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Molecular Profiling Informs Ovarian Cancer Therapy

NCI researchers are reporting that ovarian cancer cells with diminished ability to produce asparagine may be susceptible to the drug L-asparaginase (L-ASP), which has been used for more than 30 years to treat acute lymphoblastic leukemia. L-ASP metabolizes asparagine in the blood, selectively starving some types of cancer cells that cannot produce enough of the amino acid for their own needs.

Since recent studies have suggested a link between L-ASP activity and asparagine synthetase (ASNS) expression, the research team, led by Dr. John Weinstein, head of the Genomics & Bioinformatics Group (GBG) in NCI's Center for Cancer Research (CCR), analyzed expression of the ASNS gene in the NCI-60 panel of human cancer cell lines. The NCI-60 panel, used by NCI's Developmental Therapeutics Program to screen more than 100,000 compounds and natural products since 1990, is the most extensively profiled set of cancer cells in existence. Five different microarray platforms that GBG and their collaborators used for molecular profiling of the NCI-60 panel revealed a strong relationship between the anticancer

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Director's Update

NCCCP Increases Patient Access to Quality Cancer Care

NCI has created an infrastructure of clinical cancer research and cancer care that is unmatched anywhere in the world. The foundation of this successful system is the 61 NCI-designated Cancer Centers, which have been the bedrock of the continual improvements made in prevention, screening, treatment, and palliative care. However, the fact still remains that 85 percent of cancer patients receive their care at the local community level. Given this, if we are to bring the latest scientific advances to the patient, we must continue to develop programs to reach them in the communities where they live.

Cancer is a disease of the aging. This rapidly growing patient population, as well as underserved or disadvantaged populations, need more support in order to access quality care. I agree with Dr. John Seffrin, CEO of the American Cancer Society, who has said that access by patients with cancer to state-of-the-art care—to the latest advances in genomics and proteomics—will be a bigger determinant to mortality than any risk factors identified today. It is for this reason that I believe NCI needs to create a new rim of clinical cancer

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activity of L-ASP and low expression of ASNS in ovarian cancer cell lines.

When the researchers and their collaborators then used RNA interference to reduce the expression of ASNS fivefold in three of those cell lines, L-ASP became much more active. With the cell type that expressed the least ASNS, the activity of L-ASP increased more than 500-fold, and that enhanced killing was maintained in a classically multidrug resistance cell line.

"We hope the level of ASNS gene activation will one day be a useful tool for identifying ovarian cancer patients who will benefit from L-ASP treatment," said lead author Dr. Philip Lorenzi, a Pharmacology Research Associate Program fellow in GBG. "However, it should be remembered that results in cell lines don't necessarily reflect what will happen in clinical tumors."

The group's collaborators have opened a phase I clinical trial to test the safety of L-ASP in patients with solid tumors and non-Hodgkin's lymphoma and to begin assessment of ASNS as a biomarker.

The ASNS study, published online November 7 in *Molecular Cancer Therapeutics*, launches a new "Spotlight on Molecular Profiling" series of articles, which will highlight high-quality molecular profiling research and provide genomic and proteomic data for many types of cancer.

According to their interests and expertise, researchers around the world will be able to mine the molecular profiles published in the series with the ultimate goal of developing personal molecular profiles and improving cancer detection, treatment, and prevention. To facilitate those uses of the data, GBG has developed an interactive database and set of query tools called "CellMiner."

"If cancer research in the pregenomic era was a cottage industry dedicated to the study of individual molecules and processes, then the postgenomic era is an industrial revolution defined by technological advances that allow for large-scale screening of thousands of genes at once," Dr. Weinstein concluded. "This new spotlight on molecular profiling is important because it will emphasize that not all genetic changes are the same and not all cancers are the same, and they should not be treated as such." ◆

By Heather Maisey

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research and care beyond the NCI-designated Cancer Centers Program to build on the superb efforts of these Centers. By virtue of their ability to directly address issues of delivery, many Centers have invested in creating networks of affiliated community cancer programs.

