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BSA Supports Genome Pilot Project

The National Cancer Institute's (NCI's) **Board of Scientific Advisors** (BSA) last week unanimously endorsed a 3-year pilot project to assess the feasibility of sequencing genomic changes in human tumors on a large scale. The **Human Cancer Genome Pilot Project** (HCGPP) will be conducted as a partnership between NCI and the National Human Genome Research Institute (NHGRI).

"This is truly an integrated effort," said Dr. Anna Barker, NCI deputy director for strategic scientific initiatives, "not just an NCI project." Dr. Barker told BSA that by leveraging both institutes' funding, resources, and expertise, the collaboration will allow a greater return on those investments.

Enabled by the reference human sequence from the Human Genome Project, NCI and NHGRI hope the pilot project will establish a firm foundation for molecular oncology by focusing on a combination of genome characterization and resequencing to identify genetic aberrations in major cancer types. By identifying the molecular pathways that underlie cancer, the HCGPP could provide valuable new targets for cancer prevention, detection, diagnosis, and drug development.

"The mission of this pilot project is to develop a systematic approach to identifying genetic alterations in cancer that have meaningful clinical impact in a few rationally *(continued on page 2)*

Director's Update

Guest Update by Drs. James H. Doroshow, Joseph E. Tomaszewski, and Jerry M. Collins

DTP Celebrates 50 Years of Advancing Cancer Research

This month, NCI celebrates the 50th anniversary of the Developmental Therapeutics Program (DTP), which has played a key role in supplying the nation's trove of treatments against cancer. Since its inception in 1955 as the Cancer Chemotherapy National Service Center, DTP has contributed to the development of 38 anticancer drugs, including paclitaxel, bortezomib, and cetuximab. Now, as part of the **Division of Cancer Treatment & Diagnosis** (DCTD), DTP continues its role in planning, conducting, and facilitating the discovery and development of new therapeutic agents for cancer.

That concisely stated role encompasses a wide range of collaborative activities. DTP, through its own researchers and those supported by the program's grants and contracts, searches for unique anticancer agents in synthetic molecules, biologicals, and natural products. DTP staff and contractors perform the screening and related biological, toxicological, and pharmacological evaluations necessary to ensure these compounds can be introduced safely to cancer patients.

(continued on page 2)



(Genome Pilot Project continued from page 1)
selected cancer types,” said Dr.

Gregory Downing, director of NCI’s Office of Technology and Industrial Relations. “Paramount to this whole initiative is the systematic approach, which will establish public data sets and other resources to facilitate research by individual investigators.”

Investigators throughout the cancer community are already identifying and sequencing genes thought to be involved in carcinogenesis—although not in a systematic, integrated manner. The HCGPP could provide an approach to eventually consolidate this effort and make the resulting data widely and publicly available. NCI-supported genome characterization centers will utilize robust genomic technologies to measure gene copy number, expression arrays, and epigenomic and other changes, and will collaborate with NHGRI’s sequencing centers to select genes for resequencing and data integration.

“This is not just about sequencing,” said Dr. Francis Collins, NHGRI director. “This is an integrated effort that puts together sequence data with multiple other types of data, and the sum is clearly going to be much more than the parts.”

To reduce the problem of the heterogeneity of most cancers and ultimately optimize opportunity for clinical impact, the pilot project is currently planned to focus on two cancers. Although final selections will consider information provided by the cancer community through a request for information, it is likely that a hematologic tumor and a solid tumor with poor prognosis would best support the pilot project.

Because the mission of the pilot project is to assess the feasibility of a full-scale effort, BSA advised that a defined criterion be used to monitor

the initiative over the next 3 years. Several benchmarks were offered by the project team and recommended by BSA, including robust genomic analysis of two tumors to produce a “pipeline” of candidate genes/regions for resequencing; the ability to find and correlate genomic changes (e.g., copy number changes, deletions, amplifications, etc.) through in-depth sequencing; new cancer genes discovered beyond known pathways; the ability to differentiate tumor subtypes based on genomic characterization and sequence data; a precompetitive public database of genomic characterization, sequence, and clinical data to enable discovery and translational research; and technology advances that provide the capability to differentiate significant genomic changes from “noise.”

