THE CANCER LETTER

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Advisors Approve NCI's Revised Plan For $104M Proteomics Research Program

By Kirsten Boyd Goldberg

Three months after narrowly rejecting an $89-million proposal for a proteomics research program, an NCI advisory group approved a revised plan that would commit $104 million over five years to support the development of this emerging field.

In a unanimous vote, the NCI Board of Scientific Advisors approved the program at its June 27 meeting. Under the revision, NCI eliminated a proposed $16-million biospecimen repository and simplified what had been a complicated four-part program of grants, contracts, and small-business set-asides.

The new Clinical Proteomics Technologies Initiative would include

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In Brief:

Reed To Head Cancer Prevention At CDC; Mitchell Moves From UNC To Stanford

EDDIE REED was selected head of the Division of Cancer Prevention and Control, National Center for Chronic Disease Prevention and Health Promotion, of the Centers for Disease Control and Prevention. Reed, known for his translational research on platinum-DNA adduct, ERCC1 and nucleotide excision repair, and the development of new agents for ovarian cancer and metastatic prostate cancer, was director of the Mary Babb Randolph Cancer Center at the University of West Virginia University in Morgantown. For 20 years, he worked at NCI in a number of positions including senior investigator, Medicine Branch and Clinical Pharmacology Branch, 1987-2001; chief, Clinical Pharmacology Branch from 1993-1996; chief, Medical Ovarian Cancer Section from 1989-2001; and, chief, Ovarian Cancer and Metastatic Prostate Cancer Clinics from 1993-2001. . . . **BEVERLY MITCHELL**, associate director of the Lineberger Comprehensive Cancer Center at University of North Carolina, Chapel Hill, was named to the new position of deputy director of the Stanford University Medical Center's cancer center and professor of medicine at Stanford. The appointment completes the management team of the center, with **Irving Weissman** as director and **Steven Leibel** as medical director, said **Philip Pizzo**, dean of the School of Medicine. The Stanford cancer center plans to submit its application for NCI designation in February. . . . **JEFFREY FORMAN**, medical director of the Weisberg Cancer Treatment Center at Barbara Ann Karmanos Cancer Institute and the Patricia and E. Jan Hartmann professor of radiation oncology

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NCI To Support Consortia, R01s In Proteomics Program

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three elements: funding for up to five research consortia, contracts for a central supplier of reagents, and support for as many as 10 investigator-initiated R01, R21, and R33 grants.

NCI increased support for investigator-initiated grants and lengthened the reagents contracts from three to five years, which accounts for the higher total cost, said Greg Downing, director of the NCI Office of Technology and Industrial Relations.

NCI will require research teams assessing proteomic technologies to "address critical questions of validity of protein measurements and sensitivity, experimental bias and lack of reproducibility across platforms and laboratories, and design and analysis challenges that lead to statistical over-fitting," the Institute's concept statement states.

That requirement was added in response to the board's criticism of the previous proposal last March (The Cancer Letter, March 10).

"This revised concept is much improved," said board member Joe Gray, director of the Life Sciences Division at Lawrence Berkeley National Laboratory and head of the breast cancer program at University of California, San Francisco, Comprehensive Cancer Center. "This is an important area for us to be pursuing. I'm enthusiastic about it."

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The program would build a foundation of technologies, data, reagents, standards, and systems to advance the understanding of protein biology, NCI officials said. The initiative would fund:

—Clinical Proteomics Technology Assessment Consortia of multi-disciplinary teams to develop and evaluate proteomic technologies, reference reagents, sample sets, and measurement protocols, including instrumentation, platform development, reference standards development, and training opportunities.

—Investigator-initiated projects in advanced proteomic platforms, analytical methods, and computational sciences to overcome barriers in protein/peptide feature detection, identification, and quantification, and develop approaches for large-scale data analysis.

—Clinical Proteomic Reagents Resource, a central, "virtual" source for reagents, peptides, proteins, and public data.

To support these activities, a centralized communications network will be hosted by the NCI Cancer Bioinformatics Grid. The NCI Division of Cancer Epidemiology and Genetics will provide technical support for study design, analysis, and statistics, according to the Institute's proposal.