One of the missions of NCI, however, is to conduct research on how to meet the health care access crisis sitting on our doorstep, and to determine the best ways to bring prevention, early diagnosis, treatment, and new science to all of those affected with cancer. Therefore, NCI has launched a new initiative, the NCI Community Cancer Centers Program (NCCCP), which is being tested as a pilot project—not in competition with programs that do community outreach, but as a complementary program to the existing network of NCI-designated Cancer Centers, Community Clinical Oncology Program (CCOP) sites, and other academic medical center cancer programs.

NCCCP seeks to broaden and magnify the impact of our research advances and create a more comprehensive National Cancer Program that builds on our strengths. NCI's mission is to fund and perform research, not to deliver care. As a pilot, the program, which will cost $9 million over its 3-year span, is intended to help answer some of the most pressing clinical cancer-related issues, including one of the most serious problems—disparities in care.

When the NCI-designated Cancer Centers Program was being created during the 1970s, there was a need for special care units in large hospital settings to manage the side effects associated with highly toxic chemotherapeutic treatment regimens. Today, it is possible to propose this next sphere of clinical research and outreach because the new generation of drugs are targeted and less toxic, and will be able to be administered in early-phase clinical studies in a community practice setting.

To qualify for the NCCCP pilot, Centers will need to have established systems able to support clinical trials and a substantial patient base to be able to accrue patients to clinical trials, as well as effective means of serving the underinsured and uninsured. The Centers will also need to be able to apply resources effectively to build information technology capability, including electronic patient medical records, as well as support biospecimen collection. Sites must be unconditionally accredited by the American College of Surgeons Commission on Cancer, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), and the College of American Pathologists or JCAHO for laboratory services. There also is a preference for sites to be participating in national or state programs for screening and treat-
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Cancer Research Highlights

PSA Velocity Distinguishes More Lethal Prostate Cancer

Screening for prostate specific antigen (PSA) can detect early stage prostate cancer, but evidence is mixed about whether this knowledge improves health outcomes, according to the U.S. Preventive Services Task Force. However, new findings in the November 1 *Journal of the National Cancer Institute (JNCI)* indicate that the change in PSA over time (PSA velocity) is a better marker for more aggressive prostate cancers (see related article); thus, the authors concluded that PSA screening should begin earlier to capture a more dynamic view of prostate carcinogenesis.

Dr. H. Ballantine Carter and colleagues of Johns Hopkins University and the National Institute on Aging (NIA) showed that men whose PSA rises less than 0.35 ng/mL per year have only an 8 percent chance of prostate cancer death 25 years after their velocity was determined. This risk is nearly five times lower than men whose PSA velocity rises more quickly than 0.35 ng/mL per year, 46 percent of whom will succumb to their disease in that same time frame.

The researchers were able to look back at data from a large, ongoing prospective cohort study begun by NIA in 1958 and test blood samples for PSA in 980 men—124 of whom were eventually diagnosed with prostate cancer. In a related editorial, Dr. Timothy R. Church of the University of Minnesota said the study encourages optimism about the value of PSA velocity, though it had "weaknesses… and the implication of the results is not straightforward."

And while the study did not examine whether men with high PSA velocity might have benefited from early treatment, the authors concluded that "as much as 10 to 15 years before diagnosis, it would appear that PSA velocity is an indicator of disease that is destined to progress and threaten life."

Tobacco Use Decline Has Stalled, CDC Report Shows

The overall prevalence of smoking among U.S. adults was the same as in the previous year, in contrast to a steady decline seen over the last 8 years. This news, based on data from the Centers for Disease Control and Prevention's (CDC) annual National Health Interview Survey (NHIS), was reported in the October 27 *Morbidity and Mortality Weekly Report*.