BSA also recommended that funds requested to support genomic analysis technologies be increased.

In endorsing the pilot project, several BSA members noted that this is an extremely important effort for NCI to undertake at this time. ♦

(Director’s Update continued from page 1)

DTP’s extensive resources and services are available to all members of the cancer research community—academia, nonprofit organizations, and industry. DTP staff foster collaborations among scientists from the different environments, encourage use of new technology, and translate scientific findings into new cancer treatments. DTP allows researchers access to its repositories of tested synthetic and natural products, radiolabeled materials, and biological reference standards and reagents. The program also provides inbred and hybrid rats, mice, and guinea pigs to NIH-funded researchers, and offers screening services, including the testing of anticancer compounds *in vitro* in the NCI60 and *in vivo*.

DTP maintains a stable repository of transplantable *in vivo*-derived tumors and *in vitro*-established tumor cell lines from several species. Many of these samples are not available anywhere else in the world and can be provided to qualified researchers.

DTP works in close collaboration with other NCI components, especially the [Center for Cancer Research](#) and the [DCTD Cancer Therapy Evaluation Program](#). As molecules move through the internal NCI drug development pipeline, the goal is to have a smooth transition from preclinical studies in DTP to clinical investigations of efficacy, safety, and biomarkers, including noninvasive imaging. By working with the DCTD Cancer Imaging Program, DTP is helping to broaden the use of imaging in cancer treatment, especially with new molecularly targeted agents.

One recent DTP innovation, the [Rapid Access to Intervention Development \(RAID\)](#) program, is assisting extramural investigators in translating novel anticancer agents from academic laboratories to the clinic. The success of this program has led to the establishment of a number of similar programs, including the NIH-wide RAID pilot program, so that the treatments for other diseases can move more easily from the bench to bedside.

On November 29, DTP will hold its 50th Anniversary Symposium, “A History of Success in Anticancer Drug Development,” on the NIH campus to celebrate its many successes and to examine its future role in anticancer drug development. Please see <http://dtp.nci.nih.gov> for more information. ♦

By Drs. James H. Doroshow, director, DCTD; Joseph E. Tomaszewski, deputy director, DCTD and chief, DTP Toxicology and Pharmacology Branch; and Jerry M. Collins, associate director, DTP



Spotlight

Not Your Father's Mouse Model

In labs all across the country, researchers are using refined versions of an old research tool to provide critical new information on the biology of many cancers and determine which new drugs are the most promising to test in clinical trials. Their tools: laboratory mice. These next-generation mouse models differ from the xenograft models—mice, often with disabled immune systems, transplanted with human tumors—that cancer researchers have relied upon for decades. Instead, through various and often sophisticated techniques, these mice are programmed to develop specific types of cancer, and to do it in a way that substantially mimics how those same cancers arise in humans.

“In many cases, the biology of these models looks very good,” says Dr. Cheryl Marks, who administers the [NCI Mouse Models of Human Cancers Consortium](#) (NCI-MMHCC). What many of the consortium’s investigators are trying to determine now, she continues, “is whether the clinical course in the mice also mimics humans.”

Ironically, she says, “The good news is that we don’t readily cure these mice... However, we know now that when we test in these models the drugs and combination of drugs presently used in the clinic, we show that many of them would have been reasonably predictive of what actually happened in the clinic.”

Engineered models of many cancers have been developed. And although there are many potential roles for these

genetically engineered mouse models in cancer research, preclinical testing of new drugs is seen by many in the field as one of the most promising.

“But there is still much science we have to do,” Dr. Marks cautions, before it’s known whether these engineered mice routinely can be used in this way.

There is at least one successful example to date, however, of this very scenario. Results from preclinical testing of a new drug combination in engineered mouse models of acute promyelocytic leukemia (APL) led to a human trial of the drug combo that has had remarkable results.

APL is often successfully treated with one of two unconventional agents, retinoic acid or arsenic trioxide, to get patients into remission (at which point they then undergo chemotherapy). “But there were conflicting data as to whether treating patients with both agents simultaneously might be antagonistic or cooperative,” explains Dr. Scott Kogan, associate professor-in-residence at the University of California, San Francisco. Results from tests of the combination therapy in engineered APL mouse models, he says, made it “very clear that they were cooperative.”