The excerpted text of NCI's concept statement follows:

RFA for the Clinical Proteomic Technology Assessment Consortia, $8.5 million in FY 2006 to fund five U24 (Resource-Related Research Project-Cooperative Agreement) awards for five years. The total budget requested for the Consortia is $35.5 million over five years.

Initially, the Consortia will systematically compare existing technologies, improve technologies, and develop standard data sets of highly annotated specimens. The experimental designs will include blinded controls, intra-platform and inter-institutional comparisons, doping of standard reagents and development of control sets. The goal will be to dramatically refine measurement, identification, and quantitation of proteins and peptides in complex biological mixtures, and of relevance to cancer research. Specifically, the Technology Assessment Consortia will:

—Test the performance of MALDI-, ESI-TOF, and tandem mass spectroscopy platforms and compare them to Fourier Transform Ion Cyclotron Resonance MS using identical samples to determine which combination provides the best achievable combination of reproducibility, dynamic range, and mass accuracy.

—Develop rigorous protocols and internal testing methods to understand the basis for measurement variability aimed at enhancing reproducibility.

—Design, engineer, integrate, and evaluate multiplexed protein detection platforms with consideration with

consideration given to future clinical application.

—Develop, compare, and validate protocols for sample collection, fractionation, separation, labeling, and detection of proteins/peptides from complex mixtures.

—Establish reference or training sets of biological specimens and standards that are available for cross-calibration of instruments and measurements.

—Leverage existing infrastructure for the collection of clinical and animal model specimens (serum, plasma, tissues, and urine) that have a high degree of annotation.

—Perform parallel comparisons of plasma fractionation schemes to determine optimal techniques for fractionating plasma to simplify the proteome sufficiently to allow significant depth of coverage.

—Assess the reproducibility of selected schemes by performing them independently on identical aliquots of plasma and develop tools to assess reproducibility and depth of coverage.

—Test the throughput, and performance of techniques for quantitative proteomics, including isotope-coded affinity tags, ISO-labeling, N-terminal labeling, and direct quantification.

—Develop necessary algorithms for analysis of data generated on commonly-used TOF platforms to assess which techniques for quantitative mass spectrometry are sufficiently robust to support biomarker discovery efforts.

—Compare throughput and reproducibility of ELISA, SISCAP A, and visible isotope-coded affinity tags to determine the best directed discovery approach of proteins and peptides.

—Integrate the data analysis pipelines from collaborating institutions, NCI, and FDA into one pipeline (caBIG) using open source code and a shared data format so that results obtained from different laboratories can be analyzed using the same tools, enabling direct comparison of results.

—Provide training, technical service, standard protocols, and public data sets to a wide array of cancer researchers.

The Clinical Proteomic Technology Assessment Consortia will interface with cancer centers to support the training of researchers in the use and application of these technologies and will interface with programs—including EDRN and SPORE programs—to apply technologies that identify cancer protein and peptides to support discover and translational research. Once the technology platforms have been evaluated, the Consortia will interface with NCI Cancer Centers and SPOREs to apply the optimized techniques in the clinical setting. These Consortia will also serve as a critical source of protocol development, education and training to support proteomic research across the cancer research enterprise.

Advanced Proteomic Platforms, Analytical Methods, and Computational Sciences, $8 million in FY 2006 to fund seven to 10 R01, R21/R33 awards. The total budget requested is $56 million over five years.

This RFA concept would support projects by single-investigators and teams with innovative approaches to overcome barriers encountered through current technologies (e.g., protein chips, mass spectrometry, antibody production) and data analysis and computational studies of measurement data. NCI recognizes that rapid changes are occurring in protein/peptide platforms and significant challenges lie in on the path that will require higher resolution, integration, and validation of technical approaches.

Advances will likely be made in methods for fractionating complex protein mixtures, automation, microfluidics, mass spectrometry, informatics, affinity reagents, protein arrays, and other technologies. This RFA addresses the rapid identification and development of such advances. Pilot projects for new proteomic technology developments will integrate with Technology Assessment Consortia efforts to incorporate the latest advances into the cadre of tools that will support biomarker discovery platforms.

