THE CANCER LETTER

Vol. 24 No. 46
Dec. 4, 1998

Price $275 Per Year US
$295 Per Year Elsewhere

PO Box 9905 Washington DC 20016 Telephone 202-362-1809

NCI Plans $61 Million For Six-Year Program In Biomarker Research For Early Detection

NCI advisors approved the Institute's plan to spend $61 million over the next six years to form a multi-center research network for the discovery and evaluation of molecular, genetic, and other biomarkers for the early detection of epithelial cancers.

The Early Detection Research Network would consist of 10 to 12 biomarker developmental laboratories, two to three biomarkers validation laboratories, three to four clinical/epidemiology centers, and a data management and coordinating center. NCI would make the initial awards totaling $3 million in fiscal 1999.

(Continued to page 2)

In Brief:

Trials Find DiBella Treatment Ineffective; Wistar Wins $1 Million Grant For Recruitment

ITALIAN "CURE" DEBUNKED: Italy's National Health Institute has said an Italian doctor's mixture of Somatostatin, Cytoxan, melatonin, hormones, and vitamins is ineffective as a cancer treatment. Earlier this year, cancer patients held demonstrations to pressure the government to pay for the treatment offered by **Luigi Di Bella**, of Modena. The Institute said Di Bella did not have the appropriate data and decided to conduct clinical trials, results of which were released last month. Of the 386 patients treated, 57 percent died, 33 percent experienced disease progression, 3 percent had stable disease, and 6 percent were lost to followup. One percent had tumor shrinkage of at least 50 percent. These were in tumors that might be expected to respond to Cytoxan, including breast cancer, lymphoma, and chronic lymphocytic leukemia. Advising the Italian health minister in the controversy was Rhode Island oncologist **Paul Calabresi**, a member of the President's Cancer Panel, professor of medicine at Brown University, and director of the Brown-Tufts Cancer Center. Calabresi led an eight-member international panel that investigated Di Bella's claims and recommended the clinical trials. . . .

THE WISTAR INSTITUTE, of Philadelphia, has received a three-year grant of $1 million from The Pew Charitable Trusts to recruit and equip the laboratories of new investigators in the areas of regeneration, signal transduction, and brain tumor research. The institute did not specify how many new investigators are to be recruited. "We are having tremendous successes in these areas and we want to ensure our continued progress," Wistar Director **Giovanni Rovera** said. Three previous grants from the

(Continued to page 8)

Research Network Was Key Recommendation Of Advisors

(Continued from page 1)

The NCI Board of Scientific Advisors unanimously approved the concept statement for the network at a Nov. 13 meeting. The plan for the network was the main recommendation of a report by the Early Detection Implementation Group, an advisory panel that developed a blueprint for the Institute's early detection research programs, as well as recommendations from other review groups, said Bernard Levin, of M.D. Anderson Cancer Center, who served as chairman of the implementation group.

The excerpted text of the concept statement follows:

Early Detection Research Network. Concept for a new RFA, cooperative agreements, 10 to 12 awards, length of award six years, first-year set-aside $3 million, cost for project period $61 million. Program Director: Sudhir Srivastava, Division of Cancer Prevention, Early Detection Branch, phone 301-496-3983.

The initiative will support the creation of a multi-center network with resources for translational research that will include the laboratory sciences, clinical sciences, public health, biostatistics, informatics, and computer sciences. The initial goals of the network will be to discover and to coordinate the evaluation of biomarkers/reagents for the earlier detection of epithelial cancers, such as prostate, breast, lung, colorectal and upper aerodigestive tract, and for the assessment of risk. Specifically, the objectives of the network will include:

—Development and testing of promising biomarkers or technologies in institutions having the scientific and clinical expertise, in order to obtain preliminary information that will guide further testing;

—Timely and early phase evaluation of promising, analytically proven biomarkers or technologies. Evaluation will include measures of diagnostic predictive value, sensitivity, specificity, and whenever possible, medical benefits, risk, and harms, such as predictors of clinical outcome or as surrogate endpoints for early detection and for prevention intervention clinical trials;

