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Eliminating the Suffering and Death Due to Cancer

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Interim DSMB Named for National Lung Screening Trial

An interim Data and Safety Monitoring Board (DSMB) has been appointed for the 50,000-participant National Lung Screening Trial (NLST), following the resignation of the trial's original DSMB on March 26. The DSMB Chair, Dr. Sylvan Green, Arizona Cancer Center, explained that the board was resigning because individual members do not have liability insurance coverage as part of the professional services contract under which they were secured for the trial.

In response, officials from NCI (which is sponsoring the trial) and the National Institutes of Health (NIH) are working together to resolve this issue and quickly appointed an interim DSMB. The interim board is composed of NIH scientists with appropriate clinical and research expertise.

NCI policies require that all clinical trials that the institute sponsors have a DSMB. The activities of DSMBs are distinct from those performed by IRBs, which review and approve research protocols for clinical trials prior to their launch. Both IRBs and DSMBs, however, play critical roles in ensuring patient safety.

A DSMB is intimately familiar with a trial's protocol and its plans for monitoring patient safety and data

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Director's Update

A Strong Foundation for Progress Against Cancer

The news last week was replete with excellent research presented at the American Association for Cancer Research (AACR) annual meeting in Orlando. Meetings like this energize the cancer community, bringing together some of the most brilliant and dedicated researchers to share insights, educate the next generation of investigators, and celebrate progress.

At the AACR meeting, I had the privilege to give an address about the opportunities we now have to make unprecedented advances in the prevention, diagnosis and early detection, and treatment of cancer.

This talk came just a few weeks after the publication in *Fortune* magazine of an in-depth article—written by a cancer survivor—that addressed the state of cancer research in the United States.

Of course, not every story has a positive angle—nor should it. The title of the *Fortune* article was "Why We are Losing the War on Cancer (And How to Win It)" and it raised some important criticisms about how cancer research has been conducted. In my address at the AACR meeting,

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collection. The board's central function is to review interim analyses of outcome data and cumulative toxicity data summaries. Based on these reviews, the board determines whether the trial should continue as originally designed, be amended, or possibly even be terminated. The board may also recommend other actions based on these reviews.

For example, as recently reported (*NCI Cancer Bulletin*, March 16), the DSMB of a phase III clinical trial comparing five years of adjuvant chemotherapy for breast cancer using either tamoxifen alone or switching after several years to the aromatase inhibitor exemestane recommended that results data be released before the trial was complete because of the significant benefit seen in overall survival in patients treated with exemestane. The need for liability indemnification for such consultation and advice is a question that is now being addressed.

Launched in 2002, NLST is the largest trial of CT screening for lung cancer. A randomized, controlled trial, NLST is comparing spiral computed tomography and standard chest X-ray for the early detection of lung cancer. Nearly 50,000 current or former smokers have enrolled in NLST at more than 30 study sites across the country. As of February 2004, the trial reached full enrollment in record time and is closed to further enrollment. Nothing affecting patients, patient safety, or data collection has changed; the focus of the trial and its outcome have not been altered.

Further details on this development will be reported as they become available. For more information on NCI and NIH policies on data and safety monitoring of clinical trials, visit http://deainfo.nci.nih.gov/grantspolicies/datasafety.htm (NCI) and http://grants.nih.gov/grants/guide/notice-files/not98-084.html (NIH). ◆

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I discussed a number of strategic initiatives I believe, when taken up with the *Fortune* piece, address many of these criticisms.

And I believe that, with the initiatives and priorities we have established, we can fulfill our mission and reach the 2015 goal of eliminating suffering and death due to cancer. Take, for example, mouse models. We have shifted our focus away from xenograft models to the exciting work being done today with genetically engineered mouse models, much of which is being coordinated via the NCI Mouse Models of Human Cancers Consortium. These mouse models—which have physiologic properties far more reminiscent of human biology and can recapitulate human cancer both in terms of molecular biology and disease progression—are already generating important advances. For instance, an entire class of drugs, HDAC inhibitors, has been developed using an engineered mouse model of leukemia. With this highly powerful model, we will continue to make important new findings that I believe can be quickly translated into human clinical trials.

We are also making important changes to how clinical trials are conducted. At NCI, we are developing a national infrastructure for cancer clinical trials and will provide national leadership to guide and oversee the effort. I believe that this will serve to accelerate the development and testing of effective interventions and ensure that those interventions are efficiently and seamlessly incorporated into standards of care.