Based on those studies, researchers in China initiated a randomized clinical trial to test the drugs in combination up front in newly diagnosed APL patients. With more than 3 years of follow-up in 61 patients given both drugs, there have been only 2 relapses.

At Memorial Sloan-Kettering Cancer Center, Dr. Eric Holland says human clinical trials are being pursued based on the results of tests in genetically engineered mouse models of the brain cancers medulloblastoma and glioblastoma developed in his laboratory.

“For some of the small molecular inhibitors that were identified as good choices based on mouse models, there are [human] trials that are being written and going through IRBs,” he says. “This is happening now.”

The models closely mimic the response in humans to standard therapies, he adds, so the models also are being used to improve existing therapies.

One of the models developed in Dr. Holland’s lab reflects the increasing importance of advanced imaging technologies in mouse model research, which is allowing investigators to closely analyze the biologic and molecular events associated with the disease and its treatment. In the model, dubbed Efluc, cancerous cells express a built-in imaging agent, luciferase—the enzyme in fireflies that causes their tails to light up.

“In a noninvasive way, we can have a readout of a specific cellular behavior,” Dr. Holland says. “It can tell you about the activity of certain signaling pathways involved in tumor development and what the therapeutic response is in those specific pathways.”

In the laboratory of Dr. Jonathan Kurie at the University of Texas M.D. Anderson Cancer Center, imaging is also an important component of their mouse model studies. The lab has generated some significant results testing chemopreventive agents in an early-stage lung cancer model developed by Dr. Tyler Jacks and colleagues at MIT.

(Spotlight continued on page 7)



Cancer Research Highlights

Mutations in Glioblastoma Multiforme Predict Response to Targeted Therapies

Glioblastoma multiforme (GBM) is one of the most aggressive types of brain cancer and one of the most resistant to treatment. The epidermal growth factor receptor (EGFR), an important regulator of cellular signaling, is frequently mutated in GBM, and the EGFR kinase inhibitors erlotinib (Tarceva) and gefitinib (Iressa) have shown some efficacy in a subset of patients with this tumor. However, no clear correlation between mutations in the EGFR kinase domain and response to these drugs has been found.

A study, funded in part by NCI and reported in the November 10 *New England Journal of Medicine*, sheds new light on the molecular pathways associated with the response of GBM to EGFR kinase inhibitors. Investigators analyzed tumor tissue from patients with GBM who did or did not respond to treatment with erlotinib or gefitinib, and verified their results using several different molecular techniques. As in previous studies, neither mutations in the EGFR kinase domain nor amplification of EGFR were associated with the response to the drugs. However, expression of a mutant version of EGFR, known as EGFRvIII, and expression of the tumor-suppressor protein PTEN both corresponded favorably with response. Coexpression of both proteins correlated with the greatest likelihood of response. Lack of PTEN

expression corresponded to resistance to the inhibitors.

A perspective in the same issue called the results “an important first step in rational, tumor-specific therapy for glioblastoma multiforme.”

Pancreatic Cancer Vaccine Tested in Phase II Trial

An experimental vaccine to be administered along with standard treatments for pancreatic cancer may have prolonged the survival of some patients with the disease, according to preliminary results from a phase II clinical trial. The vaccine is designed to boost a patient’s immune response against cancer cells that have survived surgery, chemotherapy, and radiation.

In the study, 88 percent of the 56 patients tested were alive 1 year after treatment, and 76 percent were alive after 2 years. By comparison, the historical survival rates are approximately 60 and 40 percent, respectively. Drs. Daniel Laheru and Elizabeth Jaffee of the Johns Hopkins Kimmel Cancer Center led the trial.

Although the results are preliminary, they compare “very favorably” with the available published data, the researchers said last week at the Molecular Targets and Cancer Therapeutics International Conference in Philadelphia. Drs. Laheru and Jaffee intend to begin multi-institutional trials of the vaccine in about a year.

