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Study Strengthens Argument of Cancer as "Wounds that Do Not Heal"

A recent study provides new evidence that some types of cancer may have similarities with wound healing, demonstrating that during both processes many of the same genes are regulated in a coordinated manner.

However, the study also revealed distinct gene expression patterns, or signatures, that appear to represent the point where the two processes diverge.

This study is the first to compare and analyze the gene expression patterns of renal cell carcinoma (RCC) and gene expression during recovery from ischemia-induced damage to the kidney (renal wound healing). The study was led by Dr. Joseph Riss of the Laboratory of Biosystems and Cancer in NCI's Center for Cancer Research.

The suggestion that cancer and wound healing share many features of the same biological process dates back to the early 1970s, Dr. Riss explained.

In the July 15 *Cancer Research*, Dr. Riss and colleagues provide a comprehensive investigation of this hypothesis. They created a mouse

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Director's Update

Dr. Sanya Springfield, Acting Director, Center to Reduce Cancer Health Disparities

Guest Update by Dr. Sanya Springfield

Disparities Summit Offers Real Answers to Real Problems

During major meetings and conferences, it's easy to find ourselves caught up in the moment. Amid supportive colleagues, dramatic presentations, and positive pronouncements, we embrace the spirit of the gathering and find a wellspring of enthusiasm and energy for tackling the challenges that lie ahead. But the real test is what happens when the meeting is over. Will we keep our commitment and resolve when we return home and are faced with the realities that can sap that enthusiasm and energy?

If what happened here last week at the Cancer Health Disparities Summit is any indication, I don't think we have to worry about losing our momentum on this issue. I'm convinced that we're on course to reduce and eventually eliminate

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model of renal wound caused by a period of impaired blood flow to the kidney. Then, using microarray technology, they performed gene expression analyses several times after normal blood flow was reestablished and the damaged organ began to heal.

They compared these results with gene expression patterns of human RCC reported in the literature. They found that, relative to a normal kidney, there were 361 genes differentially expressed in both renal carcinoma and during recovery from ischemia. Of these 361 genes, 77 percent were found to be "concordant;" that is, either upregulated or downregulated in both RCC and during recovery from ischemia. The remaining 23 percent were "discordant" in that their differential expressions were in opposite directions relative to a normal kidney.

A careful gene analysis pointed to molecular pathways and gene functions involving the concordant and discordant sets.

Important orchestrated processes such as regeneration, DNA replication (e.g., MCM gene family), cell adhesion (e.g., ICAM1 and VCAM1), and immune response were reflected in the concordant genes.

The discordant gene signature revealed processes such as morphogenesis and glycolysis, and molecular pathways, such as the hypoxia-inducible factor and insulin-like growth factor-I, "that reflect the intrinsic pathologic nature of RCC," according to Dr. Riss.

"Our observations provide a conceptual framework for further efforts to understand the biology of renal regeneration and renal cell carcinoma," he continued.

"They also provide information for the development of more effective diagnostic biomarkers and therapeutic strategies for renal tumors, as well as strategies for improving recovery from renal ischemia without promoting renal cell carcinoma," he said. ◆

By Carmen Phillips

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cancer health disparities—and our determination is stronger than ever.

The summit, sponsored by NCI and the National Center on Minority Health and Health Disparities (NCMHD) of the National Institutes of Health, was something special. I believe the meeting ignited a fire to intensify our efforts going forward. I also think it sharpened our focus about what we need to do and how to do it and—most importantly—helped solidify our efforts by bringing us together to discuss commonalities and shared experiences.

More than 700 participants from as far away as American Samoa attended the summit. We also reached a broader audience through national minority media outlets, which interviewed summit representatives throughout the week.

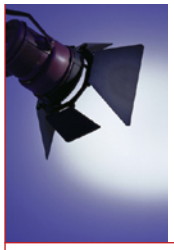
There were many positive developments from the summit, but three things stood out in particular:

First, the meeting focused on questions and answers. The goal was to develop answers to questions such as, What can we do better? Where are the research gaps? How do we enhance existing programs and resources? How can we apply what we know about cancer overall to cancer disparities research? These are just some of the questions we attempted to explore last week at the summit.