We have also embraced the concepts of team-based science and collaboration—concepts that encourage inter- and transdisciplinary research. We are actively promoting this approach with important structural and operational changes and with the launch of initiatives like the cancer Biomedical Informatics Grid (caBIG) and the Integrative Cancer Biology Program. This latter program, for example, will focus on the analysis of cancer as a complex biological system, bringing together cancer biologists and experts from fields such as mathematics, physics, imaging sciences, and computer sciences to develop reliably predictive computational models of the various cancer processes.

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Join the Tour of Hope with Lance Armstrong

The Bristol-Myers Squibb Tour of Hope™ will champion the race toward a cure for cancer this fall, and you can be a part of it. Applications for joining the 20-member Bristol-Myers Squibb Tour of Hope™ Team are available at http://www.tourofhope.org. The Tour is an extraordinary bicycle ride across the country that will mobilize America to speed the search for a cure. **The deadline for submission of applications has been extended to Tuesday, April 20, at 11:59 p.m. EDT.**

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And, finally, I believe we can achieve the 2015 goal because the cancer community has proven time and again to be a marketplace of grand ideas and, more importantly, earnest, collaborative action. Whether it's the use of proteomics and nanotechnology to improve strategies for detecting cancer at its earliest stages or investigating novel methods for eliminating disparities in care, the cancer community is clearly a hotbed of innovation.

At AACR, Dr. Leland Hartwell, president and director of the Fred Hutchinson Cancer Research Center and Nobel Laureate, gave the Distinguished Lecture, focusing on the potential of molecular diagnostics to improve cancer survival. If we can make the sort of organizational and cultural changes already under way, as well as continued advances in areas like early diagnosis and combination therapy, among others, Dr. Hartwell said, he is cautiously optimistic that we can achieve the 2015 challenge goal.

I wholeheartedly agree. Swift progress in these areas can and will happen. And cancer, no doubt, will continue to make headlines—headlines that document every advance and tell the story of how we will achieve such a remarkable goal of eliminating the suffering and death due to cancer. ◆

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

Special Report

Specialized Programs of Research Excellence: Moving Basic Research Discoveries into the Clinic

Since 1992, NCI's Specialized Programs of Research Excellence (SPOREs) have been instrumental in defining and culturing the field of translational research. The program's success results primarily from multidisciplinary teams of basic and applied researchers working together to move basic research discoveries into the clinic or, conversely, to determine the underlying mechanism of a clinical observation. As such, SPOREs have changed an important aspect of the cancer research model by breaking down communication barriers between investigators with diverse areas of expertise and focusing their collective attention on a single or related group of cancer sites. The overall program goal is to direct basic scientific discoveries toward human applications that have the potential to affect the prevention, detection, diagnosis, prognosis, or treatment of cancer in a particular organ site.

The SPORE program was conceived and implemented through a special $20 million appropriation from Congress in fiscal year 1992, representing a strategic response to the rapid expansion of cancer information being developed through basic research. At the time, no NCI funding mechanism focused exclusively on translational research; the SPORE program began as an experiment to promote interactions between basic and applied scientists and provide them with the flexibility to rapidly test new ideas and approaches.

Over the past 12 years, the program has grown from four organ sites to 14 and currently includes 56 SPOREs in breast, prostate, lung, gastrointestinal, ovarian, genitourinary, skin, brain, head and neck, lymphoma, leukemia, myeloma, pancreatic, and gynecological cancers. Unique features of SPOREs include their flexibility to change research direction to capitalize upon new translational opportunities, as well as their close ties to the patient advocate community.

Beginning in 2000, more emphasis has been placed upon the SPOREs to interact within and across organ sites. The SPORE network provides an excellent opportunity for cross-fertilization between different disciplines and enables translational goals to be quickly realized. Inter-SPORE activities are supported by administrative supplements to parent SPORE awards and are aimed largely toward the performance of early-phase clinical trials or biomarker validation studies. Many of these studies involve collaborations with other NCI networks, like the Cancer Genetics Network, the Cooperative Groups, and the NCI Intramural program. SPORE is also one of the first NCI programs to establish a public-pri-

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vate partnership with an outside funding organization. Specifically, the Avon Foundation has committed $20 million in support of administrative supplements for early-phase clinical interventions in breast cancer. The Avon-NCI Progress for Patients (PFP) Awards program was piloted within SPORE in 2002 and opened up to SPOREs and NCI-designated Cancer Centers in 2003. Currently, 21 early-phase clinical interventions in breast cancer are supported by the Avon-NCI PFP program, several of which represent inter-SPORE collaborations.