—Timely development of biomarkers and expression patterns, sometimes of multiple markers simultaneously, which will serve as background information for subsequent large definitive validation studies in the field of cancer detection and screening;

—Collaboration among academic and industrial leaders in molecular biology, molecular genetics, clinical oncology, computer science, public health, etc., for the development of high throughput, sensitive assay methods for biomarkers from an early detection viewpoint;

—Conducting early phases of clinical/epidemiological studies, e.g. cross-sectional, retrospective, to evaluate predictive value of biomarkers; and

—Encouraging collaboration and rapid dissemination of information among awardees to ensure progress and avoid fragmentation of effort.

Organizational Structure: The Network will consist of four components: 1) Consortium for Biomarkers in Early Detection Research (CBEDR), 2) a Steering Committee (SC), 3) an Advisory Committee (AC), and (a) a Data Management and Coordinating Center (DMCC).

Consortium for Biomarkers in Early Detection Research: The CBEDR will consist of three main scientific components: i) Biomarker Developmental Laboratories (BDL), ii) Biomarker Validation Laboratories (BVL), and iii) Clinical and Epidemiologic Centers (CEC). Each laboratory/center, which will be managed by a Principal Investigator, will include academic and industrial biotechnology investigators who are involved in cancer detection and diagnostic research. In order to expedite the translational research, the Consortium will be supplemented by the ad hoc participation of additional institutions (academic or community-based) that are able to validate the results of laboratory studies through patient accrual. The work of the Consortium will be coordinated by the Steering Committee.

It is anticipated that the CBEDR will consist of experts in basic molecular science, laboratory technology, clinical studies, biometry, and epidemiology. The expertise in laboratory science should include conducting research in the basic biology of preneoplasia encompassing the development and testing of biomarkers of early cancer, development of relevant technologies for biomarker detection, and analytical tools for the evaluation

THE CANCER LETTER

Member, Newsletter Publishers Association

World Wide Web: http://www.cancerletter.com

Editor & Publisher: Kirsten Boyd Goldberg
Editor: Paul Goldberg

Editorial: 202-362-1809 Fax: 202-362-1681
PO Box 9905, Washington DC 20016
E-mail: kirsten@cancerletter.com or paul@cancerletter.com

Customer Service: 800-513-7042
PO Box 40724, Nashville TN 37204-0724

Subscription $275 per year US, $295 elsewhere. ISSN 0096-3917. Published 48 times a year by The Cancer Letter Inc.

Founded Dec. 21, 1973 by Jerry D. Boyd

of biomarkers for risk assessment. Computational and informatic needs of the Consortium will be supported by the Data Management and Coordinating Center. Experts in informatics will include database developers, combinatorial data analysts, and computer application program developers/specialists.

Research Member in the Consortium: Participation in the Consortium will require expertise in one or more of its scientific components. An applicant may seek funding to participate in more than one component. They will conduct research of the consortium using their core funds supplemented in some cases, as noted below.

Steering Committee: The SC will be composed of the Principal Investigators and Co-Principal Investigators from each member of the Consortium, the director of the Data Management and Coordinating Center, NCI program staff, and the chairman of the Advisory Committee.

The Steering Committee will have major scientific management oversight, including monitoring the activities of the DMCC. Specifically, it will develop uniform criteria for the collection of clinical data, collection of tissue and blood specimens, and for instituting laboratory quality assurance.

Advisory Committee: The AC will include members who are not participating in the Consortium. Each Principal Investigator in the consortium will be asked to nominate members for the AC. The membership to the Committee and duration will be decided by NCI in consultation with the Steering Committee. The AC will include basic scientists, clinicians, prevention scientists, epidemiologists, ethicists, statisticians, and members from relevant advocacy groups. Scientific experts will be drawn from various disciplines relevant to multi-center detection research and experts in data management, biostatistics, and clinical study design.

The AC will independently advise the Steering Committee on relevant scientific issues, including study design, prioritization of biomarker development, development of study protocols. The AC will also advise the Steering Committee when to move discoveries from the laboratory into clinical testing. Prospective evaluation criteria for the success of the Network will be developed.

