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Eliminating the Suffering and Death Due to Cancer

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New Studies May Aid Movement Toward Targeted Cancer Treatment

Three new studies highlight advancements being made toward individualized molecular classification of specific cancers and the potential for more targeted therapy. Two studies released in advance online publications of *Science* and the *New England Journal of Medicine* (*NEJM*) identified mutations of the epidermal growth factor receptor (*EGFR*) gene in certain non-small-cell lung cancer (NSCLC) patients that render their tumors sensitive to the drug gefitinib (Iressa). In the third study, published in the April 29 *NEJM*, investigators reported that they had identified a six-gene "signature" using microarray analysis that can be used to predict the response of diffuse large-B-cell lymphoma patients to standard chemotherapy.

Gefitinib was approved by the U.S. Food and Drug Administration last May as a third-line therapy for NSCLC, which accounts for 85 percent of lung cancer cases. However, previous clinical trials testing gefitinib have shown significant variability in response rates. For example, 10 percent of patients responded to gefitinib in a clinical trial with mostly patients of European ancestry, whereas a 27.5 percent response rate was demonstrated in a clinical trial with solely Japanese patients.

Though a minority of patients responds to treatment with gefitinib, confirmed Dr. Frederic J. Kaye of the NCI Clinical Genetics Branch, a

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Director's Update

Conference Affirms Priorities, Strategies for 2015

"An investment in knowledge," said Benjamin Franklin, "always pays the best interest." Perhaps without officially proclaiming it, this has been the cancer community's mantra. We have made a tremendous investment in learning as much as we can about cancer and it has paid untold returns. We have amassed enough knowledge that I believe we now have the edge on this disease: We have a distinct understanding of the process by which it develops and becomes lethal and, more importantly, we have learned its vulnerabilities. And every day that store of knowledge grows, amassing more power.

This was part of the message I delivered during an intriguing and exciting meeting last week, the Milken Institute Global Conference. Nearly 2,000 leaders from the worlds of business, public and foreign policy, academia, and other arenas participated. Along with some of America's most brilliant medical minds, including Nobel Laureates Drs. David Baltimore and Lee Hartwell, I had the honor of participating in five panels that all shared a common theme: identifying the steps that must be taken to make important, needed advances in medical care. Cancer was the focus of

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coauthor of the *Science* report, these new findings will allow physicians to identify the subset of patients who are most likely to benefit from the drug.

The *EGFR* protein, the cellular target of gefitinib, is a member of the tyrosine kinase family of proteins—a class of enzymes involved in cellular signaling that is commonly mutated in a number of different cancers. These mutations are believed to disrupt *EGFR's* ability to regulate itself, thus triggering its signaling pathway to induce uncontrolled cell growth. However, these mutations also render "the mutant *EGFR* proteins much more sensitive to gefitinib," added Dr. Kaye.

In both the *Science* and *NEJM* studies, the presence of *EGFR* mutations correlated with clinical response to gefitinib. The mutations were more prevalent in Japanese patients than in Caucasian patients. Tumors from 25 new Caucasian patients were also examined: 14 that responded to gefitinib and 11 whose cancer progressed during treatment. Thirteen of the 14 tumors from responders were found to have *EGFR* mutations, whereas no *EGFR* mutations were detected in the 11 tumors from patients that progressed.

These findings should improve the outcome for many patients with NSCLC and may lead to the development of other molecularly targeted drugs to treat patients with other cancers that have known *EGFR* mutations, such as glioblastoma. "This data powerfully validates and reenergizes the approach of targeted therapy and should impact the design of future clinical trials," said Dr. Kaye.

In the *NEJM* study on diffuse large-B-cell lymphoma, instead of identifying genetic mutations that predict treatment response, researchers were able to identify six genes that, when present in patients, predicted their response to standard chemotherapy. The goal of the study, explained authors Dr. Izidore S. Lossos and colleagues from Stanford University, the University of Miami, and Applied Biosystems, was to validate previous findings that identified genes and gene signatures for predicting treatment response and to formulate these into "a model that was technically simple and applicable for routine clinical use." Their model uses the molecular characteristics of lymphoma to divide patients into three pools of risk that reflect overall patient survival and can help determine the most appropriate treatment for individual patients.