Most recently, two working groups have begun to systematically assess the pipeline of biomarkers and therapeutic agents being developed within the SPOREs. In January and February of this year, the working groups identified 10 to 12 priority projects with high potential impact within or across organ sites. The programs were struggling to overcome one or more different barriers ranging from acquiring enough material to perform a clinical trial to unraveling a complex series of intellectual property and regulatory issues surrounding the development of a panel of promising biomarkers. Interestingly, the solutions to some of these impediments may not require the expenditure of more funds, just some additional teamwork between individuals with diverse expertise, the original premise upon which the SPORE program was built.

In sum, the SPORE program represents one of NCI's many strategic opportunities to move basic discoveries into clinical applications. ◆

Legislative Update

Senate Appropriations Hearing for NIH FY 2005

The Senate Appropriations Subcommittee on Labor, Health and Human Services, and Education held a hearing on April 1 to focus on fiscal year 2005 funding for NIH. NIH director Dr. Elias Zerhouni, accompanied by all institute and center directors, talked about key research advances of the last year by NIH-funded researchers and gave examples of how the NIH Roadmap effort will shape patient-oriented research in the future.

Sen. Ted Stevens (R-Alaska) complimented Dr. Andrew C. von Eschenbach on a recent talk on imaging and inquired about the early end of the Prostate Cancer Prevention Trial to study the drug finasteride. Dr. von Eschenbach emphasized that this trial demonstrated a protective effect for prostate cancer and was ended because the clinical end points were met early. The trial has led to another clinical study of the drug's impact on disease virulence.

Senators expressed concern about NIH's reduction of inflationary increases for grantees in subsequent years from 3 to 1.9 percent and wanted to know how this change in a long-standing NIH commitment would affect researchers and the number of new grants funded. Senators asked Dr. Zerhouni to provide more specific information about how budget projections for fiscal year 2006 will have an impact on NIH initiatives.

Institute directors received questions on a number of issues, including research on obesity, complementary and alternative medicine, new technologies, stem cell research, bio-defense, neurodegenerative diseases, kidney disease, macular degeneration, and autism.

Senators Tom Harkin (D-Iowa) and Arlen Specter (R-Pa.) continued to return to the issue of stem cell lines and whether the currently available cell lines would be enough for investigators to study and whether these cell lines would be adequate for use in humans. The senators requested a comprehensive report on the "state of the art" of stem cell research to assist the subcommittee in policymaking.

Hearing on HPV and Cervical Cancer

The House Government Reform Subcommittee on Criminal Justice, Drug Policy and Human Resources held a hearing on human papillomavirus (HPV) and cervical cancer on March 11. The purpose of the hearing was to examine the latest medical science regarding cervical cancer and ongoing federal efforts to treat the disease and prevent HPV infection.

Dr. Ted Trimble, of NCI's Cancer Therapy Evaluation Program, discussed the pathology and progression of HPV infection and its relation to cervical cancer and commented on current studies on vaccine development. Witnesses from the Centers for Disease Control and Prevention and the Food and Drug Administration described their activities in HPV/cervical cancer surveillance and prevention and in labeling options for condom use. Abstinence education was also discussed as well as the failure of condoms to protect against HPV infection. ◆

Cancer Research Highlights

COX-2 Inhibitor Promotes and Inhibits Tumor Growth, Study Finds

COX-2 inhibitors, which are being studied for the treatment of a wide range of cancers, appear to be able to promote as well as inhibit tumor growth and angiogenesis, according to research reported last week at the AACR annual meeting.

In the study, conducted by Dr. Guido E. Eibl and colleagues at the UCLA David Geffen School of Medicine, the selective COX-2 inhibitor nimesulide inhibited tumor growth and angiogenesis in tumors that were COX-2 positive in two different mouse models of pancreatic cancer. However, in tumors that were COX-2 negative—which, Dr. Eibl noted, previous research has found to be the case in anywhere from 10 to 40 percent of tumors—just the opposite held true: nimesulide stimulated tumor growth.

"When we looked more carefully at these tumors, we found that on the surface there were more and larger microvessels" as well as increased production of cancerous cells, Dr. Eibl said.

The researchers also conducted *in vitro* studies to elucidate the pathway by which nimesulide acted. They found that, in COX-2 negative tumors, nimesulide increased production of vascular endothelial growth factor (VEGF), a potent angiogenesis stimulant. This occurs, they determined, primarily through the direct activation on pancreatic cancer cells of the nuclear receptor PPAR Gamma.