Second, I was gratified by NCI's level of participation. From NCI Acting Director Dr. John Niederhuber to division heads to senior researchers, NCI staff presented information and made themselves available for questions. In describing an expanded research role for the NCI-designated Cancer Centers, Dr. Niederhuber helped the cancer disparities research community see new opportunities to investigate new aspects of cancer health disparities. Dr. Niederhuber is right: We are working to deal with disparities issues at a time when there have never been more opportunities to attack cancer. The pace of discovery makes this a promising time as well as a challenging one.

Finally, I was encouraged by the collaboration that was evident during the summit. Our partnership with NCMHD helped us reach a new milestone in our intra-NIH collaboration on cancer disparities. The partnership mirrored the prevailing attitude among summit participants to cooperate across the issues, regions, and cultures to share ideas, strategies, and resources.

We're eager to begin planning for next year's summit and can't wait to put our plans and ideas for the coming year into action. The formal report of the summit will be posted soon on our Web site: http://crchd.nci.nih.gov/. So many opportunities are within reach. We simply need to reach out and grab hold of them. ◆



Spotlight

Sharing Strategies to Navigate the Drug Development Pathway

The era of molecular medicine means different things to different people. To cancer patients, it holds the promise of tailored treatments to match their particular pathobiology. To drug companies big and small, it means that thousands upon thousands of potential "new agent recipes" have been published in the human genome, exponentially increasing the number of drug targets. To Dr. H. "Kim" Lyerly, it is a call to arms: "This new era of drug development requires us to reinvent the way we perceive, pursue, and communicate about these opportunities."

Dr. Lyerly is the director of the Duke Comprehensive Cancer Center (see Conversation with Dr. Lyerly on page 8). Three years ago he organized a training workshop around the premise that young investigators—having already embarked on the discovery-development-delivery pathway with a promising cancer drug or technology—often need the kind of strategic advice that only seasoned veterans are likely to possess and that is routinely unavailable in the American system of cancer research.

This spring nearly 50 early-career cancer scientists from the United States, France, Italy, Belgium, South Korea, and England came to the third annual "Accelerating Anticancer Agent Development and Validation" workshop in Bethesda, Md. These researchers arrived at the workshop with a wide variety of projects at various stages of development. What they had in common, however, was quality: Their projects were competitively selected for merit and promise. "Yet some of the very best scientists don't necessarily have the tools needed to develop their drugs and move them through the approval pipeline," explained Dr. Lyerly.

What the participants needed most was the kind of focused mentoring that the workshop's senior faculty—more than 50 leaders in clinical and translational research from academia, industry, NCI, and the Food and Drug Administration (FDA)—had volunteered to provide.

Dr. Jerry Collins, associate director for Developmental Therapeutics in NCI's Division of Cancer Treatment and Diagnosis (DCTD), spoke in one of the opening sessions on the preclinical aspects of drug development. "The workshop delivers exactly what it promises: a concentrated experience in which learners can pick the brains of senior drug developers on how to navigate from an 'idea-and-a-molecule' to a drug and therapy for patients," said Dr. Collins. And the atmosphere was surprisingly collegial, he found. "Even the most experienced teachers can learn from the fresh approaches brought forward by talented students."

More than 9 hours of small-group sessions were spaced throughout the 3 days so that each of the participants had a chance to conceptualize a strategic plan for developing and validating the molecule they were working with as a biomarker, therapeutic agent, or cancer prevention agent.

In each of the breakout groups, four to six researchers presented their projects to an expert panel on drug development, consisting of an FDA representative; a biostatistician; senior scientists from NCI and FDA; and at least one academic, clinical, or industrial investigator; members of the advocacy community; and others experienced at matching projects and funding sources.

The researchers found themselves in a privileged position, but also occasionally in the hot seat. Some were cross-examined about possible scientific flaws in their model or misconceptions they might have about moving a product through the development pipeline. Most were asked to demonstrate their agent's potential impact and what its value might be to different constituencies.

Not every drug will target tens of thousands of patients, nor offer the kind of benefit that warrants millions of dollars in drug company investment. But other avenues of development exist: NCI has programs, initiatives, and projects to foster the development of some of these agents and strategies. Many of the participants learned of alternative opportunities for support and investment.