MS and microarrays are used extensively in proteomics for protein identification, profiling, quantification and system biology, resulting in a wealth of data collected and deposited into a variety of data repositories. While the proteomic data acquired from biological samples and processed through various instruments contains a tremendous amount of useful information, lack of standardization prohibits the facile exchange between repositories. Data collected from cancer model experiments or clinical cancer programs indicate the expression of various combinations of proteins that may be representative of a stage of the disease such as cancer. Proteomic data analysis requires sophisticated computational techniques to identify individual proteins as well as patterns or signatures in the data collected.

Data mining algorithms and emerging data exchange format standards may be leveraged to create computational software tools that support proteomics data analysis. The algorithms will address two major arrays: 1) data management and preprocessing and, 2) analysis of spectra to identify particular proteins and peptides. Several proteomic data formats are emerging for data exchange and data representation, including mzXML 13 (XML format for MS) and the Human Proteome Organization's data standards, such as mzData (XML format for MS), mzIdent (XML format for identification), and the Minimum Information About Proteomics Experiment. These approaches will facilitate the electronic exchange of spectra, archiving, and management. In addition, several existing data mining algorithms that utilize machine learning methods may be applied to proteomic data for the purposes of performing computational analysis and extracting useful protein expression patterns from biological samples.

Standardized proteomics formats and algorithms can be incorporated into the software and would allow scientists to easily obtain and analyze proteomic data across various data repositories.

This will support algorithms development for many aspects of proteomic data analysis, such as elution time normalization and peak alignment, signal processing, relative

and direct quantitation, the extraction of diagnostic "molecular fingerprints," peptide identification and sequencing, and protein identification. These capabilities will be provided to all cancer researchers through the cancer bioinformatics grid.

RFP for the Clinical Proteomic Reagents Resource, $2.5 million in research and development contracts via SAIC and in SBIR/STTR funds should fund awards over five years beginning in FY 2006. The total budget requested is $12.5 million over five years.

The Reagents Resource will organize tools, reagents, and enabling technologies to support protein/peptide measurement technology development efforts. These highly purified, standardized, and characterized reagents would be used to support improved approaches to sample preparation, fractionation, separation, detection, and quantitation as standard reference sets. This Resource will serve as a central (virtual) source for reagents, including human and mouse tissue samples, mouse models, antibodies, and other reagents as needed. Reagents include mice, mouse tissues and plasma, human tissues and plasma, antibodies for candidate enrichment, reagents for ICAT and VICAT and other labeling techniques, standard batches of plasma, standard protein and/or peptide mixtures for spiking fluids prior to analysis, and other standard reagents developed or discovered by the collaborating investigators of the Clinical Proteomic Technology Assessment Consortia. The Reagents Resource will not provide materials that are commercially available unless it is suspected that significant variation occurs between commercial lots (e.g., polyclonal antibodies).

One principle of this program is to make data as comparable as possible across laboratories and platforms. This principle will be aided by supplying standard reagents to all participating investigators. Therefore, reagents and data on reagent performance and quality will be acquired and dispersed quickly to other core facilities and satellites. The Reagents Resource will maintain a virtual database of reagents, their characteristics, and their performance data, along with reagent request forms. Priorities for access to limited or expensive reagents will be determined by an advisory committee. However, every effort will be made to enable access to program reagents by the larger scientific community.

"Let The Community Be Creative"

Gray, who led the board subcommittee that worked with NCI staff to revise the proteomics proposal, said the program "matured" over the past three months.

"I think the shift in focus toward understanding mechanisms of variability, be they genetic, clinical, biological, analytical, or whatever, is exactly right," Gray said. "The inclusion of mouse models is a major step forward. I think you have to be a little careful as this gets rolled out about not being too prescriptive about what you are asking for here. You do have to let the community be creative about the aspects of biology or the technology that they are going to explore…. Overall, I think this is an important project."