Data Management and Coordinating Center: The DMCC will provide support for the conduct of the Steering and Advisory Committee meetings, provide statistical and data management support for protocol development, conduct analysis, and informatics.

Funds: Operating funds will reside with 1) the Consortium For Biomarkers in Early Detection Research, 2) the Data Management and Coordinating Center, and 3) the Steering Committee.

Consortium for Biomarkers in Early Detection Research: The Principal Investigators will have funds available to support the development of the scientific program and clinical protocols. Collaborations will also be extended to investigators who are engaged in translational research on biomarkers, but are not funded through the consortium. It is expected that the Steering Committee will establish guidelines for including such investigators. Core funds will be made available for such investigators in order to include valuable clinical collaborators who may come from outside the core group as well as from industry.

Data Management and Coordinating Center: The DMCC will be funded through a separate RFA. While NCI plans to proceed with the funding request, its publication and timing will depend on the establishment of the Consortium and the Steering Committee first.

Discretionary funds will be available to the Steering Committee. Core funds can be used for a variety of functions: 1) Core funds would be used to expand the membership of the consortium through supplemental funding to an investigator's current funded grants; 2) Funds will often be needed in moving a new marker test to the point at which it can be validated at multiple centers and in larger populations. Test reagents will require scale-up at this point, and the Steering Committee will require sufficient funding to contract to laboratories or companies that can scale up production and maintain quality of the reagents (e.g. monoclonal antibodies, labels, etc.) Funds will also be required for data management, travel, group meetings, and other core activities.

Interaction with the clinical trial/treatment community: Plans will include collaboration with other NIH Institutes and government agencies or departments (e.g., FDA, DOD, VA), with other NCI programs (e.g., SPOREs, Cancer Genetics Network, Breast and Colon Cancer Family Registries, Cooperative Human Tissue Network), with NCI clinical research programs (e.g., CCOP, PLCO), and with active research groups with ongoing trial core functions and laboratory support such as the Cooperative Groups, NCI designated cancer centers, international collaborators, clinical epidemiologists, and health maintenance organizations interested in early detection research.

Interaction with industry: The Network will encourage collaboration with industry on a substantial cost-sharing basis. NCI funds will be used to support the underlying infrastructure and the cost of studies not having direct implications for a company's product development or marketing strategy. However, for new technologies that are part of a company's development or product plans, the individual companies will be responsible for costs in such areas as technology standardization and quality assurance as well as scale-up of laboratory techniques, in collection and formatting of specialized data required by regulatory agencies for device approvals, in the preparation of registration documents, and in supporting a portion of the accrual to studies pivotal for registration. It is anticipated that industry participating in the Network will not charge investigators or NCI for technologies/ reagents that will be evaluated in collaborative studies.

Governance: The Principal Investigator will be responsible for administering and supervising research personnel, and for conducting research. The Principal Investigator will also be responsible for the expenditure of the annual budgets. The Steering Committee will be responsible for coordinating the research effort across the Consortium, including the Data Management and Coordinating Center, and may formulate directives that will govern the operations of the Consortium.

A simplified example is provided that illustrates the functions of the Consortium and the support it offers for moving basic research findings into clinical practice: An investigator within the Consortium identifies a putative biomarker through original laboratory research. Based on the pilot research findings, the putative marker seems to be useful for early cancer detection. The investigator can then approach the Steering Committee for additional evaluation of the marker and possible support for further testing. The Steering Committee then has the responsibility to review the data on the potential marker using its standing formal criteria as a guide. The Steering Committee can consult the Advisory Committee to obtain information on the requirements and need for additional research on the marker. It also can consult the Biomarker Validation Laboratories and the Clinical Centers regarding requirements for laboratory tests, needs for quality assurance, and the availability patient groups for clinical validation. If necessary, resources from other Centers can be pooled to conduct studies. Concurrently, the informatic team in Data Management can develop tools for the analysis of results. There will also be flexibility so that investigators outside the Consortium could form a collaboration with one of the existing centers, or directly bring their discoveries to the Steering Committee (e.g., by Letter of Intent). To support such efforts, the Steering Committee will be able to use core funds to supplement the investigator's research. The investigator, in turn, will agree to share his research findings and become part of the Consortium.