Patients in the study received one vaccine injection about 8 to 10 weeks after surgery, and then four booster shots along with chemotherapy and

radiation over the next few months. The vaccine was made from irradiated pancreatic cancer cells that cannot grow and have been genetically altered to secrete a molecule called GM-CSF, which is capable of inducing antitumor immune responses in some patients.

Pancreatic cancer is the fourth-leading cause of cancer-related deaths in the United States. Each year, approximately 30,000 Americans are diagnosed with the disease, and about the same number die from it.

Higher Calcium Intake Increases Prostate Cancer Risk

Men with the highest levels of dietary calcium intake had nearly double the risk of developing prostate cancer compared with men who had the lowest intake of calcium, according to results from a large study that NCI researchers reported November 1 during a conference of the American Association for Cancer Research in Baltimore.

Researchers with NCI’s Division of Cancer Epidemiology and Genetics (DCEG) reported the latest findings from the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study, conducted on a cohort of 29,133 male smokers in Finland aged 50 to 69 years. Although the study mainly focused on whether dietary supplements of vitamin E and beta-carotene reduced cancer risk, it also examined a suspected link between consumption of dietary calcium and dairy products, and prostate cancer risk.

After 17 years of follow-up, there were 1,269 cases of prostate cancer in the cohort. “Dietary calcium intake of more than 1,000 mg/day—about 3 cups of milk—compared to intake of (Highlights continued on page 5)

(Highlights continued from page 4)

less than 1,000 mg/day was positively associated with prostate cancer risk,” said lead author Dr. Panagiota N. Mitrou with DCEG. “The highest risk was seen among men who consumed more than 2,000 mg/day, almost doubling the risk.”

They also found increased risk from dairy products. “Although this association largely disappeared when we controlled for calcium, we could not completely exclude an independent role for dairy products,” Dr. Mitrou added. The study found no links between intakes of vitamin D or phosphorus and prostate cancer risk.

Given calcium’s potential beneficial effects on osteoporosis and colorectal cancer, the DCEG scientists urge further research within other large prospective studies, examination of other noncalcium components of dairy products, and investigation of the molecular mechanisms of calcium metabolism and ways in which they could modulate prostate carcinogenesis.

NSAIDs Reduce Risk of Esophageal Cancer

Regular use of aspirin and similar painkillers reduces the risk of developing esophageal cancer, according to a prospective study from Fred Hutchinson Cancer Research Center. The development is important, the authors write, because incidence of the disease has risen sharply of late.

The researchers followed 350 people with a condition called Barrett’s esophagus, an abnormality of cells in the throat. About 10 percent of people with gastroesophageal reflux disease develop the precancerous condition, and about 1 percent of those go on to develop esophageal cancer.

During regular checkups, researchers performed endoscopies and

biopsied throat cells in the areas that showed signs of Barrett’s esophagus. Pathologists reviewed the biopsies and determined if the cells had turned cancerous.

The researchers collated that data with survey results asking about the use of aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs). Volunteers were classified as never users, current users (had used an NSAID at least once a week for 6 months), and former users (those who previously used NSAIDs but had not in the preceding year).

In the November 8 online edition of *Lancet Oncology*, the researchers reported that the 5-year cumulative risk for esophageal cancer was 14.3 percent for never users, 9.7 percent for former users, and 6.6 percent for current users.

Previous research has shown NSAIDs to be effective in reducing the risk of colon cancer in people with risk factors such as polyps.

Cetuximab Plus Radiation Proving Effective in HNSCC

Updated results from an international phase III trial testing cetuximab (Erbix) plus radiation therapy in patients with head and neck cancer continue to show favorable results.

The 424 patients in the study had locoregionally advanced squamous cell carcinoma of the head and neck (HNSCC). With a median of 45 months of follow-up, the addition of cetuximab to radiation improved median duration of locoregional control—the study’s primary endpoint—by 9.5 months, and improved median survival by 20 months, compared with patients treated with radiation alone (49 months vs. 29 months). The results were presented at the

AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in Philadelphia.

According to ImClone Systems, which manufactures the drug, the Food and Drug Administration (FDA) has accepted for priority review an application to approve the drug for marketing for this indication. Cetuximab, an antibody that blocks EGFR, is already approved by the FDA for use in combination with irinotecan to treat patients with metastatic colorectal cancer.

