NATIONAL CANCER INSTITUTE

NCI Cancer Bulletin

Eliminating the Suffering and Death Due to Cancer

September 19, 2006
Volume 3 | Number 36

In this issue:

A Publication of the
National Cancer Institute
U.S. DEPARTMENT OF
HEALTH AND HUMAN SERVICES
National Institutes of Health
NIH Publication No. 05-5498

http://www.cancer.gov

Brain, Lung, and Ovarian Cancers Selected to Initiate The Cancer Genome Atlas

The cancers to be studied first in the pilot phase of The Cancer Genome Atlas (TCGA) project will be brain, lung, and ovarian, officials from NCI and the National Human Genome Research Institute (NHGRI) announced on September 13.

The Institutes launched the pilot phase of TCGA in December 2005 to assess the feasibility of systematically identifying the significant genomic changes involved in cancer using contemporary genomic analysis technologies, including resequencing of selected genes.

The selection of brain, lung, and ovarian cancers, which collectively account for more than 210,000 cases annually in the U. S., followed a rigorous assessment of tumor collections that began over a year ago.

"The three cancer types were selected based on specific scientific, technical, and bioethical criteria," said NCI Deputy Director Dr. Anna Barker. "The biospecimen collections representing brain, lung, and ovary met or exceeded these criteria and represent high-mortality diseases that present

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Director's Update

Dr. John E. Niederhuber is sworn in as the 13th Director of the National Cancer Institute.

A Vision of Progress

Now that it is official, let me emphasize once again what a special honor it is to lead the world's preeminent cancer research organization, especially at a time when our opportunities for progress are without precedent.

There is broad agreement among NCI leaders about how best to seize these opportunities. First, we must continue to address NCI's strategic priorities, through appropriately aligned new initiatives. Second, we are committed to striving to maintain the number of competing awards near the level achieved during the period when the NIH budget doubled. In addition, we are firmly committed to funding new investigators and devising incentives that will attract the best minds to a field so vital to the health of our citizens—and to our country's future development in a changing world market.

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significant challenges to the cancer research community."

For example, each collection had to exceed a certain number of samples to achieve statistical power; contain a defined percentage of tumor cells; and have matched normal tissue, outcomes data on patients, and appropriate informed patient consent, to name a few of the criteria.

"We were looking for biospecimen sets of the highest possible quality so that we could have confidence in the results," said Dr. Carolyn Compton, director of NCI's Office of Biorepositories and Biospecimen Research.

Three institutions are donating the biospecimens for the TCGA Pilot Project.

The lung cancer samples are from the Lung Cancer Tissue Bank of the Cancer and Leukemia Group B clinical trials group, housed at Brigham and Women's Hospital; the brain cancer samples (glioblastoma multiforme grade 4) are from the University of Texas M.D. Anderson Cancer Center; and the ovarian cancer samples are from the Gynecologic Oncology Group tissue bank at the Children's Hospital of Ohio State University.

The tissue samples will be stored and processed at the TCGA Biospecimen Core Resource (BCR) facility. The International Genomics Consortium, in collaboration with the Translational Genomics Research Institute, of Phoenix, Ariz., will establish and manage the BCR.

When fully operational, the TCGA Pilot Project will have two groups of centers doing different types of genomic analyses on tissue samples provided by the BCR.

The Cancer Genome Characterization Centers, funded by NCI, will identify changes such as chromosomal rearrangements and the presence of extra copies of genes. Genes of interest will then be resequenced at Genome Sequencing Centers, funded by NHGRI.

The information generated by the centers will be integrated and managed by a Principal Bioinformatics Resource (PBR) and made available to researchers over the Internet. Data are expected to be accessible through this TCGA database by mid-2007.

"The variety of data will provide a view of the cancer problem that we have never had before," noted NHGRI Director Dr. Francis Collins.

During the pilot project, tumor samples will be assessed for alterations in DNA expression, gene regulation (including epigenetic changes that alter gene activity but not DNA sequence), gene copy numbers, and other changes. These data, along with patient outcomes and other clinical data, will be accessed through specific portals that are currently being defined.

"The revolutionary aspect of TCGA is the integration of all of these different types of genomic, biologic, and clinical data," said Dr. Barker. "TCGA promises to open up a whole world of cancer genomics that will reach far beyond these three cancers." ◆

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Sound fiscal planning, especially in today's difficult budgetary environment, will be required to achieve these goals. It will fall on the leadership of NCI to make difficult decisions among competing priorities. Scientific consensus in this process will be critical. I will rely on the NCI Executive Committee to discuss operational and scientific issues, guide the decision-making process, and help find the necessary resources, through redeployment, to maintain scientific momentum.