Budget: The Network will be funded through a cooperative agreement, $3 million for the first year, $10 million in the second year, and $12 million each year thereafter for a total of six years. The total cost is split into the following components: $4.6 million to Biomarker Developmental Laboratories (10-12 awards); $2 million for Biomarkers Validation Laboratories (2-3 awards); $3 million to Clinical/Epidemiology Centers (3-4 awards) which includes $2 million for patient accrual (2,000 patients @ $1,000/case) which will not start until year 2 and reimbursement will be on per case basis; $400,000 for Data Management and Coordinating Center (one award), and $2 million as core funds to the Steering Committee to support collaborations with investigators within and outside the Network on a competitive basis.

Board discussion: BSA members expressed enthusiasm for the network. BSA member Mary Daly, associate director, Cancer Control Science Program at Fox Chase Cancer Center, suggested that consumer advocates be included on the network's steering committee. "We're going to have to keep going back to high-risk groups," she said.

Board member Robert Young, president of Fox Chase Cancer Center, said the network should build in strong linkages to the NCI-supported Clinical Trials Cooperative Groups. "If you want to find populations of patients with stage I ovarian cancer, you're not going to find enough of them in three or four big institutions to do that kind of study," Young said. "Where you'll find them is in the Gynecologic Oncology Group, where you can do the study in three months as opposed to three years."

Barnett Kramer, deputy director of the NCI Division of Cancer Prevention, said the Request For Applications for the network would contain "a lot more of that language" on working with cooperative groups.

"The whole reason for this is to avoid the mistakes of the past, where things skipped the entire validation process and sometimes jumped to the entire population of the United States," Kramer said. Also, he noted that the network would be limited to clinical validation. "This is not the network in which to test for mortality benefits from early detection," he said.

Board member Sharon Murphy, chairman of the Pediatric Oncology Group, suggested that the board, which has approved several large extramural grants programs recently, should develop a method of tracking these programs.

NCI Director Richard Klausner said communication between the programs, NCI, and the BSA is critical. "We have developed new and sometimes very complicated ideas," he said. "Now it's going to take some effort for us to report on how they are doing, whether or not they are working as intended."

Young noted that large programs are difficult to shut down, even if they are not performing well.

"We do in fact give up on things, but you don't hear about it because we give up on them in the Executive Committee, and therefore, they are not presented to you," said Robert Wittes, NCI deputy director for extramural science.

BSA Chairman David Livingston, the Emil Frei Professor of Medicine and Genetics, Harvard Medical School, said the board would schedule a meeting to discuss the review of new programs.

Tumor Classification Scheme Based On Molecular Analysis Is Goal Of NCI "Challenge"

In a program that will attempt to apply the techniques of modern molecular biology to directly benefit cancer patients, NCI Director Richard Klausner has challenged scientists to devise new tumor classification schemes based on the molecular analysis of cancer cells.

Knowing the "molecular fingerprint" of a patient's tumor could be more useful potentially to clinicians in the diagnosis and management of the disease than the current classification of cancers by their visual appearance, Klausner said.

"I want to challenge the scientific community to propose the transformation from diagnosing cancer the way we have done for a hundred years to diagnosing cancer the way we are going to for the next hundred years, and that is by its molecular fingerprint," Klausner said at a recent meeting of the Director's Consumer Liaison Group.

Five to 10 percent of all cancers diagnosed are "tumors of unknown origin," which present difficulties in treatment. "That should be a thing of the distant past," Klausner said.

Agreeing with the director, the NCI Board of Scientific Advisors unanimously approved the formation of a new grants program that would provide $50 million over the next five years to support teams of investigators who would form National Cooperative Tumor Signatures Groups.