This "surprising" finding, he added, "suggests...that maybe a certain subset of pancreatic cancer patients may respond differently to selective COX-2 inhibitors" and that use of these drugs should be based on the tumor's COX-2 expression profile. The research team is now going to test other selective COX-2 inhibitors in these same models to see if they achieve similar results, Dr. Eibl said.

Study Links *In Utero* Arsenic Exposure to Estrogen Signaling in Liver Cancer

In the March 17 issue of the *Journal of the National Cancer Institute*, NCI scientist Dr. Michael Waalkes and colleagues report a link in mice between estrogen signaling and hepatocellular carcinoma (HCC) caused by *in utero* exposure to arsenic.

Tumors from HCC, a specific type of liver cancer, have previously been reported to be associated with arsenic exposure in humans.

The researchers found higher expression levels of the estrogen receptor-α (ER-α) gene—an indicator of changes in estrogen signaling—in the livers of adult male mice that had developed the tumors after the *in utero* arsenic exposure. Another gene, cyclin D1—a cell cycle regulator that responds to estrogen signaling—also demonstrated increased expression levels when compared to levels found in control mice. The mice with HCC had decreased methylation of the promoter region of their ER-α gene, which may be the cause for these changes in expression levels. Furthermore, the scientists looked at human liver biopsy samples from men who were exposed to high levels of arsenic and found that ER-α and cyclin D1 were also overexpressed, compared to genes in samples from people not exposed to high levels of arsenic.

"Taken together," the study report concludes, "these data indicate that aberrant expression of the ER-α gene, as a result of changes in methylation, could be an important molecular event in carcinogenesis induced by inorganic arsenic, at least in the liver."

Researchers Report a Possible Inverse Correlation between Ejaculation Frequency and Prostate Cancer Risk

In the April 7 issue of the *Journal of the American Medical Association*, researchers report the results of a prospective cohort study suggesting that higher ejaculation frequency may correlate with a decreased risk of prostate cancer in white men aged 46 or older.

The 29,342 participants received a questionnaire in 1992 that included an assessment of current and past ejaculation frequency. The researchers followed the men from 1992 until 2000, during which time the subjects completed questionnaires every two years that asked whether they had been diagnosed with prostate cancer. By the time the study ended, 1,449

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new cases of prostate cancer had been diagnosed.

The researchers found that men reporting 21 or more ejaculations per month had a lower relative risk of developing prostate cancer. They concluded that "each increment of three ejaculations per week across a lifetime" was associated with a fifteen percent reduction in total prostate cancer risk. Interestingly, the researchers found that men with the lowest ejaculation frequencies (three or fewer per month) between the ages of 40 and 49 also experienced a suggestive decreased risk of prostate cancer while men with ejaculation frequencies in the middle range showed no detectable change in risk status.

The researchers cautioned against over-interpreting their results. At most, the study indicates that an association possibly exists between higher ejaculation frequency and lower prostate cancer risk. The evidence does not definitively establish a causal linkage between ejaculation frequency and prostate cancer etiology. The study provides a direction for future research into identifying the possible biological mechanisms that give rise to prostate cancer.

"The major implications of our results are in stimulating future progress toward understanding the molecular mechanisms underlying the potential adverse effects of inhibited or suppressed ejaculation on prostate tumor growth," commented lead author Dr. Michael Leitzmann of NCI's Division of Cancer Epidemiology and Genetics. "Future research should focus on the chronic interaction of prostate glandular cells with the prostatic fluid they secrete." ◆

Featured Clinical Trial

Chemoprevention Study of Selenium for Non-Small Cell Lung Cancer

Name of the Trial

Phase III Randomized Chemoprevention Study of Selenium in Participants with Previously Resected Stage I Non-Small Cell Lung Cancer (ECOG-5597). See the protocol summary at http://cancer.gov/clinicaltrials/ECOG-5597.

Principal Investigators

Dr. Daniel David Karp, Eastern Cooperative Oncology Group; Dr. Michael Liptay, American College of Surgeons Oncology Group; Dr. Omer Kucuk, Southwest Oncology Group; Dr. Randolph Marks, North Central Cancer Treatment Group; Dr. Michael R. Johnston, National Cancer Institute of Canada; Dr. Gerald H. Clamon, Cancer and Leukemia Group B; Dr. Steven Belinsky, Lovelace Respiratory Research Institute

Dr. Daniel David Karp
Principal Investigator

Why Is This Trial Important?