Initial results from the trial were presented at the American Society for Clinical Oncology Annual Meeting in 2004.

“If approved by the FDA,” says Dr. Scott Saxman, from NCI’s **Cancer Therapy Evaluation Program**, “this will become a standard for patients who cannot tolerate or are marginal candidates for cisplatin-based chemotherapy.”

But it’s not known, he adds, whether cetuximab can eventually replace chemotherapy, or should be given in addition to chemo and radiation to improve outcomes. NCI is funding a Radiation Therapy Oncology Group-led, phase III clinical trial, which began enrolling patients today, that will compare a standard regimen of radiation and cisplatin to the same regimen plus cetuximab in patients with locally advanced head and neck carcinomas. ♦

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/cgi-bin/calendar> ♦

Funding Opportunities

Small Grants for Behavioral Research in Cancer Control

PAR-06-073

Application Receipt Dates: Apr. 20, Aug. 21, and Dec. 22, 2006; Apr. 20, Aug. 22, and Dec. 20, 2007; Apr. 20, Aug. 21, and Dec. 22, 2008.

This is a renewal of PAR-04-020. This funding opportunity will use the R03 award mechanism. For more information, see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3291. Inquiries: Veronica Chollette—vc24a@mail.nih.gov

Dissemination and Implementation Research in Health

PAR-06-071

Letter of Intent Receipt Dates: Dec. 26, 2005; Aug. 22, 2006; Apr. 24 and Dec. 26, 2007; Aug. 25, 2008; Apr. 22, 2009. Application Receipt Dates: *New, competing continuation, revised, supplemental applications:* Jan. 24 and Sep. 22, 2006; May 24, 2007; Jan. 24 and Sep. 24, 2008; May 22, 2009. *AIDS and AIDS-Related Applications (New, competing continuation, revised, and supplemental):* May 1, 2006; Jan. 2 and Sep. 1, 2007; May 1, 2008; Jan. 2 and Sep. 1, 2009.

This is a renewal of PA-02-131. This funding opportunity will use the R03 award mechanism. For more information, see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3289. Inquiries: Dr. Jon F. Kerner—kernerj@mail.nih.gov

(Funding Opportunities continued on page 7)



Featured Clinical Trial

Allogeneic Stem Cell Transplantation for Metastatic Breast Cancer

Name of the Trial

Phase I Study of T-Cell-Depleted Allogeneic Stem Cell Transplantation Followed by Donor Th2/Tc2 Cells, Administered after Immunoablative Induction Chemotherapy and Reduced-Intensity Transplantation Conditioning in Patients with Metastatic Breast Cancer (NCI-04-C-0131). See the protocol summary at <http://cancer.gov/clinicaltrials/NCI-04-C-0131>.

Principal Investigator

Dr. Michael R. Bishop, NCI Center for Cancer Research

Why Is This Trial Important?

Women whose breast cancer has recurred after treatment and metastasized (spread) to other parts of the body have few viable treatment options. Conventional chemotherapy can extend these women's lives for only a few months at best.

Allogeneic stem cell transplantation (ASCT) has been used to cure patients with hematologic malignancies (blood and bone-marrow cancers) and may represent an effective alternative treatment for some types of solid tumors, including advanced breast cancers. In ASCT, peripheral blood stem cells and T lymphocytes from a sibling donor are infused into the patient's bloodstream after preparatory chemotherapy. The donor T lymphocytes may recognize the patient's cancer cells as foreign and attack them, leading to a potentially curative graft-versus-malignancy effect.

However, ASCT is accompanied by a significant risk of death and a range of serious complications, the most potentially deadly of which is graft-versus-host disease (GVHD). GVHD results when donor T lymphocytes attack a patient's normal tissues. It develops in the majority of transplant patients and represents a major barrier to the wider application of ASCT.

Recent refinements in ASCT have begun to reduce the incidence of GVHD, making the procedure a more attractive treatment option for patients with advanced solid tumors.



Dr. Michael R. Bishop

In this study, researchers are investigating whether ASCT followed by the infusion of donor Th2/Tc2 cells—a type of T lymphocyte that is able to suppress GVHD—can be safely used to treat patients with metastatic breast cancer.