As NCI Director, I take it as my responsibility to find new ways to leverage resources. We will continue our collaborations with other NIH Institutes and Centers, nonprofit organizations, and Federal agencies. We will maintain our support of partnerships with academia that have been so successfully developed within each of the Divisions and Centers at NCI. Such programs stretch across the oncology research spectrum and include opportunities in behavioral science, clinical research, epidemiology, genetics, molecular biology, proteomics, and nanotechnology.

One of the biggest scientific challenges we will face as an Institute will be integrating our diverse research, in order to most effectively utilize new knowledge to generate better outcomes for cancer patients. I like to think of three "spaces": a chemical space, in which we develop the capacity to understand and re-engineer molecules; a biologic space that comprehends the genetic defects that comprise this disease, the signal pathways that become abnormal, the tumor stem cells, and the tissue microenvironment; and a translational space that brings new discoveries to the point where targets and markers inform drug development. Integrating these spaces is dependant on technology and technology development, which bring together the physical and biological sciences. Driving this entire continuum will be computational biology, which adds the rigors of applied mathematics and the capacity to manage, analyze, and utilize large databases. Integrating the chemical, biologic, and translational
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Cancer Research Highlights

Autoimmune Disorders Linked to Elevated Risk of Hodgkin Lymphoma

Personal and family histories of autoimmune conditions are associated with an increased risk of Hodgkin lymphoma (HL), according to study results in the September 20 *Journal of the National Cancer Institute.*

Dr. Ola Landgren of NCI's Division of Cancer Epidemiology and Genetics and colleagues conducted a population-based case control study using data from the Swedish and Danish Cancer Registries, Swedish Multi-Generational Registry, and Danish Central Population Registry. Researchers identified 7,476 case subjects with a first-time HL diagnosis and matched them to 18,573 control subjects by sex, year of birth (within 5 years), and county of residence. More than 86,000 first-degree relatives of case and control subjects also were identified. Subjects were further linked to the Swedish and Danish Inpatient Registries to collect information on discharge diagnoses and 32 autoimmune conditions. All autoimmune conditions were analyzed both individually and by grouping into categories that incorporated knowledge about similar biologic characteristics of autoimmune conditions.

Individuals with a personal history of specific systemic autoimmune conditions—in particular, rheumatoid arthritis and systemic lupus erythematosus—had a significantly increased risk of HL. The associations of both personal and family histories of sarcoidosis with increased risk of HL suggest shared susceptibility that may be important in HL pathogenesis.

These results have implications for future research. According to Dr. Landgren, "This study provides important clues to the role of immune dysregulation and inflammation in the etiology of HL. Future epidemiological and preclinical studies are needed to explain underlying mechanisms of the observed associations. We need to better understand whether they are due to systemic immune stimulation or inflammation, immune-modulating treatments for autoimmune disorders, shared susceptibility, or a combination of these factors."

NCI Study Details Celecoxib's Proteomic Impact

A new study from NCI researchers has unveiled a host of proteins not previously known to be influenced by the COX-2 inhibitor celecoxib, a drug that has shown significant potential as a chemopreventive agent for colorectal cancer. The study was published in the September 12 *Cancer Epidemiology, Biomarkers, and Prevention.*

Celecoxib's influence on these proteins was not a by-product of its inhibition of the COX-2 enzyme, lead author Dr. Iqbal Ali and colleagues from NCI's Division of Cancer Prevention reported, because the colorectal cancer cell line in which they studied its effects did not express COX-2.

"Many of these potential molecular targets of celecoxib…are of considerable significance in cancer biology, and celecoxib-mediated upregulation or downregulation of these proteins is generally consistent with the relevance of their known cellular functions to the process of carcinogenesis," they wrote.

Proteins that were modulated by celecoxib included those involved in functions such as cell cycle arrest and cell death, DNA synthesis, molecular "chaperoning," glycolysis (converting glucose into energy), and many others.

Using advanced proteomic profiling technologies, the research team conducted the first-ever effort to globally profile the proteins affected by celecoxib in a cancer cell line. Profiling was performed before celecoxib treatment and then afterward, using two doses of celecoxib—one small and one significantly larger. Although celecoxib had different effects depending on the dose administered, at either dose there was approximately 30 percent overlap in the proteins with altered expression.