The NHIS questionnaire was administered to a nationally representative sample of 31,428 people aged 18 years or older. The survey found that, in 2005, an estimated 20.9 percent of U.S. adults—45 million people—were current cigarette smokers (people who had smoked at least 100 cigarettes during their lifetimes, and were now smoking every day or on some days); 80.8 percent smoked every day, and 19.2 percent smoked some days. As in past years, there were striking differences between population groups. For example, smoking prevalence among highly educated Americans (those with graduate degrees) fell to 7.1 percent, while prevalence among those with a GED was 43.2 percent. Prevalence was also higher among people living below the poverty level than among those at or above the poverty level (29.9 percent vs. 20.6 percent).

The authors cite smaller annual increases in the price of cigarettes, increased tobacco industry expenditures on price discounts, and a significant drop in state tobacco control program funding as possible contributors to their findings. "The huge differences in smoking rates associated with income, education, and other factors are of great concern to tobacco control researchers and practitioners," said Dr. Cathy Backinger, acting chief of NCI's Tobacco Control Research Branch in the Division of Cancer Control and Population Sciences (DCCPS).

More information about tobacco use and cancer can be found at http://www.cancer.gov/cancertopics/smoking.

New Therapeutic Target Identified in Retinal Tumors

A new study published in the November 2 *Nature* has shown that overexpression of a protein in the p53 cell-signaling pathway called MDMX allows retinoblastoma cells to survive and proliferate. While previous studies have implicated mutations in the tumor-suppressor gene *RB1* as necessary for the formation of retinoblastoma, researchers had thought that these tumors developed independently of mutations in the p53 pathway.

The investigators from St. Jude Children's Research Hospital in Memphis first determined that MDMX was overexpressed in retinoblastoma tissue samples and that the p53 pathway downstream of MDMX

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was fully functional in several retinoblastoma cell lines. They next induced MDMX expression in a mouse model of retinoblastoma. Expression of the protein promoted both proliferation and survival in cells that were genetically susceptible to malignant transformation.

When the investigators introduced MDMX into cultured human retinas, cell death was suppressed even if *RB1* was inhibited at the same time. When a mutant form of MDMX that cannot bind to p53 was introduced in place of normal MDMX, cells underwent apoptosis (cell death).

The investigators next tested a small-molecule inhibitor called nutlin-3 on retinoblastoma *in vitro* and *in vivo*. Nutlin-3 was able to inhibit MDMX from binding to p53 *in vivo*, and a subconjunctival injection of nutlin-3 plus the chemotherapy drug topotican synergistically killed retinoblastoma cells in a mouse model, with no systemic or eye complications.

The authors encourage further clinical examination of this drug combination: "On the basis of our preclinical studies, we propose that subconjunctival administration of these two drugs could achieve the same synergistic effect in individuals with retinoblastoma without causing the side effects associated with prolonged systemic exposure to broad-spectrum chemotherapeutic drugs."

Epirubicin Improves Standard Breast Cancer Chemotherapy

The addition of several treatment cycles with the anthracycline drug epirubicin (Ellence) to the standard adjuvant chemotherapy regimen for early breast cancer significantly increased relapse-free and overall survival rates compared with patients using the standard therapy alone, according to an analysis of two studies in the November 2 *New England Journal of Medicine*.

The National Epirubicin Adjuvant Trial (NEAT) and the BR9601 trial included 2,391 women who received either the combination of four cycles of epirubicin and the standard CMF regimen (cyclophosphamide, methotrexate, and fluorouracil) or CMF alone. At a median follow-up of 48 months, the relapse-free and overall survival rates were significantly higher in the epirubicin-CMF groups than in the CMF-alone groups—the 2-year relapse-free survival was 91 percent vs. 85 percent, and the 2-year overall survival was 95 percent vs. 92 percent.

"The overall incidence of adverse effects was significantly higher with epirubicin plus CMF than with CMF alone but did not significantly affect the delivered-dose intensity or the quality of life," reported the researchers, led by Dr. Christopher J. Poole of the Cancer Research U.K. Clinical Trials Unit in the United Kingdom.