Who Can Join This Trial?

Researchers will recruit 45 women, aged 18 to 75, with metastatic breast cancer that has recurred after treatment. See the list of eligibility criteria at <http://www.cancer.gov/clinicaltrials/NCI-04-C-0131>.

Where Is This Trial Taking Place?

The study is taking place at the NIH Clinical Center in Bethesda, Md.

Contact Information

For more information, call the NCI Clinical Studies Support Center at 1-888-NCI-1937. 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

Science Writers' Seminar to Highlight Cancer Health Disparities

NCI's Science Writers' Seminar, "Improving Cancer Survival by Understanding Racial/Ethnic Disparities," will take place November 30 at the Herbert Irving Comprehensive Cancer Center (HICCC) in New York City. The seminar will explore why many ethnic minorities experience lower cancer survival rates than others, including differences in biological tumor types, timeliness of treatment, and lack of compliance with treatment regimens. Discussions will highlight plans to reduce cancer health disparities through programs that address prevention, diagnosis, and treatment. Speakers include Drs. I. Bernard Weinstein, Alfred I. Neugut, Dawn L. Hershman, Regina M. Santella, and Victor R. Grann from HICCC, and Dr. Harold Freeman from NCI.

Journalists who wish to attend should contact the NCI Press Office at (301) 496-6641 or ncipressofficers@mail.nih.gov.

New Edition of Monograph Available

NCI recently released *Theory at a Glance: A Guide for Health Promotion Practice (Second Edition)*.

The first edition was hailed as a welcome resource for public health practitioners seeking a single, concise summary of health behavior theories. The updated edition includes information from recent health behavior research and suggests theoretical approaches to using emerging technologies and developing programs for diverse populations. Copies of the monograph can be ordered through the Cancer Information Service at <http://www.cancer.gov/publications> or by calling 1-800-4-CANCER (1-800-422-6237).

NCI Hosts Inaugural Biorepository Symposium

On November 10, NCI hosted the first-ever NCI Symposium on International Harmonization of Biorepository Practices. The day began with a welcome from NCI Director Dr. Andrew C. von Eschenbach, who spoke of the need for high-quality biorepositories to advance genomics- and proteomics-based biomarker research. More than 80 experts from 15 nations then explored areas of critical importance to biorepositories: ethical and legal issues; biospecimen collection, processing, storage, and dissemination; and informatics systems.

At the end of the meeting, participants decided to form an International Biorepository Working Group to support harmonization by fostering demonstration projects, and developing a data and information portal for evaluation of biorepository standards to encourage international research collaborations.

Cancer Booklets Updated

NCI has updated four booklets in its award-winning *What You Need To Know About Cancer* series, which is produced to answer cancer patients' questions about symptoms, diagnosis, staging, and treatment. Updates of the following booklets are now available: *What You Need To Know About Breast Cancer*, *What You Need To Know About Prostate Cancer*, *What You Need To Know About Skin Cancer*, and *What You Need To Know About Stomach Cancer*. The booklets 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). ♦

(Funding Opportunities continued from page 6)

Dissemination and Implementation Research in Health PAR-06-072

Letter of Intent Receipt Dates: Dec. 26, 2005; Aug. 22, 2006; Apr. 24 and Dec. 26, 2007; Aug. 25, 2008; Apr. 22, 2009. Application Receipt Dates: *New, competing continuation, revised, supplemental applications*: Jan. 24 and Sep. 22, 2006; May 24, 2007; Jan. 24 and Sep. 24, 2008; May 22, 2009. *AIDS and AIDS-Related Applications (New, competing continuation, revised, and supplemental)*: May 1, 2006; Jan. 2 and Sep. 1, 2007; May 1, 2008; Jan. 2 and Sep. 1, 2009.

This is a renewal of PA-02-131. This funding opportunity will use the R21 award mechanism. For more information, see http://cri.nci.nih.gov/4abst.cfm?initiativeparfa_id=3290. Inquiries: Dr. Jon F. Kerner—kernerj@mail.nih.gov ♦

(Spotlight continued from page 3)

"We do CT scans on all of the mice," he says. "We also do a lot of biochemistry, trying to understand what pathways are being modulated and what cell types are being modulated."