"Lossos and coworkers have passed a milestone in the development of clinical diagnostic tests for cancer," wrote Dr. Sridhar Ramaswamy in an *NEJM* editorial. Their findings translate diagnostics, he continued, "from unbiased, genome scale surveys of gene expression in human tumors to the creation and initial validation of a novel diagnostic tool that should fit easily into clinical practice and might refine the currently available measures used for risk stratification." ◆

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several of these sessions.

It was immensely encouraging to witness the participants' almost uniformly positive feelings about our ability to defeat cancer. Beyond that, however, was the agreement about the roles technology and communication must play in this process. At NCI, we have embraced these same conclusions and have launched initiatives to make them a reality.

Take the cancer Biomedical Informatics Grid, or caBIG. With this initiative, we are using technology to connect all cancer researchers and provide unprecedented access to data and tools that will improve research efficiency. Then there is the National Advanced Technologies Initiative for Cancer, with which we are creating a coordinated national infrastructure to improve the availability of and access to key technologies. We also have made important investments in fields such nanotechnology and proteomics, and are driving advances in areas like imaging.

On several occasions, panel members bemoaned the expense and time now required to bring a new drug to market: approximately $800 million and more than 15 years. Greg Simon, president of the Center for Accelerating Medical Solutions, put it bluntly when he called the latter figure an "awful number." I agree. And I believe that technological advances can and will dramatically shorten this time.

But technology is only part of the solution. Again and again, conference participants talked about the necessity of collaboration and communication—not just between one or two segments of the medical establishment, but among all those with a stake in preventing illnesses from taking more lives. That means researchers, clinicians, advocacy groups, patients, technology companies, pharmaceutical companies, regulators, and others.

Again, NCI is leading the way. Through our partnership with the U.S. Food and Drug Administration, for example, we are developing processes to ensure that clinical trials are more efficient and effective, and that positive results are more quickly translated into new diagnostic or treatment options for patients. With caBIG, we are creating an entirely new portal to connect researchers, clinicians, advocates, patients, and others.

Overall, I returned to NCI late last week with a strong affirmation that we are indeed on the right track—on the path to 2015. And if the conference participants' attitude is any indication, I think we can count on a lot of help. ◆

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

Cancer Research Highlights

Study Provides New Insights into Tumor Cell Survival

A new study from NCI researchers has provided the first evidence that a specific transcription factor, C/EBPβ, is required for the transformation of macrophages into tumor cells, as well as the identification of a C/EBPβ-regulated gene that allows these cells to elude cell death and proliferate despite the absence of exogenous growth factors. The study, by Dr. Peter F. Johnson and colleagues, was published in the April 2004 *Molecular and Cellular Biology*.

The researchers infected bone marrow cells from mice lacking C/EBPβ with a transforming virus that carried the *Myc* and *Raf* oncogenes. This virus has been shown to produce myeloid tumor cells that are "self sufficient," no longer requiring external growth factors to proliferate. In this study, however, the authors showed that macrophage transformation is dependent on C/EBPβ. Further investigation using microarray analysis indicated that C/EBPβ activated the insulin-like growth factor I (*IGF-I*) gene, thus triggering a signaling pathway that is essential for tumor cell survival and proliferation.

Tumor cells' ability to avoid cell death is considered a central component of cancer development, the authors write. As a result, finding ways to interrupt the molecular pathways to tumor cell immortality, such as by inhibiting the activity of implicated transcription factors or the genes that they target, "has emerged as a promising strategy for cancer intervention."

A preliminary analysis, the authors noted, indicated that other transcription factors also are likely to play a role in *IGF-I* expression. The combination of their findings with future studies that further elucidate the mechanisms by which *IGF-I* is regulated, the authors concluded, "may facilitate the development of anticancer strategies based on inhibiting *IGF-I* production."

Evidence Shows Dynamic Nature of Steroid Receptor-Mediated Transcription

Dr. Gordon Hager and scientists in his laboratory have developed evidence that challenges the 30-year-old paradigm of how our cells respond to hormones. The classic view is that nuclear receptors such as the glucocorticoid receptor (GR) bind statically to chromatin—a complex of DNA and histone proteins in the cell nucleus—and nucleate large transcription complexes, which in turn mediate the transcription of genes that the receptor controls.

In a report published in the April 23 issue of *Molecular Cell*, Dr. Akhilesh Nagaich and colleagues in the Hager lab demonstrate that, contrary to widely held belief, the interaction of receptors such as GR with chromatin is highly dynamic and periodic; the interaction may last on the order of seconds rather than minutes or hours.