In an accompanying editorial, Dr. Mark N. Levine and Timothy Whelan noted as background that the 2000 NIH Consensus Conference recommended anthracycline-containing regimens for the adjuvant treatment of breast cancer. Although the analysis of the two studies showed modest benefit from adding epirubicin to the standard CMF regimen, the editorial cautioned that the considerable toxic effects and costs require that physicians "tailor the aggressiveness of the chemotherapy to the risk of recurrence" in each patient. ◆

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ment to incorporate other efforts to improve cancer care.

A major goal of NCCCP will be to create a cohort of oncology patients linked through electronic records and common bioinformatic databases. If we hope to accelerate the timeline to drug approval, we need to establish linked multisite clinical trial networks. NCCCP offers the infrastructure that reaches deeper into the community to bring together these patient cohorts.

The interplay of the NCCCP pilot will be an important step in transferring the rigors of clinical cancer care to local hospitals and clinics. I believe that by introducing clinical research standards to the local setting, it will raise the quality of care and acquaint community physicians with state-of-the-art cancer care management.

Through this pilot, we hope to identify effective ways to increase accrual to clinical trials, assess programs to bridge the disparities gap, develop standardized tissue banks that will enable future research in carcinogenesis, and bring community-based oncology into the era of electronic medical record keeping and information technology networks.

Like any well-designed project of this nature, evaluation metrics will be established for NCCCP, and independent assessments will help us determine whether it is something that, approximately 3 years from now, we need to revisit, revise, or even expand.

With NCCCP, we are trying to answer some ambitious questions for which there are no easy answers. But I am a firm believer that if we make the effort to identify the parameters and imperatives behind delivering high-quality care to people in communities across the country, we will reap the benefits—as measured by many cancers prevented and lives saved. ◆

Dr. John E. Niederhuber
Director, National Cancer Institute

Spotlight

Helping Radiologists Improve Breast Cancer Screening

The radiologists who read mammograms in the United States face the daunting task of finding 3 to 6 cancers in every 1,000 mammograms. But despite the challenge, a recent study reported that most radiologists exceed performance levels set in the early 1990s.

The study, which appeared in the October *Radiology*, used data from the NCI-sponsored Breast Cancer Surveillance Consortium (BCSC) to evaluate how well 807 radiologists around the country were performing different aspects of breast cancer screening.

"We now have a baseline of where physicians are practicing," says lead author Dr. Robert Rosenberg of the Radiology Department at the University of New Mexico in Albuquerque. "If you look at cancer outcomes, the radiologists are doing a good job."

The performance levels set back in the early 1990s were basically educated guesses about how well a radiologist could do. Today, thanks to the BCSC, a wealth of data exists, and researchers are using the information to improve breast cancer screening.

The findings by Dr. Rosenberg's team provide performance "benchmarks" that may help radiologists identify which areas of their practices could be improved, says Dr. Stephen Taplin of NCI's DCCPS.

"Until you know where you stand, you can't figure out what you need to do to improve your performance," adds Dr. Taplin, who oversees the BCSC program.

Dr. Rosenberg's team analyzed 2.5 million mammography screening exams done between 1996 and 2002 involving 1.1 million women. They compared screening exam results with each woman's clinical outcome in the 12 months following her initial exam.

After follow-up work, cancer was diagnosed in 4.8 per 1,000 women. When a radiologist advised that a biopsy be performed immediately, 34 percent of the results indicated cancer.

The 807 radiologists came from nearly 200 different facilities that provide information on screening mammography to the BCSC.

The consortium, launched in 1994, includes five research sites currently gathering information on mammography through partnerships with facilities in their geographic areas. The facilities range in type from traditional radiology practices and hospital-based services to mobile mammography vans and pathology laboratories.

More than 225 published studies have used data collected by the BCSC.