"The course provides a comprehensive view of the drug development process," said faculty member Dr. Richard Pazdur, director of FDA's Office of Oncology Drug Products. "Few individual investigators possess this viewpoint, and the workshop illustrates the interplay of the many stakeholders throughout the drug development process." And of course the FDA oversees more than just

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Cancer Research Highlights

HPV Co-Infections May Increase Risk of Precancerous Lesions

Simultaneous infection with multiple types of human papillomavirus (HPV) significantly increases the risk of developing abnormal lesions that can lead to cervical cancer, researchers reported last week. Co-infections that include two HPV types in particular, HPV 16 and HPV 58, seemed to confer the greatest risk of developing these lesions.

"Women who harbor multiple infections are at higher risk for cervical lesions than those ever infected with one type only and should be followed more closely," said the study's lead investigator, Dr. Eduardo L. Franco, director of the Division of Cancer Epidemiology at McGill University in Montreal.

The epidemiologic study, partly funded by NCI and published in the July *Cancer Epidemiology, Biomarkers, and Prevention,* involved more than 2,400 Brazilian women participating in a long-term HPV cohort study. Participants were seen once every 4 months for the first year, and then two times a year for the next 3 years, with cervical specimens collected at each visit.

Previous studies have not found an increased risk associated with co-infections with multiple HPV types, the authors noted. In their study, however, the greater the number of HPV types involved in the co-infection, the greater the risk of the precancerous lesions, suggesting that the different types "seem to act synergistically in cervical carcinogenesis."

While HPV 16 alone increased the risk for developing the lesions by nearly 25 times compared with women who were HPV-negative, an additional threefold increased risk was associated with co-infection of HPV 16 and at least one other HPV type, whether the infections were simultaneous or were detected concurrently during follow-up visits. Co-infections that included HPV 58 also significantly increased risk, regardless of whether the infection included HPV 16.

There is a need for more research to determine whether the elevated risk represents true synergy or the combination of independent viral risks, noted Dr. Mark Schiffman of NCI's Division of Cancer Epidemiology and Genetics.

Test for Bladder Cancer Analyzes DNA in Urine

Researchers have developed an experimental test for detecting bladder cancer that screens urine for DNA changes associated with the disease. The noninvasive test, which needs more study before entering the clinic, detects DNA methylation, a chemical change that can alter the activity of genes, including those associated with cancer. Many researchers are investigating whether abnormal methylation can be a biological marker for cancer.

To develop the test, Dr. David Sidransky of Johns Hopkins School of Medicine and colleagues profiled the methylation patterns of nine key genes that are altered in various cancers, including bladder cancer. They then analyzed the genes in urine from 15 bladder cancer patients and 25 healthy individuals. For all 15 patients, the methylation pattern in urine matched that in the primary tumors.

"All of the 15 primary tumors tested in this study harbored at least one methylated marker," the researchers wrote in the July 19 *Journal of the National Cancer Institute (JNCI).* "Moreover, the methylation status of the urine sample always matched that of the tumor sample from the same patient."

Among a larger group of 175 bladder cancer patients, 121 showed methylation in at least 1 of 4 genes, whereas none of the nearly 95 healthy individuals did.

The detection method, quantitative methylation-specific PCR assay, is sensitive enough to identify 1 methylated gene among more than 1,000 unmethylated genes, the researchers say. The gold standard for diagnosing bladder cancer is cystoscopy, but the procedure has limitations, is expensive, and is uncomfortable for the patient.

Tissue Growth Factor Inhibits Metastatic Activity in Lung Cancer

Scientists showed that connective tissue growth factor (CTGF) inhibits metastatic activity of human lung cancer cells in mice by inhibiting angiogenesis, according to a study in the July 19 *JNCI.*

The researchers, led by Dr. Cheng-Chi Chang at National Taiwan University, transfected the lung cancer cells with either CTGF or hypoxia-inducible factor 1α (HIF-1α), a protein associated with metastatic activity and angiogenesis. The

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cells were then injected into mice to form xenograft tumors. Tumors that grew from the CTGF-transfected cells grew more slowly and the mice survived longer, the investigators reported.

"We have shown that CTGF expression can inhibit tumor growth in primary or metastatic sites by reducing *VEGF-A* gene expression and its subsequent angiogenic effects in tumor cells," they explain. "Most importantly, we have provided functional evidence that CTGF acts as an angiogenesis suppressor, inhibiting tumor growth and metastasis in mouse models of human lung adenocarcinoma."