The researchers applied a technique called ultraviolet (UV) laser crosslinking to their novel *in vitro* chromatin model system, which closely approximates the *in vivo* state of a natural promoter. The UV laser crosslinking allowed the researchers to make fast measurements of GR binding and dissociation from the chromatin. They show the receptor first binds cooperatively to promoter DNA during chromatin remodeling, then is actively ejected from the template as the remodeling reaction proceeds.

Transcriptional regulation by nuclear receptors is now a major focus of pharmaceutical drug screening. The new results point to ligand-modified receptor interactions with chromatin remodeling systems as a new target for drug discovery.

Higher NHL Risk Among Asthmatics Linked to Pesticide Use

NCI researchers have found a higher risk of non-Hodgkin's lymphoma (NHL) among asthmatics who have been exposed to common agricultural pesticides than among individuals without asthma.

To conduct the study, published online April 12 in the *International Journal of Cancer*, Dr. Won Jin Lee, of NCI's Occupational and Environmental Epidemiology Branch, and colleagues pooled data from two population-based, case-controlled NHL studies conducted in three Midwestern states. They looked at cases of NHL diagnosed between 1980 and 1983 among white males over age 30 from Iowa and Minnesota, and NHL cases diagnosed between 1983 and 1986 among white men and women over age 21 in Nebraska. They compared the resulting 872 NHL case histories with 2,336 healthy controls from the same geographic areas and interviewed either the subjects or their next-of-kin to collect information on use of and exposure to pesticides and other known or suspected risk factors for NHL.

"We found that farmers with potential exposure to pesticides and a history

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Special Report

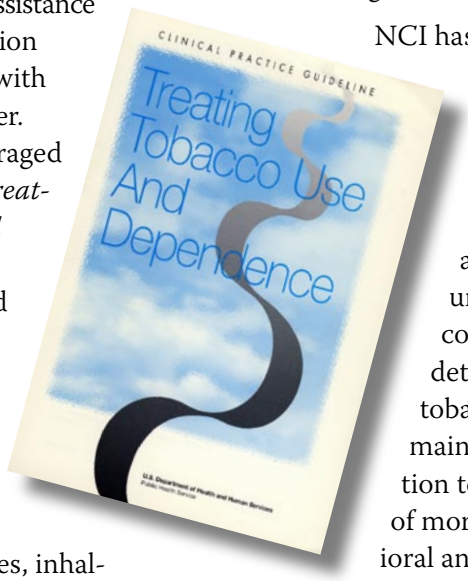
The Health Care Provider's Role in Helping Smokers Quit

Tobacco use is the leading preventable cause of death in the United States. Cigarette smoking is responsible for the vast majority of lung cancer deaths, and it is a major contributor to deaths from coronary artery disease, chronic obstructive pulmonary disease, and stroke. In 2004, approximately 160,440 people will die from lung cancer—the leading cause of cancer mortality. Cigarette smoking also causes cancers of the larynx, mouth, esophagus, pharynx, and bladder. In addition, it plays a role in cancers of the pancreas, kidney, and cervix. Seventy percent of smokers say they would like to quit, but the interaction of nicotine addiction and behavioral and social factors makes quitting very difficult.

The good news is that current evidence serves to remind us that health care providers can play a key role in helping smokers quit. As reported in the April 21 *Journal of the National Cancer Institute*, Katz et al. found that providers who used a brief intervention to help their patients quit smoking significantly increased abstinence rates six months later, especially among heavy smokers. The authors noted that for the 70 percent of American smokers who visit their physicians at least once a year, exposure to an intervention could lead to smoking cessation for approximately 2 million patients annually.

The study highlights both the effectiveness of interventions and barriers to implementing behavioral risk-reduction strategies in health care settings. It was based on the 1996 Agency for Healthcare Research and Quality (AHRQ) *Smoking Cessation Clinical Practice Guideline*, which has since been updated and expanded in the 2000 U.S. Public Health Service publication, *Treating Tobacco Use and Dependence* (http://www.surgeongeneral.gov/tobacco/treating_tobacco_use.pdf).