"You could not do this particular study without the BCSC," notes Dr. Taplin. "It's very complicated to standardize data collection and definitions."

The findings suggest the need for more research on the recall rate—the proportion of women called back by radiologists for more evaluation based on a finding in a mammogram.

The recall rate should be less than 10 percent, and it has been higher in the United States than in Europe. The study reports a wide range, with some radiologists recalling 4 to 5 percent of women while others recall 20 percent or more.

"The question is whether we can narrow the range down," says Dr. Rosenberg, noting that the challenge will be to do so while detecting cancer at the same level.

A second study in the October *Radiology* used BCSC data to explore another aspect of screening mammography: whether radiologists are making the appropriate recommendations for follow-up care after assessing a mammogram.

This question is related to performance benchmarks because if the assessments are not properly linked to recommendations, then the benchmarks will be inaccurate and so will the audits that radiologists do to compare themselves to the benchmarks.

To answer the question, Dr. Berta Geller of the University of Vermont and colleagues analyzed several years of data before and after the final rules of the Mammography Quality Standards Act (MQSA) went into effect in April 1999.

These rules dictate the terminology that radiologists should use when making recommendations based on a finding in a mammogram. Previous studies found that assessments do not always match recommendations; the new study reports progress.

For example, in 1996 only 51 percent of the screening mammograms

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Funding Opportunities

Development, Application, and Evaluation of Prediction Models for Cancer Risk and Prognosis

Announcement Number: PA-07-022

Application Receipt Dates: Feb. 1, June 1, and Oct. 1, 2007; Feb. 1, June 1, and Oct. 1, 2008; Feb. 1, June 1, and Oct. 1, 2009

This funding opportunity will use the R21 award mechanism. See http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3552. Inquires: Dr. Andrew N. Freedman—freedmaa@mail.nih.gov; Dr. Isis S. Mikhail—mikhaili@mail.nih.gov; Dr. J. Milburn Jessup—jessupj@mail.nih.gov

Facilitating Interdisciplinary Research via Methodological and Technological Innovation in the Behavioral and Social Sciences

Announcement Number: RFA-RM-07-004

Application Receipt Date: Feb. 23, 2007

This funding opportunity will use the R21 award mechanism. See http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3549. Inquires: Dr. Patricia L. Mabry—mabryp@od.nih.gov; Dr. Lisa Onken—Lisa_Onken@nih.gov

Understanding and Promoting Health Literacy

Announcement Number: PAR-07-018

Letter of Intent Receipt Dates: April 24, 2007; Dec. 24, 2007; Aug. 22, 2008; April 24, 2009; Dec. 24, 2010

Application Receipt Dates: May 24, 2007; Jan. 24, 2008; Sept. 24, 2008; May 25, 2009; Jan. 25, 2010

This funding opportunity will use the R21 award mechanism. See http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3550. Inquires: Dr. Sabra F. Woolley—sabra_woolley@nih.gov ◆

Featured Clinical Trial

Treating Adult T-Cell Leukemia/Lymphoma

Name of the Trial

Phase II Study of Denileukin Diftitox in Patients with Tac-Expressing HTLV-1-Associated Adult T-Cell Leukemia/Lymphoma (NCI-05-C-0185). See the protocol summary at http://cancer.gov/clinicaltrials/NCI-05-C-0185.

Principal Investigators

Drs. John Janik and Deirdre O'Mahony (Protocol Chair), NCI CCR

Dr. John Janik

Why This Trial Is Important

Adult T-cell leukemia/lymphoma (ATLL) is an aggressive form of non-Hodgkin's lymphoma caused by the human T-cell leukemia virus type 1 (HTLV-1). Patients with ATLL may experience bone and skin lesions; high calcium levels; or enlargement of the lymph nodes, spleen, or liver. Most patients die within a year of diagnosis. The development of effective therapies for the treatment of this aggressive cancer serves as a model for the treatment of other forms of lymphoma.