A *JNCI* editorial noted that "the elucidation of the interplay between central and tributary pathways in tumor progression, such as those highlighted here for the putative metastasis suppressor gene *CTGF*, will help in deciding which molecular target in the network will more specifically affect aberrant tumor angiogenesis without compromising the physiological process." Targeting the tumor microenvironment, in addition to attacking tumor cells, "may permit important improvements to clinical outcomes in the future."

Smoking Blamed for Half of Difference in Death Rates

Numerous research studies have documented that men and women from lower socioeconomic backgrounds have a higher mortality risk than those from higher socioeconomic backgrounds. Now a new study from researchers at the University of Toronto and the University of Oxford attributes more than half of this difference, in middle-aged men at least, to smoking.

Regardless of whether this discrepancy is due to factors such as smoking prevalence, smoking intensity, or lung cancer treatment, the authors concluded, "a substantial increase in cessation could approximately halve these…social inequalities in adult male mortality."

Released early online on July 15 by the *Lancet*, the study team, led by Drs. Prabhat Jha and Richard Peto, used what they describe as an "indirect method" to estimate the contribution of smoking to the mortality difference between these two groups of men, "based solely on the national age-specific death rates for lung cancer and for various other [smoking-related] diseases."

They looked at nearly 600,000 deaths that occurred in 1996 in men aged 35 to 69 years in the United Kingdom, Canada, the United States, and Poland. They used different measures of "social strata" for each country. For men in the United Kingdom, for example, they used a national social classification system based on occupation, whereas for men in the United States they used completed years of education.

Although they admitted that the estimation method they used was "crude," they argued that the "major pattern in these populations is clear."

The study results confirm the role of smoking in health disparities worldwide, Dr. Michael Marmot from the University College London noted in an accompanying editorial. It also highlights the need to answer important questions about how to reduce smoking rates in lower income populations, as well as address "the other major social causes of inequalities in health."

SPORE Investigators' Workshop Held July 16–19

The goal of NCI's Specialized Programs of Research Excellence (SPORE) program is to conduct translational research to rapidly move promising laboratory results into early-phase clinical trials. The 14th SPORE Investigators' Workshop, held in Baltimore, July 16–19, drew researchers from 58 SPOREs representing 14 individual organ sites.

NCI is increasing its focus on translational research, explained Dr. Ernie Hawk, director of the Office of Centers, Training and Resources, in the conference's opening session, because "advances in cancer biology offer enormous opportunities to improve cancer treatment and prevention. Translation of these new concepts into drugs, devices, and interventions that can be tested in the clinic or population has not kept pace with advances in fundamental research. Expanding opportunities and high expectations coupled with limited resources require a translational research system that can identify and pursue the most promising opportunities efficiently and productively."

A day of breakout sessions allowed organ-site programs to discuss the most important recent scientific advancements within their SPOREs and in their fields, and explore opportunities for future collaborations. Mini-symposia and working groups gave investigators the chance to discuss new findings and identify new research challenges.

The conference closed with a morning of plenary sessions, highlighting the best efforts of each SPORE to achieve a human application or intervention from its basic research. Investigators presented promising new research and novel uses for established drugs and techniques.

Dr. John Park, of the University of California, San Francisco, Brain

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Funding Opportunities

Following are newly released NCI research funding opportunities:

Mechanisms of Immune Modulation

Announcement Number: RFA-AT-06-005

Application Receipt Date: Dec. 12, 2006

This funding opportunity will use the R21 award mechanism. For more information, see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3507. Inquiries: Dr. Young S. Kim—yk47s@nih.gov

Assay Development for High Throughput Molecular Screening

Announcement Number: RFA-RM-07-001

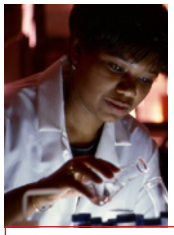
Letter of Intent Receipt Date: Sept. 8, 2006

Application Receipt Date: Sept. 22, 2006

This is a renewal of RFA-RM-06-004 and will use the R21 award mechanism. For more information, see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3508. Inquiries: Dr. Mark Scheideler—scheidelerm@ninds.nih.gov

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

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



Featured Clinical Trial

Adjuvant Bisphosphonates for Breast Cancer

Name of the Trial

Phase III Randomized Study of Adjuvant Zoledronate Versus Clodronate Versus Ibandronate in Women with Resected Primary Stage I-III Adenocarcinoma of the Breast (SWOG-S0307). See the protocol summary at http://cancer.gov/clinicaltrials/SWOG-S0307.