The excerpted text of the program's concept statement approved by the BSA follows:

Director's Challenge: Toward A Molecular Classification of Tumors. Concept for a new RFA, 8-10 awards, five years, first-year set-aside $10 million, estimated cost for project period $50 million. Program Director: James Jacobson, chief, Technology Development Branch, Cancer Diagnosis Program, Division of Cancer Treatment and Diagnosis, phone 301-496-8639.

Since its beginnings as a scientific discipline, diagnostic pathology has been rooted in morphology: the visual appearance of tumor tissue has served to classify cancers. Progressively finer levels of resolution and greater specificity in the staining of tissues has permitted substantial refinements in diagnostic criteria for many cancers, but morphology remains the cornerstone. The limitations of our current classification schemes are serious: they often do not discriminate between tumors of similar histopathologic appearance that will follow significantly different clinical courses. The Director of the National Cancer Institute now challenges the scientific community to harness the power of contemporary molecular analysis to place the classification of tumors on a vastly more informative footing. This "Director's Challenge" is intended to lay the groundwork, over a five-year period, for changing the language of tumor classification from morphological to molecular.

This challenge is based on the assumption that a comprehensive knowledge of the molecules (or a relevant subset of molecules) expressed in a tumor is potentially much more informative clinically than the morphological characteristics of the tumor. The knowledge that a specific molecular profile correlates with important clinical parameters should allow physicians to base management decisions on the molecular changes present in the patient's tumor. Molecular profiles should also improve identification of tumors of unknown origin at the time of their detection. Determination of comprehensive patterns of molecular alterations of tumors should allow researchers to address these problems.

Background: The application of high-throughput technologies to human tumors should make it possible to generate molecular profiles of tumors. To date, the technologies have primarily been applied to the analysis of model systems, cell lines or lower eukaryotes. A few of the most mature technologies are being applied to the analysis of clinical tissue specimens. For example, serial analysis of gene expression (SAGE) has been applied to the analysis of gene expression patterns in colon tumors, lung tumors and tumors from several other sites. Studies are just being initiated to correlate gene expression patterns determined by SAGE with clinical parameters. Oligonucleotide and cDNA arrays are being used to analyze gene expression in colon, breast, and certain other tumors. Although these and some other early studies are demonstrating the potential power of these technologies, the extensive research needed to apply molecular-based strategies to actual tumor specimens is just beginning.

This is an opportune time to apply these technologies to analysis of tumor specimens. The technologies are developing to the point where translation to analysis of tumor specimens is feasible. The Cancer Genome Anatomy Project and other research efforts are providing the resources and reagents needed for these efforts to be successful. This initiative is designed to bring together the expertise necessary to coordinate the development and application of these powerful new technologies.

The purpose of this [proposed] RFA is to identify potentially useful patterns of molecular alterations of tumors. Multidisciplinary groups will be funded to focus on the translation of comprehensive molecular technologies to the analysis of tumor specimens. These National Cooperative Tumor Signatures Groups (NCTSGs) will be expected to accomplish one of two goals within the five-year funding period. They will be expected to either develop new molecular classification

schemes for tumors from one or more sites or to develop schemes for the accurate identification of the primary sites of tumors of unknown origin. These schemes will be based on patterns of molecular alterations rather than on the classical histopathological criteria currently in use. The new classification schemes should be annotated with all available, relevant clinical information.

—The NCTSGs will be focused on developing molecular profiles for specific sets of tumors. Each NCTSG applicant should propose use of one technology or a class of technologies such as DNA array technologies, mutation detection technologies or proteomics technologies for developing molecular profiles from tumor specimens. The selected technology should be able to generate a comprehensive analysis of each tumor specimen and should be amenable to high-throughput analysis so that large numbers of specimens can be characterized.

Development of new molecular classification schemes will depend on a systematic approach to the analysis of tumor specimens. Applicants should propose a rational basis for selecting the spectrum of tumor specimens to ensure that enough specimens of a given tumor type will be analyzed to generate informative molecular signatures. For example, an applicant could propose to initially analyze only specimens of node-negative breast cancer or specimens of multiple foci of organ-confined prostate cancer. Applicants may expand the analysis to related tumor specimens during the course of the project.