Board member Thomas Curran, chairman of the Department of Developmental Neurobiology at St. Jude Children's Research Hospital, agreed that the revised concept was "significantly improved," but questioned its potential.

"I do believe that this will fund improved technologies in the proteomics arena," Curran said. "My issue is with the biology. I think the focus, which is still on serum proteomics, is somewhat flawed. What we have learned so far from serum proteomics analysis is that you can measure breakdown products of major cell proteins, which are not necessarily measuring the biomarker that you think you are measuring…. I'm concerned that what you will get biologically at the end of the day is a finely-resolved, well-documented characterization of several more fragments of haptoglobin."

NCI's Downing said the program wouldn't focus exclusively on serum proteomics, but would include work in the mouse, in tissue, and linking genetic mutations to protein biology.

Board member Jane Weeks, associate professor of health policy and management, Dana-Farber Cancer Institute, said the concept is "considerably better and more focused," but she was "disappointed that in the focusing, the price tag didn't come down."

The consortia and the reagents resource "would be extraordinarily useful in increasing the ratio of useful to useless science going on in this field," Weeks said. "I'm quite enthusiastic about that. I'm less enthusiastic about the $56-million R01 pool. I'm a little concerned that to invest that amount of money in technology development in the absence of proof of concept that this is clinically useful, is extremely poor, in my opinion…. If we decide to go ahead with this, I would urge you to think about whether it might be useful to focus it a bit in areas that are most likely to be clinically useful.

"I think the most important application of proteomics is going to be in the setting of very low volume disease," Weeks said. "I'm much less enthusiastic about using proteomics to monitor response to therapy, because I don't think that's going to lead to better outcomes for cancer patients."

Downing said the investigator-initiated grants would be "focused on specific questions." The exploratory grants have "nominal" budgets for the first year, and only receive additional funding if they are deemed successful, he said.

Other board members also said they were concerned about the R01 component. "R01s are not

very compatible with technology development," said board member Leroy Hood, president of the Institute for Systems Biology.

Anna Barker, NCI deputy director for advanced technologies and strategic partnerships, said it will be up to R01 investigators to make the case for their ideas. The exploratory R21/R31 grants are designed to develop technology and include specific milestones that investigators have to meet to continue to receive funding, she said.

"We're confident we can actually do this," Barker said.

One Concept Withdrawn, One Approved

Robert Croyle, director of the NCI Division of Cancer Control and Population Sciences, presented and then withdrew a concept for a new RFA on the molecular epidemiology of pancreatic cancer.

The division proposed to fund four to seven U01 grants for a total of $16.5 million over three years to develop a better understanding of the etiology of pancreatic cancer. Members of NCI's Cohort Consortium would be invited to apply for the awards.

Board members said the RFA appeared unnecessary given the size of the study population. "You don't need four or five R01s to do what I think is a single R01," said Margaret Spitz, chairman of the Department of Epidemiology at M.D. Anderson Cancer Center.

NCI should encourage the consortium to apply for an R01 grant, Spitz and other board members said.

Paula Kim, a board member and advocate for patients with pancreatic cancer, said the RFA concept was the first involving pancreatic cancer to come before the board and would "carve out a niche for pancreatic cancer."

BSA Chairman Robert Young, president of Fox Chase Cancer Center, said that while board members expressed "a universal enthusiasm for more work in pancreatic cancer," they had "serious concerns" about the proposal. He appointed a subcommittee to work with NCI staff to improve the concept.

In another action, the board unanimously approved NCI's plans to reissue an RFA for the Small Animal Imaging Resource Projects.

The excerpted text of the concept statement follows:

Small Animal Imaging Resource Projects. Reissuance of an RFA for U24 grants, eight awards. Estimated first-year set-aside $3.6 million. Total estimated cost $18 million over five years.