"Detailed analysis of the functional role of novel candidate molecular targets identified in this study," Dr. Ali and co-authors concluded, "would extend our understanding of the chemopreventive effects of celecoxib" and can help lead to "more effective chemoprevention."

Chemotherapy Fails to Improve Survival in Rectal Cancer

Advanced rectal cancer patients benefit from radiotherapy before surgery to remove their tumors, but there is no clear consensus on whether chemotherapy should be given before or after that surgery. Results from a large European study published in the September 14 *New England Journal of Medicine* suggest that fluorouracil chemotherapy will reduce local

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recurrence regardless of when it is given, but does not have an effect on progression-free and overall survival.

Using those who received only preoperative radiotherapy as a standard, the researchers evaluated three different ways to add fluorouracil chemotherapy to the treatment: before surgery, after surgery, or both. They found no statistically significant survival differences among any of these groups, yet "regardless of timing, chemotherapy provides a significant benefit with respect to local control," said the study's lead author, Dr. Jean-François Bosset, from the University of Franche-Comté in Besançon, France, a member of the EORTC (European Organization for Research and Treatment of Cancer) Radiotherapy Group.

The 1,011 patients were followed for a median of 5.4 years; 17.1 percent of those who received radiotherapy alone before their surgery had local recurrence, compared with 8.6 percent who had some form of chemotherapy. Fluorouracil was shown to facilitate surgery by shrinking rectal tumors and reducing pathology, though local recurrence was still significantly reduced even when the drug was given only after surgery.

The results suggest that "future trials should focus on eradicating micrometastases," said Dr. Bosset, because distant recurrence was found to be three times more likely than local recurrence.

Response to Antiangiogenic Drugs for Kidney Cancer Linked to Mutations

Researchers have identified an association between certain mutations in the Von Hippel-Lindau (VHL) gene and the response to drugs that inhibit the growth of tumor blood vessels (angiogenesis) in patients with metastatic clear cell renal cell carcinoma (cRCC), an aggressive form of kidney cancer.

Antiangiogenic therapies are more effective than traditional treatments for some patients with metastatic cRCC, but physicians need ways to identify responders. Mutations in VHL, a tumor-suppressor gene, could potentially be used to help predict response if the association can be confirmed in larger studies.

In this study, the cancer took longer to progress in patients who took antiangiogenic agents such as bevacizumab (Avastin) and had mutations that severely altered the VHL protein. Twenty-five of 43 tumors had a VHL mutation. The median time to disease progression was 13.7 months for patients with mutations that extensively altered the structure of the VHL protein, compared with 7.4 months for patients with less extensive alterations, and 5.5 months for patients with no VHL mutation.

Mutations in the VHL gene are responsible for half of noninherited cases of cRCC. The mutations result in greater expression of the vascular endothelial growth factor (VEGF) and its receptor. VEGF, a regulator of angiogenesis, is a target of drugs such as bevacizumab.

The researchers concluded that the response to therapies targeting the VEGF pathway in patients with metastatic cRCC may be associated with VHL mutations that extensively alter the structure of the VHL protein. The findings were presented by Dr. Erich Jaeger of the University of California, San Francisco, on September 13 at the first meeting on Molecular Diagnostics in Cancer Therapeutic Development, organized by the American Association for Cancer Research. ◆

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spaces—with informatics as a common thread—will make the process of interventional discovery much faster, and as we make this continuum faster, we will make it less costly.

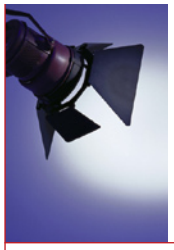
One element of our research—from which informatics will be inseparable—will be to study how we can improve the delivery of cancer care to patients in the communities where they live. In an era of highly targeted cancer treatments, I believe that access to care could potentially be the greatest determinant of cancer mortality. NCI will work to extend its clinical trials infrastructure and its science into the community. We will research how to bring the best science to patients—with electronic medical records and interconnected informatics systems helping create a national cohort of cancer patients. This cohort will help us address the translational space and will be a significant factor in reducing the cost of drug discovery.

We live in a time of unparalleled scientific opportunity. NCI will face the challenges that come its way, with a clear vision of how to exploit scientific advances and lessen the burden of cancer. ◆

Dr. John E. Niederhuber
Director, National Cancer Institute

NCI Funding Opportunities

For a complete listing of current NCI funding opportunities, please go to the HTML version of today's *NCI Cancer Bulletin* at http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_091906/page7. ◆



Spotlight

Afterbirth No Longer an Afterthought: Cord Blood for Cancer Patients

A gentle smack on the bottom, a quick whisk to the warming table for cleanup, and sighs of relief fill the room. A baby is born. New life has come into the world. But the potential for life doesn't rest only with the infant. In the umbilical cord and placenta, leftover blood capable of regenerating tissue is helping doctors to treat cancer patients.