Principal Investigators

Dr. Julie Gralow and Dr. Robert Livingston, SWOG; Dr. James Ingle, NCCTG; Dr. Carla Falkson, ECOG; Dr. Alexander Paterson, NSABP; Dr. Elizabeth Dees, CALGB; and Dr. Mark Clemons, NCIC-CTG.

Dr. Julie Gralow

Why This Trial Is Important

When breast cancer spreads (metastasizes), it often spreads first to the bones. Bone metastases can lead to complications such as pain, fractures, spinal cord compression, bone marrow suppression, and hypercalcemia (abnormally high blood calcium).

Drugs called bisphosphonates have been shown to slow the progression of bone metastases and reduce skeletal complications in women with metastatic breast cancer. Bisphosphonates may also prevent the development of bone metastases in newly diagnosed patients with no evidence of metastasis.

"Breast cancer cells stimulate bone cells called osteoclasts, and these osteoclasts in turn stimulate the growth of breast cancer cells," said Dr. Gralow. "A bisphosphonate called clodronate has been shown to interrupt the relationship between osteoclasts and breast cancer cells in early stage breast cancer. With this trial, we're comparing clodronate with two newer, more potent bisphosphonates—zoledronate and ibandronate.

"If we can eliminate bone as a safe harbor for breast cancer cells in women who would have experienced bone metastases as the first site of metastasis, we may be able to prevent the spread of breast cancer in these women altogether and save lives. Additionally, we hope to determine which types of breast cancer preferentially metastasize to bone," Dr. Gralow added.

Who Can Join This Trial

Researchers will enroll 6,000 women aged 18 or over whose tumors have been surgically removed and who are receiving, or will receive, standard adjuvant hormonal therapy, chemotherapy, or both. See the list of eligibility criteria at http://cancer.gov/clinicaltrials/SWOG-S0307.

Study Sites and Contact Information

Study sites in the United States are recruiting patients for this trial. See the list of study contacts at http://cancer.gov/clinicaltrials/SWOG-S0307 or call NCI's Cancer Information Service toll free at 1-800-4-CANCER (1-800-422-6237). The call is confidential. ◆

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

Notes

Dr. Tsuyoshi Kakefuda Dies at 77

NCI researcher Dr. Tsuyoshi Kakefuda died on June 16 in Potomac, Md., at the age of 77.

Dr. Kakefuda joined NCI's Department of Molecular Carcinogenesis in 1967, capturing one of the first images of DNA replicating itself. He later worked in the Office of International Affairs and became executive secretary of the U.S.-Japan Cooperative Cancer Research Program. He was dedicated to fostering U.S.-Japan relations and to providing opportunities for young Japanese scientists. He also published two books, *Life Science Strategies of NIH* and *Tracking Down the Oncogene*, and occasionally wrote a column for the *Asahi Shinbun* newspaper.

Dr. Kakefuda is survived by his wife, a sister, two children, and three grandchildren.

NIH Roadmap Featured

The June 15 issue of *Genetic Engineering News* reports on the progress of the NIH Roadmap initiative. Now in its third year, the program funds organizations and companies focusing on emerging areas of science, with the goal of moving research from lab to clinic as quickly as possible.

The article notes that the response to date from industry and academia has been enthusiastic and cites examples of successful collaborations between NIH and other organizations. The article also reports on NIH's ability to shift the focus of Roadmap activities, based on experience gained as the initiative progresses.

Additional information about the NIH Roadmap is available online at http://nihroadmap.nih.gov. The *Genetic Engineering News* article can be accessed at http://www.nih.gov/about/director/interviews/geneng-news.pdf.

NCI Symposium Celebrates Progress in Cytogenetics

More than 300 scientists from around the world attended the NCI-sponsored symposium, "50 Years of 46 Human Chromosomes: Progress in Cytogenetics," on July 20–21. In her opening remarks, NCI Deputy Director Dr. Anna Barker said, "This discovery set in motion the basis for unraveling the genetics of man and ultimately understanding the origin of disease."

Dr. Daniela Gerhard, director of NCI's Office of Cancer Genomics, reviewed the history of cytogenetics. Other speakers included Dr. Francis Collins, director of the National Human Genome Research Institute; Dr. Janet Rowley of the University of Chicago; and Dr. Felix Mitelman of the University of Lund. The organizers plan to publish a summary of the meeting within the next few months.