NCI proposes an open recompetition of the second Small Animal Imaging Resource Program RFA. Imaging allows the study of a cohort of animals for the entire course of an experiment, which might include tumor initiation, growth, treatment, and re-growth. In vivo imaging facilitates the use of fewer animals, better control of the experiments, and acquisition of data from the tumor-host system. The characterization and use of genetically engineered mice, stimulated by The Mouse Models of Human Cancer Consortium, is entering a new era with emphasis on utilization of mouse models. Small animal imaging is essential to gain full knowledge about the model and its behavior under experimental conditions.

The second five funded SAIRP sites, as well as the two unsuccessful contenders for the last round of funding, will be strong applicants in a new competition, but we believe that making the RFA open to all applicants will improve the overall strength of applications. More institutions now have the capability to perform small animal imaging, and the MMHCC awardees would like to see some of their institutions compete for one of these research resources.

The RFA would require that programs provide: At least 2 imaging technologies for small animals; research and development on innovative imaging methods applicable to or required for oncology questions in small animals; facilities and personnel to assist in the development of necessary molecular probes for the cancer imaging technologies provided; facilities and personnel to aid in small animal anesthesia, management, and care, as well as to consult on the optimal use of animals in connection with the imaging experiments; and training of individuals from institutions throughout the country in the science and techniques of small animal imaging.

The structure of the SAIRP must ensure that the small animal imaging technologies available under this mechanism are state of the art or innovative. In addition, the SAIRP should support the broadest range of cancer research possible. SAIRPs offer a unique opportunity for multidisciplinary teams within the cancer research community to address critical cancer research questions. Scientific personnel in the SAIRP must include professional scientists from a variety of fields including radiology, oncology, physics, chemistry/radiochemistry, biochemistry, cell and molecular biology, computer science, pharmacology, veterinary anesthesiology, and pathology.

The SAIRP must use at least 1/2 of its resources and time to provide imaging services and to collaborate with cancer-related research projects. Some projects require intensive imaging of a small number of animals, while other projects require high-throughput screening of large numbers of animals. Some projects require much interaction with the imaging scientists to develop or adapt methods for the particular experimental question. As part of the initial application, there must be commitments from at least 8 cancer-related research projects that will use the small animal imaging resource within year 1.

Applicants must demonstrate that at the time of application they have available at least two state-of-the-art

imaging technologies optimized for small animals. They must show evidence of experience with in vivo imaging of small animals using the available technology.

The SAIRP will use approximately 1/3 to 1/2 of its resources and time for research and development of small animal imaging methodology related to cancer. This could be further development and optimization of existing technologies or exploration of novel technologies. Methods to produce valid quantitative results are particularly encouraged.

A plan for training of individuals including basic scientists, clinicians, technologists and others interested in learning the techniques and science of small animal imaging is required. Some of the trainees must come from institutions other than the awardee institution. The training should include both didactic education and hands-on instruction. This training may take the form of courses for multiple individuals at a time, or on-site individual training experiences for short periods of time.

Applicants must describe their plan for governance, and methods to be used to evaluate and select protocols to support with the SAIRP. A scientific advisory board of collaborators and other cancer investigators should be established for this purpose. Plans for partial or complete cost recovery for services and collaborative efforts must be discussed in the application, because cost-recovery for on-going service projects represents the standard for shared resources. It is expected that there might be a sliding scale of charges, starting from developmental grants to prove a concept, through Cancer Center researchers, then to other university investigators, and finally to commercial investigators.

Cancer Prevention:

Vitamin E Doesn't Prevent Heart Attack, Stroke Or Cancer

Vitamin E supplements do not protect healthy women against heart attacks, stroke, or the most common cancers, according to results from the Women's Health Study, a long-term clinical trial of the effect of vitamin E and aspirin on both the prevention of cardiovascular disease and of cancer.

The vitamin E results of the study were published in the July 6 issue of the Journal of the American Medical Association. The study was funded by the National Heart, Lung, and Blood Institute and NCI.

Vitamin E had no effect on total cancer or on the most common cancers in women—breast, lung, and colon cancers, the study found.