The next step in this process is important: directly comparing the results from the mouse model investigations to similar analyses in human tumors. By looking at measures such as the activation of intracellular signaling pathways in early lesions as well as more advanced lesions, they can determine just how closely the model resembles the real deal.

"We're lucky enough," Dr. Kurie says, "to be at the cusp of a revolution in the mouse model field." ♦

By Carmen Phillips



Community Update

NCI Focuses on Native Americans

During a celebration of the [Fifth Annual NIH American Indian/Alaska Native \(AI/AN\) Heritage Month Program](#), sponsored by the [American Indian/Alaska Native Employee Council](#) and the [NIH Office of Equal Opportunity and Diversity Management](#), a number of research scientists, clinicians, and program specialists gathered to reflect on the unique challenges of fighting cancer in these Native American groups. Lakota storyteller Dr. Joseph M. Marshall, III—author, historian, and cancer survivor—reminded the attendees that the struggles of the original Americans continue into the 21st century.

Cancer strikes different racial and ethnic groups in different ways. Health disparities often arise because culture, outlook, biology, and access to resources all influence the ways in which different people experience cancer.

“This country provides inadequate resources to Native Americans for cancer education, screening, prevention, and treatment,” wrote Dr. Harold P. Freeman, on behalf of the President’s Cancer Panel, in the 2002 Annual Report, *Facing Cancer in Indian Country*. Exacerbating these problems, he said, are “important but remediable cultural misunderstandings...Facing cancer in Indian Country should not be more arduous than it is elsewhere in our Nation.”

Dr. Thomas Becker agrees, citing 2 basic lessons learned from nearly 20 years of work with Native communi-

ties. First, he says, bring your focus down to the local level—to individual tribes, groups, and regions. Second, “You need to reduce the barriers between Native communities that serve as study populations and the mainstream researchers who are usually from another racial group.”

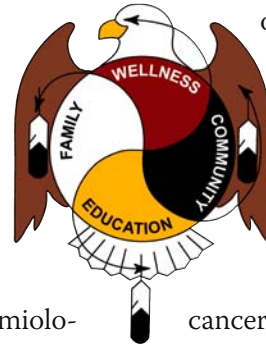
Dr. Becker is a medical epidemiologist. Each summer, he, Dr. Jennie Joe, and other colleagues invite Native researchers to their NCI-funded [Native Researchers’ Cancer Control Training Program](#). For 3 weeks, trainees get intensive hands-on training in the clinical and research skills they will need to make cancer control programs work better in the unique AI/AN community settings.

Dr. Joe, a Navajo, is one of the charter members of the [Network for Cancer Control Research Among American Indian/Alaskan Natives Populations](#), which grew out of Dr. Becker’s drive to create “a de facto think tank in the mid-1990s,” says Judith Swan from NCI’s Surveillance Research Program. She and Dr. Brenda Edwards, head of

NCI’s Cancer Statistics Branch, host the Network’s annual meetings at NCI “where the crucial needs, cutting-edge ideas, and most-likely-to-succeed projects eventually rise to the surface. It’s probably the most exciting meeting I attend each year,” she says.

Currently, Dr. Judith Kaur chairs the Network, which also meets annually at the Mayo Clinic Cancer Center (a partner with NCI in supporting the Network). Dr. Kaur is a medical oncologist and a Choctaw/Cherokee, whose NCI-supported [Native C.I.R.C.L.E.](#) (Cancer Information Resource Center and Learning Exchange) is a national clearinghouse providing cancer-related materials to health care professionals and lay people engaged in the education, care, and treatment of AI/ANs with cancer.

NCI’s [Center to Reduce Cancer Health Disparities](#) funds the Community Networks Program, which supports another Mayo partnership, Spirit of EAGLES, which is dedicated to building the infrastructure to support comprehensive cancer control. It also provides small community grants aimed at lowering incidence and increasing survival in communities in Indian Country, including Alaska. Both Mayo projects, said Dr. Kaur, “translate information and resources into ideas, concepts, and language to which Native peoples are more likely to respond.” ♦



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>.

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