Lung cancer kills more Americans than any other cancer. Surgical removal of tumors is the preferred treatment for non-small cell lung cancer. However, the incidence of a second tumor developing in patients who have been treated surgically for early-stage non-small cell lung cancer is about 20-30 percent.

Researchers are investigating selenium as a chemoprevention agent against development of secondary lung tumors. "With stage 1 non-small cell lung cancers that have been treated successfully with surgery, the more likely risk is development of a second tumor rather than recurrence of the original tumor," said Dr. Karp. "So we are interested in seeing if selenium will be effective in preventing the growth of new tumors in patients who have undergone curative surgery for non-small cell lung cancer.

"In a previous study, selenium appeared to cause decreases in both prostate and lung cancer, but those results were not statistically validated. Subsequent studies, including this one, seek to validate those observations," Dr. Karp said.

Who Can Join This Trial?

Researchers seek to enroll 1,960 patients 18 years of age and older who have had stage I non-small cell lung cancer completely removed by surgery. See the full list of eligibility criteria for this trial at http://cancer.gov/clinicaltrials/ECOG-5597.

Where Is This Trial Taking Place?

Study sites in the United States and elsewhere are enrolling patients in this trial. See the list of study sites at http://cancer.gov/clinicaltrials/ECOG-5597.

Who to Contact

See the list of study contacts at http://cancer.gov/clinicaltrials/ECOG-5597 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

Three Top NCI Positions Filled

NCI Director Dr. Andrew C. von Eschenbach recently announced three new appointments—a new director for the Division of Cancer Treatment and Diagnosis (DCTD) and two new deputy directors within his office.

As the new DCTD director, Dr. James H. Doroshow fills a position vacant since 2001. He comes to NCI from Los Angeles, where for 20 years he served as both chair of the Department of Medical Oncology and Therapeutics Research and as associate director for clinical research at the City of Hope Comprehensive Cancer Center. In addition to his division responsibilities, Dr. Doroshow will lead NCI's Clinical Trials Working Group.

In the director's office, Dr. Karen Antman will lead strategic scientific efforts in her new role as deputy director for Translational and Clinical Sciences. She will direct a broad national research program that includes the Cancer Centers Program, the Specialized Programs of Research Excellence, and other translational programs. Dr. Antman had been director of the Columbia University's Herbert Irving Comprehensive Cancer Center and chief of the Division of Medical Oncology.

As reported in the Feb. 10 *NCI Cancer Bulletin*, Dr. Mark Clanton was recently named the new deputy director for Cancer Care and Delivery Systems at NCI. With a strong background in managed care and health plan administration, Dr. Clanton will bring his expertise to bear on expanding and enhancing NCI's research portfolio to have a greater impact on cancer care delivery.

Telephone Education Workshop on Cancer Survivorship

On March 10, NCI's Office of Cancer Survivorship and Office of Education and Special Initiatives kicked off the Second Annual Cancer Survivorship Series, "Living With, Through & Beyond Cancer." More than 1,300 participants from around the world phoned in to hear expert speakers discuss "Living with Uncertainty" and the feelings that accompany the period following cancer treatment. The program, a collaboration with CancerCare, the Intercultural Cancer Council, Living Beyond Breast Cancer, and the National Coalition for Cancer Survivorship, is co-funded by the Lance Armstrong Foundation and NCI. The second survivorship education workshop, "Talking About Cancer with Children of All Ages," is scheduled for April 14. The topic for the third and final installment on May 19 will be "Turning Research into Action." Calls take place on Wednesdays from 1:00 to 2:00 p.m. Eastern Time, and participants can register online at www.cancercare.org or call Cancer Care at 1-800-813-HOPE for more information.

NCI Director Receives Cancer Public Service Award

On April 2, NCI Director Dr. Andrew C. von Eschenbach received the first Distinguished Cancer Public Service Award from the George Washington University Cancer Institute. The award is presented to an individual who has "provided outstanding public leadership in cancer health care and public policy."

Other awards from the GW Cancer Institute included the Cancer Advocacy Achievement Award to Dr. Ellen Sigal, Chair, Friends of Cancer Research; the Cancer Compassion Award to Zora Brown, Founder and Chair of the Cancer Awareness Program Services and Breast Cancer Resource Committee; and the Celebration of Life Award to Lance Armstrong, Tour de France champion and founder of the Lance Armstrong Foundation.