Months before birth, stem cells travel from the fetal yolk sac to the baby's bone marrow where they are ready to replace red blood cells, immune cells, and platelets after birth. In the fetus, the stem cells circulate until the time of birth. After the umbilical cord is cut, cells remaining in the placenta may be collected and frozen for later use.

Like the stem cells that patients receive in bone marrow transplants, these cord blood stem cells can be injected into another person to repair damage caused by radiation or chemotherapy, migrating to the recipient's bone marrow in a process called engraftment.

"The limits of cord blood have yet to be defined," says Dr. Ron Gress, who heads the Transplantation Therapy Section of the Experimental Transplantation and Immunology Branch in NCI's Center for Cancer Research, "but the field has moved far enough forward that we know cord blood as a source of stem cells for transplantation is a viable treatment possibility."

The immune system attacks transplanted tissues when antigens on the new cells' surfaces are too different from those of native tissue. In turn, transplanted immune cells can attack a recipient's body in a condition known as graft-versus-host-disease (GVHD). This is why finding a matched donor is so important in transplantation.

Less than a third of patients who need bone marrow transplants are able to find an ideal match—a blood relative with the same human leukocyte antigens (HLAs)—in time to have the procedure. The next best option is an unrelated matched donor. For African Americans, Asians, and people from other minority groups, this process is particularly restricted because the pool of donors from similar ethnic backgrounds is so small. But there's data to indicate that cord blood could solve many of these problems.

Unlike bone marrow, cord blood is easy to get and poses no harm to the donor. Cord blood is also almost always free of viruses or bacteria, and appears to be more "recipient friendly" because units only need to match in four out of six HLA categories. In additon, there's lower incidence of GVHD than in bone marrow recipients.

The clinical potential is so great that, after receiving recommendations in a report from the Institute of Medicine, Congress passed legislation to increase the nation's inventory of cord blood for use in transplantation. The first contracts for blood banks to begin implementing the plan will be announced by the Health Resources and Services Administration before the end of this fiscal year.

"Cord blood transplants are already the standard practice in Japan, and in Europe and the U.S., the approach is steadily being adopted," says Dr. John Wagner, a pioneer in the field of cord blood transplantation at the University of Minnesota. "Once we begin receiving reports from the U.S. and Europe that document results similar to ours, I think that use of cord blood will dramatically change for adults as well as children."

Much of Dr. Wagner's results come from studies in adults with leukemia. Beyond showing that cord blood transplants can work, researchers have found that HLA-mismatched cord blood units actually attack the cancer, decreasing the chance of relapse. While HLA-mismatching carries a higher risk of transplant-related mortality, new information suggests that this can be minimized by increasing the number of transplanted cord blood cells. "While survival after HLA-mismatched cord blood parallels that of HLA-matched marrow, we continue to look for ways to make it better," says Dr. Wagner.

Then why aren't cord blood transplants standard practice in the United States today for adults? The principal limiting factor is cell dose—the number of cells given to a patient based on body weight. Cord blood is a rich source of stem cells, but the number of cells in the collection is often small. Adults need at least 25 million nucleated cells per kilogram of weight for successful engraftment, and very few of the cord blood units

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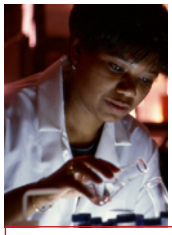
available today through blood banks meet this criterion. As a result, most of the 8,000 transplants conducted during the past 16 years have been in children, whose body weight is generally lower than that of adults.

To overcome this barrier, researchers are combining two individual cord blood units to increase the number of transplanted cells. "For patients who have received a double cord-blood transplant, we have observed a greater chance of survival compared with single-unit transplants," Dr. Wagner says. "While we expected to see less transplant-related mortality with the higher cell dose, we were surprised to see a markedly lower risk of relapse in patients transplanted with two cord blood units."

Dr. Wagner's team has performed nearly 300 double cord-blood transplants in adults and children so far, with 76 percent mismatched at 2 HLA antigens. The next step is to determine how results compare in patients transplanted with two cord blood units versus HLA-matched marrow.