National data suggest that many smokers are not advised to stop smoking or offered assistance with smoking cessation during a given visit with a health care provider. Providers are encouraged to review and use *Treating Tobacco Use and Dependence*. It contains evidence-based information about effective behavioral counseling, first-line pharmacologic therapies (bupropion SR, nicotine gum, patches, inhalers, and nasal sprays) and second-line pharmacologic therapies (clonidine and nortriptyline). It also recommends a simple five-step approach to cessation counseling: ASK about smoking; ADVISE smokers to quit; ASSESS willingness to quit; ASSIST the patient in trying to quit; and ARRANGE follow-up. This approach can save lives. And it is important to note that an intervention need not be delivered by a physician to be effective. Katz et al. utilized intake staff: nurse practitioners and physician's assistants.



In this week's guest commentary on page 8, Dr. Carolyn Clancy, director of AHRQ, offers insights on the clinical practice guidelines and the importance of provider-patient interaction in achieving smoking cessation success. One of NCI's many collaborations with AHRQ was the partnership effort on the *National Blueprint for Disseminating and Implementing Evidence-Based Clinical and Community Strategies to Promote Tobacco Use Cessation* (http://www.ctcinfo.org/upload/blueprint_adult.pdf). NCI continues to work with AHRQ, NIH colleagues, and many other partners to ensure that providers have the resources they need to learn about and implement effective cessation strategies in clinical settings.

NCI has long supported tobacco use and treatment research. Studies range from transdisciplinary approaches to understanding the complex interactive determinants of tobacco use initiation, maintenance, and cessation to the development of more effective behavioral and pharmacologic approaches to tobacco use cessation. NCI's clinical trials include several smoking cessation trials (http://clinicaltrials.gov/ct/search?term=smoking+cessation) to which we encourage health care providers to refer patients. Through state-of-the-art research efforts, the opportunity exists to improve health directly while identifying clinical applications, successful interventions, and knowledge

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that can be used in health care settings around the world.

NCI offers several options for smokers who are trying to quit. The information and professional assistance available at http://www.smokefree.gov helps support smokers as they become—and remain—nonsmokers. The site provides immediate assistance in the form of an online step-by-step cessation guide; access to local and state telephone quitlines; NCI's personalized telephone-based service (1-877-44U-QUIT) and instant messaging; and targeted publications, which may be downloaded, printed, or ordered. In addition, providers will find a section with evidence-based resources they can use to help patients quit.

Clearly, NCI cannot achieve its goal to eliminate suffering and death due to cancer without dramatically reducing and treating tobacco use and tobacco-related cancers. Health care providers must be full and active partners in these efforts to take the steps necessary to reduce tobacco use in the United States. ◆

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of asthma tended to have higher relative risks for NHL than pesticide-exposed farmers not reporting asthma," the researchers observed. One possible explanation, they said, is that immunologic changes sparked by asthma may inhibit the immune system's ability to respond to potentially carcinogenic elements in specific pesticides. "Considering the widespread use of pesticides and the relatively high prevalence of asthma," the authors concluded, "further studies, particularly with carefully defined asthma diagnoses and biomarkers … are needed to confirm these findings and clarify the mechanisms involved."
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Legislative Update

House Hearings Focus on NIH Appropriations

The House Appropriations Subcommittee on Labor, Health and Human Services, Education and Related Agencies held hearings relating to the NIH on April 21 and 22. The first day focused on NIH scientific research, and the second day highlighted NIH management. The principal witness for both hearings was NIH Director Dr. Elias Zerhouni.

In his opening testimony, Dr. Zerhouni spoke about the public health challenges facing the nation in the 21st century, which will drive NIH research priorities. He discussed the NIH roadmap initiatives and his plans for developing a national electronic clinical trials and research network that would eventually link community-based clinical systems with academic health centers throughout the country.

In addition to questions about topics that reflected members' individual interests—Duchenne muscular dystrophy, transient ischemic attacks, strokes, estrogen therapy, pancreatic cancer, and stem cell research—the hearing was characterized by questions and discussion about obesity and the need for a sound public health policy to promote healthy lifestyles. NCI's National 5 A Day for Better Health Program was cited as an example of a good public health initiative.

Rep. Nita Lowey (D-N.Y.) requested an update on the early detection and treatment of breast cancer. Dr. von Eschenbach described the latest methods to detect breast cancer, using nipple aspirants coupled with proteomics analysis to identify molecular signatures that will lead to the development of targeted therapies.