Call for Posters Deadline Extended

The deadline to submit poster abstracts for the 2006 NIH Research Festival, to be held October 17–20 on the NIH campus, has been extended to August 8. For more information, contact Paula Cohen at 301-402-4507 or cohenp@mail.nih.gov. For additional information about the event, go to http://researchfestival.nih.gov.

AIDS Malignancy Program Conference Scheduled for October

The 10th International Conference on Malignancies in AIDS and Other Acquired Immunodeficiencies will take place in Bethesda, Md., on October 16–17.

The conference is intended for clinical and laboratory investigators, postdoctoral fellows, students, physicians, health care workers, and others involved, interested, or participating in malignancy research in AIDS and other immunodeficiencies and in tumor virology.

The conference is free, but registration is required. For additional information, go to http://www.palladianpartners.com/aidsmalignancy/index.htm. ◆

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oncology drugs, added Dr. George S. Johnson, of DCTD's Developmental Therapeutics Program, who called the workshop "a model for translational research fully applicable to other diseases."

Information about the workshop is available at http://www.acceleratingworkshop.org. Major sponsors of the event included the American Association for Cancer Research, the American Society of Clinical Oncology, FDA, NCI, and the Duke Comprehensive Cancer Center. ◆

By Addison Greenwood

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SPORE, stressed the contribution of this cutting-edge translational drug development in his plenary session remarks: "I think that the development of new therapeutics…within the SPOREs and within academic centers is a critical part of global oncology drug development and the cancer therapeutics enterprise. I think that it represents a sorely needed and very complementary process to…industry and biotechnology." ◆

A Conversation With...Dr. Kim Lyerly

Dr. H. "Kim" Lyerly is director of the Duke Comprehensive Cancer Center, and a member of NCI's Translational Research Working Group. He is one of the originators of the workshop "Accelerating Anticancer Agent Development and Validation" (see Spotlight, page 3).

Why was the workshop created?

There's a perception that it takes too long to get a drug to market and that the system is broken. You see people pointing fingers at the FDA, at NCI, at the big drug companies. But active attempts are being made. Nonetheless, when a patient asks me directly why he or she can't get access to some new anticancer treatment in the pipeline, I want to be able to say that we are working on tangible solutions as a team. With leadership and support from the FDA, NCI, American Association for Cancer Research, American Society for Clinical Oncology, and consumers, I hope the workshop has evolved into just that.

What is your own take on the problem?

The molecular era has spawned undreamed of advances in science, which the drug development process has not been able to keep up with. Ten years ago, the scientific community was aware of perhaps 500 "conceivable" drugs they might work on. In the wake of the Human Genome Project, that number has grown to more than 50,000. And yet the system that has evolved produces only 1 successful drug for every 20 that enter into clinical evaluation, often at a cost of more than a billion dollars. Hence, people working in every sector want to solve this problem.

Does the workshop provide a solution?

The workshop illustrates what we think is the most immediate solution by shining a light on a historically closed-door process. We provide lectures from experts in the drug development process and match younger scientists grappling with how to further develop their specific agent with some of the best minds in the country who are actively involved in drug development and approval, and with consumers, representing cancer patients. It's an open forum—no secrets, no cautious regulatory doublespeak, no self-interest. The FDA, in particular, has been a leading contributor and a crucial player, letting their best people provide guidance and insight into the approval process in a way they could not do when responding to an actual drug application. They've embraced the opportunity to deliver this practical but unofficial guidance.

What do you think should happen?

In order of importance, if not feasibility: Continued dialogue throughout the development process that allows more open and collaborative discussions about a drug's viability. Funded research focused on developing new endpoints, such as highly predictive markers of clinical efficacy and more realistic ways to define toxicity. Immediate and sustained action on the NCI working group recommendations to improve clinical trials and translational research. While the latter [TRWG] has yet to issue recommendations, clearly we need a team approach and a coordinated development context. Finally, national-level solutions to the imbalance between the cost of conducting clinical trials in this country and abroad. ◆

Featured Meetings and Events

A calendar of scientific meetings and events sponsored by the National Institutes of Health is available at http://calendar.nih.gov ◆

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

For more information on cancer, call 1-800-4-CANCER or visit http://www.cancer.gov. Contact the *NCI Cancer Bulletin* staff at ncicancerbulletin@mail.nih.gov.