Beyond testing double cord-blood transplants, Dr. Wagner's group is also looking into cord blood-derived natural killer cells in patients with refractory leukemia, cord blood-derived regulatory T cells to enhance engraftment and reduce GVHD, and injection of cord blood right into the bone marrow space to speed marrow recovery. ◆

By Brittany Moya del Pino



Featured Clinical Trial

Monoclonal Antibodies for Metastatic Colorectal Cancer

Name of the Trial
Phase III Randomized Study of Cetuximab and/or Bevacizumab in Combination with Either Oxaliplatin, Fluorouracil, and Leucovorin Calcium (FOLFOX) or Irinotecan Hydrochloride, Fluorouracil, and Leucovorin Calcium (FOLFIRI) in Patients with Previously Untreated Metastatic Adenocarcinoma of the Colon or Rectum (CALGB-C80405). See the protocol summary at http://cancer.gov/clinicaltrials/CALGB-C80405.

Principal Investigators
Dr. Alan Venook, Cancer and Leukemia Group B; and Dr. Charles Blanke, Southwest Oncology Group

Why This Trial Is Important
Colon and rectal cancer (colorectal cancer) are highly treatable if caught at an early stage. Yet, colorectal cancer is expected to cause more than 55,000 deaths in the United States in 2006, many because the cancer will not be detected until it has spread (metastasized) beyond the colon or rectum. Patients with metastatic colorectal cancer face a poor likelihood of survival. Consequently, the need for more effective treatments is great.

In this trial, patients will receive one of two targeted agents, or a combination of the two, that were recently approved by the U.S. Food and Drug Administration for use with combination chemotherapy in the treatment of metastatic colorectal cancer.

The two targeted agents, bevacizumab (Avastin) and cetuximab (Erbitux), are monoclonal antibodies that seek out and block the activity of different proteins important for tumor cell growth and spread. These proteins, vascular endothelial growth factor (VEGF) and epidermal growth factor receptor (EGFR), respectively, are often found in much greater abundance on cancer cells than on normal cells.

"We want to see if combining these agents along with standard chemotherapy can help these patients live longer and possibly shrink their tumors enough to allow potentially curative surgical treatment," said Dr. Venook.

Who Can Join This Trial
Researchers will enroll 2,300 patients with metastatic colorectal cancer who have not received prior treatment. See the list of eligibility criteria at http://cancer.gov/clinicaltrials/CALGB-C80405. This clinical trial is eligible for special Medicare coverage.

Study Sites and Contact Information
Study sites in the United States and elsewhere are recruiting patients for this trial. See the list of study contacts at http://cancer.gov/clinicaltrials/CALGB-C80405 or call NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237) for more information. The toll-free call is confidential. ◆

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

Notes

Gallahan Appointed Deputy Director of DCB

Dr. Daniel Gallahan has been appointed deputy director of NCI's Division of Cancer Biology (DCB). As deputy, Dr. Gallahan will support DCB's mission of furthering cancer biology research through effective management of grants, as well as facilitation of new ideas, concepts, technologies, and opportunities while continuing to oversee the division's efforts in technology and systems biology, specifically the new Integrative Cancer Biology Program.

Prior to his appointment, Dr. Gallahan had been serving as DCB's associate director and chief of its Structural Biology and Molecular Applications Branch. He played a major role in developing and managing NCI's IMAT program, which has led to the development of new technologies for cancer research.

Dr. Gallahan trained as a cancer biologist and had a distinguished career as a bench scientist within NCI's intramural program. His postdoctoral training included molecular biology, proteomics, bioinformatics, and cancer biology.

Current, Former NCI Grantees Win Lasker Awards

On September 17, the Albert and Mary Lasker Foundation announced the winners of the 2006 Lasker Awards. Three scientists, who are current and former NCI grantees, were honored with the Lasker Award for Basic Medical Research.

Dr. Elizabeth Blackburn of the University of California, San Francisco; Dr. Carol Greider of Johns Hopkins University School of Medicine; and Dr. Jack Szostak of Harvard Medical School were recognized for their work in predicting and discovering telomerase, an RNA-containing enzyme that synthesizes the ends of chromosomes, protecting them and maintaining the integrity of the genome. Their work laid the foundation for studies that have connected telomerase and telomeres to human cancer and age-related conditions. Drs. Blackburn and Greider currently hold NCI grants; Dr. Szostak is a former NCI grantee.

