidelines on long-term care and monitoring of cancer survivors, and support additional research on interventions to improve long-term care, said ASCO President **David Johnson**. Another initiative involves having a cancer prevention symposium at the annual meeting. . . . **INTERNATIONAL HapMap Consortium** is making all of its data publicly available. The consortium is developing a map of common patterns, or haplotypes, of human genetic variation. The $130 million project, begun in 2002, is a partnership of scientists and funding agencies from Canada, China, Japan, Nigeria, the UK, and the U.S. The National Human Genome Research Institute leads the U.S. component. Information on the project at http://genome.gov/10001688. . . . **DANIEL IHDE**, former NCI deputy director and a lung cancer expert, died Dec. 9 in Rio Rancho, N.M. He was 61. Ihde worked at NCI from 1973 to 1994, serving as director of the Division of Hematology and Oncology at the Uniformed Services University of the Health Sciences, editor-in-chief of the Journal of the National Cancer Institute, and NCI deputy director from 1991 to 1994. He was chief of oncology at the Washington University School of Medicine in St. Louis from 1994 to 1997. Ihde was the first to report on the role of drug combinations for the treatment of both small cell and non-small cell lung cancers. He received a degree in mathematics from Eastern New Mexico University in 1964, a medical degree from Stanford University Medical School in 1969, and served his internship and residency at New York Hospital and Memorial Sloan-Kettering Hospital.

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