On the second day of hearings, Dr. Zerhouni, Dr. Allen Spiegel, director of the National Institute of Diabetes and Digestive and Kidney Diseases, and Dr. Story Landis, director of the National Institute of Neurological Disorders and Stroke, described the rationale and streamlining of decision making at NIH and how science is managed within NIH's institutes and centers.

Several subcommittee members asked questions about cancer. Rep. Rosa DeLauro (D-Conn.) expressed concern about the current level of funding for ovarian cancer research and SPOREs. Rep. Roger Wicker (R-Miss.) mentioned long-term cancer survivors and praised the work of Dr. Julia Rowland, director of NCI's Office of Cancer Survivorship. Rep. Jesse Jackson, Jr. (D-Ill.) inquired about the amount of money NIH spends on projects that address health disparities and minority health issues and expressed interest in how much NCI is spending in these areas. NIH is currently working on responding to Rep. Jackson's request. ◆

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UTF Adjuvant Chemo for Lung Adenocarcinoma Improves Patient Survival

Adjuvant chemotherapy with uracil-tegafur (UTF) improves survival among patients with completely resected stage I lung adenocarcinoma, according to the results of a new study from Japan. In the study, published in the April 22 *New England Journal of Medicine*, 979 patients aged 45 to 75 with stage I lung adenocarcinoma were randomized to surgery alone followed by observation, the standard therapy, or surgery plus UTF twice daily for 2 years. The UTF group, reported study authors Dr. Harubumi Kato and colleagues, had a statistically significant 5-year overall survival rate of 88 percent, compared with 85 percent for the standard therapy group.

There were few severe adverse reactions associated with UTF, with 10 patients (2 percent) developing a grade 3 adverse reaction. The authors reported that in patients with tumors 2 cm or less, the survival rate was 91 percent. Therefore, they recommended that patients with small tumors be excluded from adjuvant trials unless a subgroup with a poor prognosis is identified. "Our study indicated that patients with completely resected stage I disease, especially T2 N0 adenocarcinoma, will benefit from adjuvant chemotherapy with uracil-tegafur," the authors noted.

UTF has not been approved in the United States "and has been used in relatively few clinical trials in this country, despite widespread approval elsewhere," wrote Dr. Robert Diasio of the Comprehensive Cancer Center at the University of Alabama at Birmingham in an accompanying editorial. But given the "compelling evidence" of its effectiveness among patients with adenocarcinoma of the lung in the study by Kato and colleagues, he argued, newer forms of this class of drugs, fluoropyrimidines, may prove to have an even greater effect on survival. ◆

Funding Opportunities

Community Clinical Oncology Program

RFA-CA-05-014
Letter of Intent Receipt Date: June 14, 2004
Application Receipt Date: July 14, 2004

NCI invites domestic institutions to apply for cooperative agreements in response to this Community Clinical Oncology Program (CCOP) RFA. Applicants for new and currently funded CCOPs and research bases may respond. This reissuance of RFA-CA-04-008 seeks to build on the strength and success of the network over the past 20 years by continuing to support community participation in cancer treatment, prevention, and control clinical trials through research bases; expanding and strengthening the cancer prevention and control research effort; utilizing the CCOP network for conducting NCI-assisted cancer prevention and control research; and evaluating CCOP performance and impact in the community.

The RFA will use the NIH U10 award mechanism.

For more information see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=2040

Inquiries: Dr. Lori Minasian, lm145a@nih.gov

Minority-Based Community Clinical Oncology Program

RFA-CA-05-015
Letter of Intent Receipt Date: June 15, 2004
Application Receipt Date: July 15, 2004

NCI is continuing the established cancer control effort involving oncologists who serve large minority populations in the NCI clinical trials program, providing a network of support for clinical research in cancer centers, major university centers, and community programs. Domestic institutions with the capability and intent to serve new cancer patients largely from minority populations are invited to apply for cooperative agreements in response to this Minority-Based Community Clinical Oncology Program (CCOP) Request for Applications (RFA). Currently funded Minority-Based CCOPs are also invited to respond.

This RFA will use the NIH U10 award mechanism.