Applicants should describe the demographic and clinical data associated with the tumor specimens that will be available to annotate the molecular profiles. Applicants should specifically describe plans to maintain patient confidentiality.

Development of schemes for identifying tumors of unknown origin will require the determination of profiles that uniquely identify tumors from a number of individual organ sites. The identification of these characteristic profiles for tumors from multiple organ sites should allow the accurate identification of tumors of unknown origin at the time of detection.

The applicants should propose a strategy for making these valuable molecular data sets available to the cancer research community.

—The NCTSGs will need special tissue resources to meet their project goals. Applicants will be asked to present a strategy for obtaining high quality tissues and describe how they will assess the effects of specimen handling on data quality.

The NCTSGs should have access to enough appropriate tissue specimens to initiate their programs for the development of new tumor classification schemes. NCI program staff will assist grantees to obtain access to additional tissue resources by facilitating interactions and collaborations between the NCTSGs and other NCI supported research efforts. Appropriate collaborations can be established between the NCTSGs and the clinical trials groups, CCOPs, SPOREs, NCI supported collaborative research networks, NCI Cancer Centers and other NCI supported specimen resources.

—The NCTSGs will develop and utilize innovative bioinformatics and statistical approaches to data analysis. The application of comprehensive analytical technologies will generate large quantities of data. The NCTSGs will need to develop and apply innovative bioinformatics and statistical tools to analyze the data. Each applicant should describe the analytical approach that will be developed and/or used to identify patterns of molecular alterations. The statistical strategies that will be used to develop and compare molecular profiles must be discussed.

—The NCTSGs will bring together the expertise needed to successfully develop new molecular-based tumor classification schemes. The team of investigators for an individual NCTSG will assemble prior to submitting their application. Each group should include the expertise necessary to support continued development and/or adaptation of the technologies selected and the expertise to ensure the selection of appropriate specimens for analysis. The necessary expertise is expected to include a mix of technology developers, engineers, basic cancer researchers, oncologists, pathologists, statistician and experts in bioinformatics.

Collaborations between investigators from academic and commercial organizations may be necessary in order to include all of the expertise required for the project. Applications may be submitted by either academic or commercial organizations.

Collaborations between investigators from academic and commercial institutions often are difficult to establish because of concerns over issues of intellectual property. Applicants will be asked to provide a detailed plan for minimizing possible intellectual property problems. Assessment of the adequacy of the plan will be included in the review criteria.

The NCTSGs should be able to respond to new scientific opportunities as they arise. Applicants will be invited to request developmental funds in their budget so they are able to respond to these opportunities. Applicants may budget up to $100,000 for this purpose. These funds may also be used to offset unexpected administrative costs associated with obtaining the clinical specimens.

Program staff propose the use of the U19 and U01 funding mechanisms to support the NCTSGs. Applicants proposing a large, complex structure containing groups of related but independent projects, similar to a P01 format, should use the U19 mechanism. Applicants proposing projects without defined independent components can be supported by the U01 mechanism. Program staff initially request support for up to 10 NCTSGs with an average annual budget of $1 million per group per year.

Cooperative Groups:

Insurer Agrees To Cover Patient Care Costs In Trials

United HealthCare Corp., of Minneapolis, and the Coalition of National Cancer Cooperative Groups Inc. have agreed to begin a pilot project in which the insurer would pay the patient care costs of members enrolled in adult and pediatric cancer clinical trials.

United HealthCare said it will encourage eligible members to enroll in any multi-institutional clinical trial sponsored by any of the six cooperative groups belonging to the coalition.

"This program offers choices of treatments to members suffering from cancer," said Lee Newcomer, director of health policy and strategy for United HealthCare. "Their participation in the trials, in turn, will help researchers find the best ways to prevent, detect, or treat cancer."