Constance Percy Dies at 89

Former NCI statistician Constance

Percy died of lung cancer on March 24 at her home in Rockville, Md. Ms. Percy was with NCI for 31 years and was internationally recognized for her work in cancer nomenclature and classification standards. She was instrumental in the development of NCI's Surveillance, Epidemiology and End Results Program. She also contributed to the establishment of international cancer nomenclature with the *International Classification of Diseases for Oncology*. Before joining NCI in 1970, Ms. Percy worked for the American Cancer Society for 22 years. She was part of the research team that produced the seminal study linking smoking with lung cancer and heart disease; she was an advocate for tobacco control. Ms. Percy was a chemistry graduate of Cornell University and received a master's degree in public health from Columbia University. She is survived by a sister, two daughters, and two granddaughters. ◆

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.

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Guest Commentary by Dr. Leland Hartwell

Basic Science Leads the Charge in the War on Cancer

In an article in a recent edition of *Fortune* magazine, Clifton Leaf, a cancer survivor, assesses the state of the war on cancer and concludes that we are losing. Moreover, he proposes a game plan for winning it. Is he right? In many ways, yes, he is right. He argues that we should focus on cancer as a process and fight it at its earliest stages when it is highly curable rather than at later stages where battle after battle has failed. He argues that drugs should be tested on patients earlier in the cancer process rather than on patients who have failed to respond to all other treatments, as is currently done. He argues that cancer, like AIDS, will require multiple drugs and that we need to test multiple drugs in combination, some of which may have no efficacy in isolation. While I agree with each of these recommendations, he fails to note that they are only now becoming possible and that these new opportunities derive from the very source he denigrates: fundamental knowledge provided by basic science.

Consider each of his points above in turn. There is currently no technology able to examine comprehensively all of the molecules in the blood for early diagnosis of disease. This means that it will be necessary to focus molecular diagnosis on molecules known to be abundant in tumors or involved in tumor processes. This knowledge is coming from basic research in cancer. It may well be productive to test new drugs in patients with earlier stages of cancer and to test new drugs in combinations, although both approaches would face ethical and regulatory hurdles. If either can be accomplished, that would not be done without excellent information suggesting potential efficacy. That information would come from drug target validation in human cells, a technology dependent on small RNA molecules, only discovered in the last couple of years as a result of basic research. It is definitely too soon to throw out basic science!

NCI Director Andrew C. von Eschenbach has called for the cancer community to eliminate the suffering and death from cancer by the year 2015. Given the poor state of progress toward it to date, one must ask: Is this possible? What is important about this challenge is not the precise date but the sense of urgency, the same sense of urgency expressed by Mr. Leaf. As a cancer center director, I have experienced the sense of urgency of our patients, donors, and board members. People who support cancer research and experience cancer in their families expect us to focus on eliminating this disease now. I think they are all correct in thinking that a more effective approach is possible and should be applied post haste. I believe the answer is in methods to detect cancer earlier and monitor the effectiveness of drug interventions quickly and individually. We know that early detection of disease cures cancer by surgery alone for cervical, colon, and esophageal cancer.

Implementing this new approach relies on exploiting recent technology and knowledge in the area of molecular diagnostics. The completion of the human genome project provides us a guide to all potential protein molecules in our blood. Recent advances in the technology of mass spectrometry allow for an unprecedented analysis of those proteins. Knowing the proteins associated with cancers will allow us to exploit recent advances in molecularly targeted imaging to locate very small tumors and interrogate their molecular features. Drugs attached to agents that seek out the proteins on cancer cells can deliver therapy directly where it is needed. I believe this is what the winning battle with cancer will look like.

Mr. Leaf calls for a coordinated assault on this disease, an approach also championed by Dr. von Eschenbach. Why a coordinated assault? We learned from the human genome project that achieving some goals in biology requires the type of coordination that is common in physics and engineering but rare in biology and medicine. This is one of those goals. Many players in the cancer community are needed to implement a major direction change from a focus on drugs for late-stage disease to one using effective diagnostics at earlier stages for detection and treatment. A paradigm shift cannot be effective if it does not engage the entire community. With NCI leading a coordinated effort involving the research community, the Food and Drug Administration, pharmaceutical and biotechnology industries, and advocacy groups, we can win the war on cancer. ◆

Dr. Leland Hartwell is President & Director of the Fred Hutchinson Cancer Research Center

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.