In ATLL, HTLV-1 causes abnormal and uncontrolled growth of T cells (immune system cells that normally fight infections and disease). These malignant T cells often express high amounts of a protein called Tac, which is a receptor protein for the immune system hormone interleukin-2.

Denileukin diftitox (Ontak) is a genetically engineered protein that combines segments of interleukin-2 and diphtheria toxin. Diphtheria toxin is a poison made by the same bacterium that causes the disease diphtheria, which can be fatal.

Denileukin diftitox binds to the Tac protein on ATLL cells and is subsequently absorbed by them, causing the cells to die. Researchers hope that administering denileukin diftitox to patients with ATLL will help these patients survive longer.

"Denileukin diftitox is approved by the Food and Drug Administration to treat cutaneous T-cell lymphoma, and it is fairly well tolerated by patients," said Dr. O'Mahony. "We hope that this drug will prove to be a more effective treatment than traditional chemotherapy for patients with ATLL, a rare disease that is usually associated with a poor outcome."

Who Can Join This Trial

Researchers seek to enroll 29 patients aged 18 or over with Tac-expressing ATLL. See the list of eligibility criteria at http://cancer.gov/clinicaltrials/NCI-05-C-0185.

Study Site and Contact Information

This study is taking place at the NIH Clinical Center in Bethesda, Md. For more information, call the NCI Clinical Studies Support Center (CSSC) at 1-888-NCI-1937. The call is toll free and confidential. ◆

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

Notes

Conference Moves Transdisciplinary Science Forward

An international audience participated onsite and via videocast in the "Science of Team Science (STS): Assessing the Value of Transdisciplinary Research" conference on October 30–31, jointly sponsored by NCI's Behavioral Research Program in DCCPS, the NIH Office of Behavioral and Social Sciences Research, and the American Psychological Association. The conference integrated existing knowledge in the STS field, opened new avenues of research on several cutting-edge topics, and identified high-priority topics for future investigation. The archived videocast can be found at http://videocast.nih.gov, and presentations soon will be posted at http://behavioralresearch.cancer.gov.

OSPA Releases 21 Disease-Specific Snapshots

NCI's Office of Science Planning and Assessment (OSPA) recently developed and released a set of 21 disease site-specific "Snapshots," including 4 new ones on pediatric cancer, head and neck cancer, sarcoma, and Kaposi's sarcoma, plus 17 that were updated. The compact one-page, double-sided documents provide a snapshot of trends in disease incidence and mortality, NCI's investment by fiscal year, examples of current relevant NCI initiatives, and selected opportunities for advancement. To view or download the snapshots, visit http://planning.cancer.gov/disease/snapshots.shtml.

Nanotech Investigators Meeting Embraces Team Science

On October 25–26, NCI leadership welcomed members of the Alliance for Nanotechnology in Cancer to the first annual Investigators Meeting hosted by the University of California, San Diego's Center for Cancer Nanotechnology Excellence. More than 200 members of the Alliance teams—including cancer biologists, engineers, chemists, and clinical oncologists—shared their new nanotech-enabled approaches to targeted therapies, cancer imaging, and detection techniques, and identified new opportunities for collaboration.

Challenges in translation of technologies to the clinic, as well as featured experts from industry and the FDA who defined key steps toward commercialization, were highlighted. Various Alliance work groups presented progress on bioinformatics tools development, data and research tools sharing, and multifunctional nanoscale drug delivery systems. Several poster sessions fostered connectivity among Alliance investigators and encouraged the development of new ideas for research collaborations. Students and postdoctoral candidates currently working within their Alliance programs also attended.

New Ovarian Cancer Booklet Available

NCI has updated *What You Need To Know About Ovarian Cancer*, which answers cancer patients' questions about symptoms, diagnosis, staging, and treatment. The booklet can be downloaded from http://www.cancer.gov/publications. Print copies can be ordered online or by calling 1-800-4-CANCER (1-800-422-6237).