"So often, patients and their physicians do not consider entering a clinical trial because most managed care organizations and health care insurers typically do not pay for the costs," said Robert Comis, president of the Philadelphia-based coalition. "United HealthCare is helping to change that and shows its commitment to its members through this pilot program."

• • •

PILOT PROJECTS testing the proposed reform of the clinical trials system are scheduled to be operational by next summer, an NCI official said.

Jeffrey Abrams, of the Cancer Therapy Evaluation Program, said NCI formed two internal committees to carry out the plan developed by the Clinical Trials Implementation Committee to broaden patient and physician access to clinical trials and increase accrual (**The Cancer Letter**, Oct. 9).

At a recent meeting of the chairmen of the NCI-supported Clinical Trials Cooperative Groups, Abrams provided an update on the status of the three pilot projects:

—Disease-specific clinical trials concept review committees: Membership of the committees will be selected this winter and will begin operation by next April or May.

—State-of-the-science meetings to identify new research opportunities: CTEP plans to hold four to six of these meetings in fiscal 1999.

—Clinical Trials Support Units to consolidate administrative tasks, to be conducted by contract to NCI: CTEP will develop a Request for Proposals.

Funding Opportunities:

NCI Request For Applications

RFA CA-98-026: The NCI Scholars Program. Letter of Intent Receipt Date: Feb. 16, 1999. Application Receipt Date: March 22, 1999.

The purpose of the NCI Scholars Program is to provide an opportunity for outstanding new investigators to begin their independent research careers within the National Cancer Institute and to continue their careers at an institution of their choice. This program is designed to encourage exceptionally well qualified new investigators to establish themselves in the cancer research field by providing them with independent research funding.

Individuals with a research or health professional doctoral level degree or equivalent, who are recognized by their peers and mentors as exceptional but with no more than five years of postdoctoral research training at the time of application, are eligible to apply.

Inquiries regarding eligibility and other programmatic issues: Lester S. Gorelic, Ph.D., Office of the Deputy Director for Extramural Sciences, NCI, Executive Plaza North, Room 520, Bethesda, MD 20892-7390, phone: 301-496-8580, fax: 301-402-4472, email: lg2h@nih.gov

Program Announcements

PA-99-016: Mechanisms Underlying Individual Variations In Drug Responses

The purpose of this program announcement is to stimulate research into identifying the critical candidate proteins and/or genes that play essential roles in determining individual variations in drug responses. The aim is to identify the fundamental mechanisms that appear to play a role in determining individual variations in drug responses, through biochemical, pharmacological, genetic, and/or genomic studies, and to accelerate the pace of discovery in pharmacogenetics.

Inquiries: Kumiko Iwamoto, M.D., Dr.P.H., Division of Cancer Control and Population Sciences, NCI, EPN Room 535, Rockville, MD 20852, phone 301-496-9600, fax 301-402-4279, email ki6n@nih.gov

Mary Wolpert, Ph.D., Division of Cancer Treatment and Diagnosis, NCI, EPN Room 841, Rockville, MD 20852, phone 301-496-8783, fax 301-402-5200, email wolpertm@nci.nih.gov

PAR-99-019: Non-Mammalian Organisms As Models For Anticancer Drug Discovery. Letter of Intent Receipt Dates: Jan. 15 and Sept. 15, 1999. Application Receipt Dates: Feb. 19 and Oct. 19, 1999.

This PA encourages the use of non-mammalian organisms to discover new cancer therapies. The goal is to identify key genes, enzymatic activities, components of signaling pathways, or cellular processes, which are altered in human cancer, as potential intervention points

or targets that could be used in the design of new cancer drugs.

Inquiries: George Johnson, Ph.D., Division of Cancer Treatment and Diagnosis, NCI, EPN Room 841, Bethesda, MD 20892-7456, phone: 301-496-8783, fax: 301-402-5200, email johnsong@exchange.nih.gov

PAR-99-020: Non-Mammalian Organisms As Models For Anticancer Drug Discovery: SBIR/STTR Initiative. Letter of Intent Receipt Dates: Jan. 15 and Sept. 15, 1999. Application Receipt Dates: Feb. 19 and Oct. 19, 1999.