The study was conducted between 1992 and 2004. The participants were 39,876 healthy women age 45 years and older who were randomly assigned to receive 600 IU of vitamin E or placebo and low-dose aspirin or placebo on alternate days. The participants were followed for an average of 10.1 years. The aspirin results published last March found no benefit of aspirin (100 mg every other day) in preventing first heart attacks or death from cardiovascular causes in women, but did find a reduced risk of stroke overall, as well as reduced risk of both stroke and heart attack in women aged 65 and older.

Participants in the Women's Health Study were monitored for major cardiovascular "events"—a combination of nonfatal heart attack, nonfatal stroke, or cardiovascular death. By the end of the study, participants in the vitamin E group had 482 such events compared to 517 in the placebo group. However, this difference was not statistically different.

Study investigators also found no significant effect of vitamin E on deaths from all causes. By the end of the study, there were 636 deaths in the vitamin E group compared to 615 in the placebo group.

FDA News:

Tea "Unlikely" To Prevent Cancer, FDA Review Finds

By Eric Lai

It's "highly unlikely" that drinking green tea reduces the risk of breast cancer in women or prostate cancer in men, FDA said, but the agency will allow manufacturers to make a "qualified health claim" using the following wording:

—"Two studies do not show that drinking green tea reduces the risk of breast cancer in women, but one weaker, more limited study suggests that drinking green tea may reduce this risk. Based on these studies, FDA concludes that it is highly unlikely that green tea reduces the risk of breast cancer."

—"One weak and limited study does not show that drinking green tea reduces the risk of prostate cancer, but another weak and limited study suggests that drinking green tea may reduce this risk. Based on these studies, FDA concludes that it is highly unlikely that green tea reduces the risk of prostate cancer."

As a result of a scientific review, FDA concluded that there is no credible evidence to support qualified health claims for green tea consumption and a reduced risk of gastric, lung, colon/rectal, esophageal, pancreatic, ovarian, and combined cancers.

The agency conducted the review in response to a health claim petition filed by Sin Hang Lee, president of Fleminger Inc., who sells green tea under the brand name Dr. Lee's TeaForHealth.

FDA's letter responding to the petition is available at: http://www.cfsan.fda.gov/~dms/qhc-gtea.html.

President's Cancer Panel:

Barriers To Translational Work Stall Progress, Panel Says

By Eric Lai

Barriers in the research translation continuum have stalled the progress of cancer research and treatment, the President's Cancer Panel said in its annual report to the White House, issued last week.

Lack of clinical research resources, an inadequate translational research infrastructure, a paucity of collaborative scientific projects, and regulatory issues that stall clinical trials and FDA drug approval are just a few of the barriers the panel identified.

"Unless the nation confronts these barriers to delivering research advances to the American people, the national investment in cancer research will be tragically squandered, for discoveries that do not lead to improved patient outcomes are tantamount to no discovery at all," the report said.

The panel made the following recommendations:

Team Science and the Culture of Research

—A task force of stakeholders in academic research should be established to examine and change existing rewards systems to promote collaborative research.

—Governmental and private research sponsors must substantially increase funding for clinical and human tissue research.

—NIH and other research sponsors should collaborate in large research projects focusing on more team approaches, and should designate a percentage of project funding for such efforts.

—NIH and other research sponsors should devise implementation plans for allowing co-principal investigators to share grant funding and credit for this work.

Infrastructure Required

To attract and retain young investigators to translational and clinical research careers:

—Longer and earlier protected research time and mentoring must be provided in academic institutions.

—New or expanded student loan buy-back programs should be started to encourage young investigators to pursue additional research training.

—Academic institutions should make efforts to recruit young scientists from underrepresented population groups.

—NCI's Rapid Access to Intervention Development program should be expanded and revitalized.

—NCI's Specialized Programs of Research Excellence should be expanded with some SPOREs focusing more on clinical than basic research.

—The Center for Medicare and Medicaid Services should investigate the possibility of collecting cancer stage data at least at the time of diagnosis.

—The proposed Human Cancer Genome Project should be supported with funding coming from a special supplement rather than from participating agencies' budgets.

Regulatory Issues Affecting Translation

—Current partnerships between NCI and FDA to expedite cancer drug reviews and between NCI and CMS to produce clinical data on new interventions to support Medicare coverage decisions should both be continued and strengthened.