Science Offers Online Alerts and Research Summaries

Science magazine offers a variety of e-mail alerts to registered users and subscribers. Select from Content Awareness alerts, CiteTrack Personal Research alerts, and Career and Grant alerts. Most alerts are free for registered users with username and password. More information is available at http://sciencemag.org/ema. ◆

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appropriately recommended a short-interval follow-up (usually 6 months) for women with lesions classified as "probably benign." By 2001, the number was up to 76 percent.

"The surprise is how quickly people adopted the new terminology," says Dr. Taplin.

Dr. Geller attributes the improvement to several factors, including greater familiarity with the terminology among radiologists due to the American College of Radiology's Breast Imaging Reporting And Data Systems (BI-RADS) and to the MQSA regulations.

More radiologists also are using computer software that automatically suggests recommendations when findings are entered on the computer. "This is a teaching tool, and radiologists who have difficulty with the terminology may find it useful," says Dr. Geller.

"Because breast cancer affects so many women and because mammography is the best current screening method, we're always trying to find ways to improve mammography," she says. ◆

By Edward R. Winstead

Community Update

NCI-FDA Training Program Focuses on Translation

Dr. Robert J. Lechleider was on a familiar path for many cancer researchers. He had received research grants and co-authored published, peer-reviewed papers, and most recently served as an associate professor in cell biology at Georgetown University Medical School.

These days, however, he's spending most of his time in training sessions and meetings at the Food and Drug Administration (FDA) learning how to review applications from drug companies seeking approval to market a new drug or conduct a clinical trial of an investigational agent.

"It's a hard thing to train for," he says. "But it's just like anything else. You have to jump in and do it."

Dr. Lechleider is one of the first fellows in a novel training program developed by NCI and FDA's Interagency Oncology Task Force (IOTF). Its goal: To develop a cadre of basic and clinical researchers who also understand the legal and regulatory aspects of delivering new drugs or diagnostics to the clinic.

"It's definitely a unique program," says Dr. Jonathan Wiest, associate director for training and education in NCI's CCR. "It's especially rare to have two agencies within HHS working together on a program like this." Dr. Wiest, along with Drs. Mary Poos and David Brown of the FDA, oversee the training program.

The IOTF Joint Fellowship Program is composed of four different programs, each with curricula that are tailored somewhat differently depending on a fellow's education, training, and interest. For Dr. Lechleider, the program offered him an opportunity to move in a new direction.

"I was a basic scientist, with no clinical involvement," he says. "I wanted to be more directly involved in drug development."

The first year of Dr. Lechleider's 3-year program was dedicated to clinical training at the Bethesda Naval Medical Hospital and at the NIH Clinical Center with patients enrolled in NCI clinical trials.

Now more than a month into the regulatory training, he admits it's quite a change.

"It's a different way of thinking," he says. "The clinical training has been great because when I start to look at trial designs, having seen patients treated on clinical trials makes it easier to interpret applications and evaluate them for risk and benefit."

Another fellow in the program, Dr. M. Stacey Ricci, agrees that the program has given her a different mindset.

"Coming from a background in basic research, it has been a great way to learn what it takes to get a promising cancer drug into clinical trials," says Dr. Ricci, who came to the program after completing her postdoctoral training at the University of Pennsylvania. "Training at the FDA has provided an opportunity to understand, in great detail, what the critical safety and manufacturing issues are for successful drug development." Much of Dr. Ricci's training at the FDA has focused on biologics, particularly monoclonal antibodies.

In addition to their regulatory training, both Drs. Ricci and Lechleider will continue conducting research in FDA and NCI laboratories, respectively.

Established as a 3- to 5-year pilot, the program definitely addresses a pressing need.

"When you look at the cost of getting a drug through to the market, one of the most expensive and time-consuming aspects is meeting the requirements for gaining regulatory approval," says Dr. Wiest. "This program is about training world-class scientists who understand how to make that happen." ◆

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.