For more information see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=2041

Inquiries: Dr. Worta McCaskill-Stevens, wm57h@nih.gov

Support for Human Specimen Banking in NCI-Supported Cancer Clinical Trials

RFA-CA-05-017
Letter of Intent Receipt Date: June 21, 2004
Application Receipt Date: July 21, 2004

The purpose of this initiative is to support the infrastructure needed to ensure the collection of, storage of, and access to high-quality, well-annotated human specimens collected from and representative of the patient populations entered into NCI-funded, phase III clinical treatment trials.

The RFA will use the NIH U24 Cooperative Agreement award mechanism for Resource-Related Research Projects.

For more information see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=2043

Inquiries: Dr. Roger L. Aamodt, ra32u@nih.gov

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(Funding Opportunities continued from page 6)

Community Networks to Reduce Cancer Health Disparities

RFA-CA-05-012
Letter of Intent Receipt Date: June 14, 2004
Application Receipt Date: July 13, 2004

NCI, through its Center to Reduce Cancer Health Disparities (CRCHD), invites cooperative agreement grant applications for Community Networks to Reduce Cancer Health Disparities Through Education, Research, and Training (Community Networks Program, CNP). The purpose of the CNP is to reduce cancer health disparities by conducting community-based participatory education, training, and research among racial/ethnic minorities and underserved populations. The overall goals of this program are to significantly improve access to and utilization of beneficial cancer interventions in communities with cancer health disparities, thereby reducing these disparities. This RFA is a reissue of RFA-CA-99-003.

The RFA will use the NIH cooperative agreement U01 award mechanism.

For more information see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=2042

Inquiries: Dr. Kenneth C. Chu, KC10D@NIH.GOV

Paul Calabresi Award for Clinical Oncology (K12)

PAR-04-096
Letter of Intent Receipt Dates:
Jun. 1, 2004; May 2, 2005
Application Receipt Dates:
Jul. 1, 2004; Jun. 1, 2005

The purpose of the Paul Calabresi Award for Clinical Oncology is to increase the number of medical doctors and doctorally degreed nurses and basic scientists who are highly motivated and trained to: (1) perform clinical oncology therapeutic research; (2) design and test hypothesis-based, clinical therapeutic protocols; and (3) conduct cancer therapeutic research in team research settings to expedite the translation of basic research discoveries into patient-oriented therapeutic cancer research. This Program Announcement replaces PAR-03-083.

The PA will use the NIH Mentored Clinical Scientist Development K12 Program Award.

For more information see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=2020

Inquiries: Dr. Lester S. Gorelic, gorelicl@mail.nih.gov ◆

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

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

NIH Publication No. 04-5498

Notes

Workshop Results in Research Framework

Presentations from the workshop, "Models and Procedures for Evaluating Radioprotectors," held in Dec. 2003 and sponsored by NCI's Radiation Research Program (RRP) were summarized in the April 30 issue of *Science*. Drs. C. Norman Coleman and Helen B. Stone of RRP and their colleagues described a number of approaches to prevent, mitigate, and treat radiation injury, which results from whole- and partial-body exposure to radiation. Research presented at the meeting is expected to lead to developments that will improve survival and reduce normal tissue injury following accidental or intentional exposure to radiation. Dr. Coleman also noted that the meeting laid the groundwork for the discovery and delivery of new radiation modulators, which will require input and collaboration from experts in radiation biology, inflammation, immunology, tissue injury, drug development, and clinical radiation oncology. A new initiative is under development with NCI, NIAID, and NIH for the development of countermeasures to radiation exposure (http://www3.cancer.gov/rrp/default.shtml).

NCI and NHGRI Host Tumor Sequencing Workshop

"Exploring Cancer Through Genomic Sequence Comparisons," a workshop co-chaired by Dr. Anna Barker, NCI, and Dr. Francis Collins, NHGRI, was held on April 14-15 in Bethesda, Md. The meeting convened genomics experts, technology developers, and cancer biologists from the public and private sectors to discuss how new genomic resources could support the development of diagnostics and therapeutics specifically tailored to the disease.