—To stimulate private sector investment in cancer therapies, all new chemoprevention/chemotherapy drugs and biologics should be designated "orphan drugs" under the Orphan Drug Act of 1983.

—A task force of stakeholders affected by barriers relating to intellectual property and patent issues should convene and agree on a standard language for patent exemptions for research purposes, standard clauses for contracts governing collaborative research, and other agreements to resolve intellectual property and data-sharing issues.

—The Institute of Medicine should evaluate the impact of the Health Insurance Portability and Accountability Act provisions, guide legislators on amendments needed to remove obstacles in cancer research and make the law better suited to serve the interests of cancer patients and survivors.

Dissemination, Education, and Communication

—A lead agency for cancer-related dissemination research and activities should be designated and provided with the budget and authority to carry out the dissemination.

—NCI should increase funding for implementation activities to improve dissemination and adoption of cancer research advances. Comprehensive Cancer Centers should also take an active role in disseminating new cancer-related interventions into their communities.

—The translation process should be expedited through bi-directional education between regulators and cancer researchers.

Public Trust, Community Participation

—Clinical and prevention research funders should require community participation early in protocol design and in research implementation.

—Research results must be shared with individuals who participate in clinical trials.

—Clinical and prevention research grantees should be required to include a plan for disseminating new interventions into the community as part of their grant application.

—Existing community-based participatory research models should be evaluated to determine the potential for adopting them in other geographic areas.

Also, the panel recommended that Congress reauthorize the National Cancer Act, preserving the statutory authorities the Act provides NCI. In five years, an evaluation should be conducted of activities designed to accelerate translational research, the panel said.

The panel's report is available at http://pcp.cancer.gov.

Funding Opportunities:

RFA Available

RFA-NR-06-001: Research on Research Integrity. Letters of Intent Receipt Date(s): Aug. 16. Application Receipt Date: Sept. 16.

Participating centers and institutes, including NCI, invite applications relevant to biomedical, behavioral health sciences, and health services research. Research objectives include empirical information on the standards that guide responsible practice, how are they set, and the extent to which researchers routinely adhere to these standards; the effectiveness of professional self-regulation in research; and the factors that influence students, researchers and research institutions to adhere to or deviate from integrity in research and how these factors can be reinforced or modified to promote responsible practices; and the economic and intellectual impacts of behaviors that fail to adhere to rules, regulations, guidelines, and commonly accepted professional codes or norms. The participating programs are especially interested in quantifiable information relevant to PHS research communities and/or research interests. Projects relevant to NIH Roadmap Initiatives are also encouraged. The RFA is available at http://grants1.nih.gov/grants/guide/rfa-files/RFA-NR-06-001.html.

Inquiries: For NCI, Ann O'Mara, program director, Research Areas: Symptom Management/End of Life, Community Clinical Oncology Program, phone 301-496-8541; fax 301-496-8667; e-mail Omaraa@mail.nih.gov.

Program Announcement

PAR-05-133: Short-Term Courses In Human Embryonic Stem Cell Culture Techniques. Letters of Intent Receipt Date: Aug. 8. Application Receipt Dates: Sept. 8.

NIH invites applications for the development, implementation and evaluation of short-term continuing education programs on skills and techniques in human embryonic stem cell research, and the dissemination of course materials to the larger scientific community. Educational programs should improve the skills of biomedical researchers in the maintenance of human embryonic stem cells in culture and their application of this research tool in basic research studies. Applicants are encouraged to propose innovative programs with new approaches for teaching and learning human embryonic stem cell culture techniques. Both didactic and hands-on training experiences are appropriate. To help NIH assess the long-term impact of the training courses, NIH will work with course directors to develop assessments, based on information provided by the attendees, on their current and subsequent activities or responsibilities in the area of embryonic stem cell biology. The NIH Continuing Education Training Grant T15 mechanism will be used. The PA is available at http://grants1.nih.gov/grants/guide/pa-files/PAR-05-133.html.