The awards will be presented on September 29 in New York City. Additional information about the Lasker Awards and the other award winners for 2006 is available at http://www.laskerfoundation.org.

eHealth Conference Focuses on Patient-Centered Care

Last week, nearly 200 scientists from government, academia, survey research, and public- and private-sector practitioners gathered in Bethesda, Md., for the second annual conference on "Critical Issues in eHealth Research." The meeting focused on patient-centered care and consolidated the conceptual, methodological, and technological issues that emerge as health information of all kinds is managed and communicated through electronic media.

Dr. Jon Kerner, deputy director for research dissemination and diffusion in NCI's Division of Cancer Control and Population Sciences, summarized a number of trends that are driving the field, including the shift to paperless health records in the electronic domain. Referring to the interface between electronic and interpersonal activities, he said, "We have to realize that at the end of the day, all of the electronic data represent real people and patients."

Joining NCI as meeting sponsors were the National Institute on Drug Abuse, the National Library of Medicine, the NIH's Office of Behavioral and Social Sciences Research and Office of Disease Prevention, the Agency for Healthcare Quality and Research, the Office of Disease Prevention and Health Promotion, the American Medical Informatics Association, and the Health e-Technologies Initiative, a national program office of the Robert Wood Johnson Foundation. ◆

CCR Grand Rounds

September 26: Dr. Javed Khan, Principal Investigator and Attending Physician, Oncogenomics Section, Pediatric Oncology Branch, Center for Cancer Research. "Translational 'omics' in Cancer."

October 3: Dr. Steven K. Libutti, Head, Tumor Angiogenesis Section, Surgery Branch, CCR. "Targeting the Tumor Microenvironment for Cancer Therapy."

CCR Grand Rounds are held 8:30 to 9:30 a.m. at the NIH campus in Bethesda, Md., in the Clinical Center's Lipsett Amphitheater. ◆

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 ◆

A Conversation with Dr. Anna Barker and Doug Ulman

Dr. Anna Barker is Deputy Director of NCI and Deputy Director for Advanced Technologies and Strategic Partnerships. Doug Ulman is Chair of the NCI Director's Consumer Liaison Group, Chief Mission Officer of the Lance Armstrong Foundation, and a three-time cancer survivor. They spoke with the NCI Cancer Bulletin *about The Cancer Genome Atlas Pilot Project.*

Why were these three tumor types chosen?

Dr. Barker: We selected cancer types that were scientifically and technically appropriate to build TCGA and prepare the teams to analyze other tumors in the future. We also needed to locate and qualify existing biospecimen collections that were of high quality and sufficient quantity to meet the needs of the project. To accomplish these complex goals, we developed a rigorous, three-part selection process that allowed us to make the final selections.

Mr. Ulman: I think it's important for cancer patients to know that, while the cancers to be studied by this project come from existing biorepositories, samples to be studied will eventually be prospectively collected in clinical trials. Participating in clinical trials that meet TCGA criteria will be an excellent way to support the expansion of TCGA.

How will studying these cancers help patients with other cancers?

Dr. Barker: This pilot phase has been designed to study a few cancer types that hold the most promise for helping researchers understand how to design and conduct future studies on a wide range of tumors. TCGA will support the development of new technologies aimed at overcoming the current limitations in genomic analysis and bioinformatics technologies. Another goal is to develop data analysis tools that will allow clinicians to use this new molecular information to better understand subtle differences between subtypes of certain cancer, how tumors develop and progress, and why some cancers respond to certain treatments and not others.

Mr. Ulman: By focusing first on the cancers that will be studied in the pilot phase of TCGA, we expect that researchers will begin to understand how genomic changes at the molecular level may impact all types of cancer. These findings will eventually help to find new ways to target therapies and improve outcomes for all cancer patients.

How will TCGA affect diagnosis and treatment of cancer patients?

Dr. Barker: Achieving the long-term goal of TCGA will benefit patients by enabling the discovery and development of the molecular biomarkers needed to develop targeted interventions to stratify patients for clinical trials, monitor patients on therapy, and define and develop new molecular targets. Discoveries in cancer genomics already have helped identify several new treatments that target cancer-related molecules. For example, Gleevec effectively treats chronic myelogenous leukemia, gastrointestinal stromal tumors, and several other cancers. Another product of cancer genomics research, Herceptin, effectively treats about 20 percent of breast cancers that capitalize on a specific genetic anomaly.

Mr. Ulman: Understanding the genetic changes that cause the uncontrolled cell growth that characterizes cancer will enable researchers and clinicians to develop new diagnostic techniques and targeted therapies, leading to improved outcomes for all cancer patients and, eventually, cancer prevention. ◆