Participants highlighted recent discoveries such as work correlating EGFR somatic mutations with response to Iressa by Dr. Matt Meyerson's group at Dana-Farber (published in *Science* this week; see lead story, this issue), and research identifying mutational patterns that could help characterize new oncogenes from Dr. Victor Velculescu's laboratory at Johns Hopkins (*Science* 304:554). Attendees further emphasized the potential for tumor sequencing initiatives to stimulate new approaches for early cancer detection. Said Dr. Maynard Olson, University of Washington, "The enthusiastic dialogue at the workshop illustrates that we are transitioning to the next generation of genomic resources that will inform the development of novel cancer interventions." ◆

Guest Commentary by Dr. Carolyn M. Clancy

Putting Science into Practice

In their article in the April 21 issue of the *Journal of the National Cancer Institute*, Dr. David A. Katz and his colleagues present the findings of the first randomized controlled trial to test the feasibility of implementing the smoking cessation guideline in primary care clinics and the effective behavioral counseling strategies in the guideline. The bottom line: It is feasible to use this guideline in primary care practice and its implementation leads to increased abstinence from smoking.

The Agency for Healthcare Research and Quality (AHRQ) is proud to have supported the development of the Smoking Cessation Clinical Practice Guideline in 1996 and, in 2000, to have been part of the consortium that developed its successor, the U.S. Public Health Service (PHS) Clinical Practice Guideline: *Treating Tobacco Use and Dependence*. However, we recognize that synthesizing the evidence is only the first step; we need to put this evidence into the hands of people who can use it immediately to change health and health care.

AHRQ's mission is "to improve the quality, safety, efficiency and effectiveness of health care for all Americans." We are working with public and private sector partners to translate the Guideline into improved health care practice. We also have developed a successful series of products and publications targeted to health care systems, clinicians, and consumers.

Our current partners include the American Cancer Society, Blue Cross and Blue Shield of California, the American Legacy Foundation, the Oregon State Health Division, and the Oklahoma Association of Optometric Physicians. As part of the National Partnership to Help Pregnant Smokers Quit, AHRQ has supported the implementation of the PHS guideline by prenatal care providers, resulting in quit rates of at least 30 percent among pregnant women.

AHRQ is building new partnerships with a variety of clinicians and organizations that directly influence care delivery. For example, AHRQ recently convened "Building Nursing Leadership in Tobacco Control," a historic meeting of 21 nursing organizations, representing almost a half million nurses. Nurses play a critical role in patient counseling and education, and we hope this will be the start of a broad-based effort by the nursing profession to support the implementation of cessation of tobacco use in clinical practice.

An essential component of strategies to promote smoking cessation is the identification of likely targets of opportunity. One AHRQ-supported study is evaluating rural emergency departments as an access point for teen smoking intervention, and another is studying smoking cessation interventions in maternal and child health clinics. Still other studies are examining physician profiling to increase smoking cessation, tailored outpatient nicotine replacement therapy, and evaluation of strategies to reduce smoking among Native American elders.

While effective smoking cessation efforts are, by definition, multipronged, primary care clinicians have important "teachable moments" with their patients. Moreover, patients who trust their primary care clinicians are far more likely to attempt lifestyle changes, including smoking cessation. Thus we are excited about our collaboration with the Robert Wood Johnson Foundation to help AHRQ-funded practice-based research networks (PBRNs) to develop creative, practical strategies for promoting healthy behaviors among patients that can be easily adopted by other primary care practices. The PBRN projects target the four health risk behaviors that represent the nation's leading causes of preventable disease, disability, health care burden, and premature death: tobacco use, sedentary lifestyle, unhealthy diet, and risky drinking.

Finally, in 2003, AHRQ's U.S. Preventive Services Task Force released a recommendation on counseling to prevent initial tobacco use that is consistent with the evidence in the PHS Clinical Practice Guideline. The Task Force's companion program, Put Prevention Into Practice, helps clinicians determine which services their patients should receive and makes it easier for patients to understand and keep track of their preventive care.

The PHS Clinical Practice Guideline on cessation of tobacco use provides evidence of what works, and with the Katz study we know that it can be implemented and lead to positive results. The imperative now is to identify effective incentives to sustain what works and spread successes across the nation to increase the number of Americans who successfully stop using tobacco. Please visit AHRQ's tobacco pathfinder Web site at www.ahrq.gov/path/tobacco.htm for a full menu of guideline tools. ◆

Dr. Carolyn M. Clancy, Director, Agency for Healthcare Research and Quality

This *NCI Cancer Bulletin* is produced by the National Cancer Institute (NCI). NCI, which was established in 1937, leads a national effort to eliminate the suffering and death due to cancer. Through basic and clinical biomedical research and training, NCI conducts and supports research that will lead to a future in which we can 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.