Inquiries: For NCI, John Sogn, phone 301-594-8782; e-mail JS150x@nih.gov.

In Brief:

Hillman Foundation Gives UPCI $20 Million For Fellows

(Continued from page 1)

at Wayne State University, will head expansion efforts of the institute to satellites and affiliates. Forman will coordinate outreach in Southeast Michigan and create cancer diagnosis and treatment centers to provide clinical trials and cancer care at local hospitals. . . . **UNIVERSITY OF PITTSBURGH** Cancer Institute and UPMC Cancer Centers received $20 million from the Henry L. Hillman Foundation and the Hillman Foundation for The Hillman Fellows Program for Innovative Cancer Research. The program gives seed money to stimulate collaboration between junior and senior investigators. The gift is part of a five-year plan to expand the Hillman Cancer Center research laboratories and facilities, recruit clinicians and scientists, broaden clinical research studies, community outreach, and education, and increase the research endowments, said **Ronald Herberman,** director of UPCI and UPMC Cancer Centers. . . . **VANDERBILT-INGRAM** Cancer Center received a $10 million gift from Jim Ayers, a West Tennessee businessman, to establish the Jim Ayers Institute for Pre-Cancer Detection and Diagnosis. The center will use proteomics to identify patterns of protein expression to predict pre-cancers and early cancers.... **UNIVERSITY OF IOWA** has dedicated its Center of Excellence in Image-Guided Radiation Therapy, a $39.6 million facility for cancer and benign lesions. The center specializes in the delivery of image- and optic-guided stereotactic radiation. . . . **STEVEN CLAUSER** was named chief of Outcomes Research Branch in the Applied Research Program of the NCI Division of Cancer Control and Population Sciences. Clauser joined NCI in 2002 to develop research related to cancer care outcomes measurement and quality of care. Before joining NCI, Clauser held several senior policy research positions at the Centers for Medicare and Medicaid Services. . . . **GRAND CHALLENGES** in Global Health initiative, established by the Bill & Melinda Gates Foundation, selected 43 research projects totaling more than $436 million to create disease-fighting health tools for developing countries. Accordingly, most of the awards involve infectious disease. **Robert Garcea**, professor of pediatric hematology, oncology, and bone marrow transplantation at UCDHSC received a $3.5 million grant to study immunological methods to cure latent and chronic infection in diseases such as tuberculosis and hepatitis C.

A Notch-Signaling Pathway Inhibitor in Patients with T-cell Acute Lymphoblastic Leukemia/Lymphoma (T-ALL)

An investigational study for children, adolescents and adults with relapsed and refractory T-cell acute lymphoblastic leukemia/lymphoma is now accruing patients at various centers around the country.

This study's goal is to evaluate the safety and tolerability of a Notch inhibitor as a rational molecular therapeutic target in T-ALL, potentially uncovering a novel treatment for these cancer patients.

Eligibility criteria and treatment schema for the study include:

Notch-Signaling Pathway Inhibitor in Patients with T-ALL	
Eligibility Criteria	Patient must be = 12 months with a diagnosis of T-cell acute lymphoblastic leukemia/lymphoma AND must also have: • Relapsed T-ALL • T-ALL refractory to standard therapy • Not be a candidate for myelosuppressive chemotherapy due to age or comorbid disease ECOG performance status =2 for patients >16 years of age OR Lanksy performance level >50 for patients 12 months to =16 years of age Fully recovered from any chemotherapy and >2 weeks from radiotherapy, immunotherapy, or systemic steroid therapy with the exception of hydroxyurea or intrathecal therapy Patient must be >2 months following bone marrow or peripheral blood stem cell transplantation No treatment with any investigational therapy during the preceding 30 days No active or uncontrolled infection
Treatment Plan	Open label and non-randomized, this study is conducted in two parts. Part I is an accelerated dose escalation to determine the maximum tolerated dose (MTD), and Part II is a cohort expansion at or below the MTD. MK-0752 will be administered orally. Plasma concentrations will be measured at defined time intervals.

For information regarding centers currently open for enrollment, please contact 1-888-577-8839.

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