This PA encourages the use of non-mammalian organisms to discover new cancer therapies (see PAR-99-019). This PA must be read in conjunction with the Omnibus Solicitation Of The Public Health Service For Small Business Innovation Research Grant Applications (PHS 98-2) And The Omnibus Solicitation Of The National Institutes Of Health For Small Business Technology Transfer Grant Applications (PHS 98-3).

Inquiries: George Johnson, Ph.D., DCTD, NCI, 6130 Executive Blvd Room 841, Bethesda, MD 20892-7456, phone: 301-496-8783, fax: 301-402-5200, email johnsong@exchange.nih.gov

PA-99-021: Biobehavioral Pain Research

Applications are encouraged to study individual differences in pain response which may be due to factors such as genetic differences, endocrine activity, neural activity, immune function, psychological state, disability state, age, gender, and cultural background. Ten NIH Institutes are taking part in this PA. For NCI inquiries contact: Claudette Varricchio, Community Oncology and Rehabilitation Branch, NCI, EPN Suite 300, Bethesda, MD 20892, phone: 301-496-8541, email: varriccc@dcpcepn.nci.nih.gov

In Brief:

Coriell Wins Expansion Funds

(Continued from page 1)

Trusts supported recruitment of 12 researchers. . . . **CORIELL INSTITUTE** for Medical Research, of Camden, NJ, received a $500,000 grant from The Pew Charitable Trusts for the expansion of cryogenic storage facilities for cell collections. In addition to the Pew grant, about $3 million has been raised for the estimated $5 million expansion. Requests for biomaterials have near quadrupled since 1990, according to Coriell President **David Beck**. . . . **AMERICAN CANCER SOCIETY** presented Distinguished Service Awards to three leaders in cancer control: **James Marks**, director, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention; **Donald Shopland**, coordinator for smoking and tobacco control, NCI; and **Amy Langer**, executive director, National Alliance of Breast Cancer Organizations. . . . **MORE ACS AWARDS**: **Gilbert Friedell**, director emeritus, University of Kentucky Markey Cancer Center, and head of the Kentucky Cancer Registry and the NCI Region 9 of the Cancer Information Service, received the ACS Humanitarian Award for his work on behalf of the poor and underserved in Appalachia. **Genevieve Foley**, vice president, patient care services, St. Jude Children's Research Hospital, Memphis, received the ACS Volunteer Leadership Award. . . . **S. B. GUSBERG**, distinguished service professor of obstetrics and gynecology emeritus at Mt. Sinai School of Medicine, New York, was honored for his contributions to medical science at the 100th anniversary celebration of the alumni of the Sloane Hospital for Women of the Columbia-Presbyterian Medical Center at Columbia University. . . . **DAN MCCRONE** was named medical director and chief medical officer of Quality Oncology Inc., of McLean, VA, a cancer disease management firm. McCrone was senior vice president and chief medical officer of HealthAmerica, a for-profit insurer in Pennsylvania, Ohio, and West Virginia. With clients in Florida and New Hampshire, Quality Oncology has 284,000 managed care lives under contract, the company said. . . . **MASSACHUSETTS** Board of Registration in Medicine suspended **James Foran** for prescribing four times the proper dosage of chemotherapy drugs to two breast cancer patients at the Dana-Farber Cancer Institute in November 1994. The overdoses killed Betsy Lehman, a health columnist for The Boston Globe, and caused heart damage to Maureen Bateman, a teacher. "Dr. Foran engaged in conduct which calls into question his competence to practice medicine, including practicing medicine with negligence on repeated occasions," the board wrote in a consent order signed by Foran last month. The board issued a three-year suspension retroactive to October 1995. Lehman died of a heart attack in December 1994. Bateman recovered, but died in May 1997 of cancer.

Where To Find Cancer Meetings

The Cancer Letter meetings list is located on the Web at http://www.cancerletter.com/html/documents.html#top

NCI maintains an extensive list of oncology meetings at http://calendar.nci.nih.gov/internal/