THE CANCER LETTER

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NCI, Dept. Of Veterans' Affairs Sign Agreement On Clinical Trials Access

NCI and the Department of Veterans Affairs have signed an interagency agreement that would provide U.S. Armed Forces veterans with greater access to NCI-sponsored cancer clinical trials.

The three-year agreement, which becomes effective Jan. 1, expands on existing affiliations between VA hospitals and NCI clinical cooperative groups and cancer centers. About 2.9 million veterans receive care annually in the VA's 173 medical centers and 400 clinics. Of the 45,000 veterans who are treated for new cancers each year, about 4 percent are enrolled on NCI-sponsored clinical trials.

The agreement, signed by Undersecretary for Health Kenneth Kizer,

(Continued to page 2)

In Brief

Fraud By Trainee Leads Collins To Retract Five Papers; Weinstein Retires At Columbia

FRANCIS COLLINS, director of the National Center for Human Genome Research at NIH, retracted five research papers on leukemia genetics published in leading scientific journals because a research trainee fabricated data, according to news reports. The student, who worked in Collins' lab, admitted systematically fabricating data over two years, Collins said. The New York Times in an Oct. 30 article identified the student as **Amitov Hajra**, a graduate student at the University of Michigan in Ann Arbor. The research dealt with the role of a defective gene in producing acute leukemia. The work did not involve patients. Two of the papers were published in the Proceedings of the National Academy of Sciences; others appeared in Genomics; Molecular and Cellular Biology; and Genes, Chromosomes and Cancer. University of Michigan and the HHS Office of Research Integrity are conducting an investigation. The fraud was discovered when a geneticist became suspicious while reviewing a paper Collins and Hajra submitted to the journal Oncogene. In an Oct. 1 letter to 100 scientists, Collins disclosed the problem. The letter was described in an Oct. 29 article in The Chicago Tribune. . . . **I. BERNARD WEINSTEIN** has retired as director of the Columbia-Presbyterian Comprehensive Cancer Center after serving in this role for the past 10 years. He will concentrate his efforts on his own research in molecular carcinogenesis and will serve as a senior advisor to the cancer center. He also holds the position of Frode Jensen Professor of Medicine, Professor of Genetics and Development and Public Health. **KAREN ANTMAN** has been appointed as the new director of the cancer center.

NCI, Dept. Of Veterans' Affairs, Sign Clinical Trials Agreement

(Continued from page 1)

of DVA, and NCI Director Richard Klausner, covers NCI-sponsored studies in diagnosis, treatment, and prevention.

These include trials reviewed and approved by NCI staff, NCI cooperative group studies, studies conducted in clinical and comprehensive cancer centers under an NCI-approved protocol review and surveillance mechanism, and protocols performed under the direct support of an NCI peer-reviewed grant.

"The potential mutual benefit as a result of this agreement is great," said Tom Holohan, chief of patient care services for DVA. "In any protocol, the assumption is that the research arm is likely to be at least as beneficial as the standard treatment, so the veteran gets the opportunity to have cutting-edge treatment."

The agreement covers all phases of cancer research studies, NCI officials said. "We think it is a terrific agreement because of the flexibility," said Robert Wittes, director of the NCI Division of Cancer Treatment, Diagnosis and Centers. "It lets us work across the spectrum of cancer research including prevention, diaganosis and treatment."

Under the terms of the agreement, VA will be responsible for all medical care for eligible veterans participating in trials at VA sites, including tests, treatment, follow-up, management of complications and costs of commercially available drugs.

For veterans who meet the VA criteria for participation in clinical trials outside of the VA system, the VA will reimburse all medical care required as a result of participation in the NCI-sponsored trial, including follow-up care and testing after the protocol is completed.

Whether a veteran is enrolled in a protocol within or outside of the VA system, NCI will pay the research costs of participation in the protocol.

"The agreement's success depends on identifying a number of VA sites that are motivated to participate in trials with us and on bankrolling their participation," Wittes said to **The Cancer Letter**. "The potential is large for a significant increase in accrual to NCI-sponsored studies."

The anticipated amount of the research costs or the estimated cost to the VA system were not available.

"The presumption has been that this kind of treatment is more expensive, but that is an assumption not based on data, and that's one thing NCI might be able to find out through this agreement and the agreement with CHAMPUS" the Department of Defense healthcare system, Holohan said to **The Cancer Letter**.

The VA collaboration is broader in scope than NCI's clinical trials agreement signed earlier this year with DOD, said Mary McCabe, special assistant in the NCI DCTDC. "The CHAMPUS agreement predominantly provides coverage for beneficiaries receiving care outside of the military system," McCabe said. "Under the VA agreeement, the benefits and trials coverage will be by VA physicians working within the NCI clinical trials program. The predominant activity will be a patient being treated at a VA facility by VA physicians."

"There is the option that when the VA has an interest in a particular trial or where a disease is rare and a clinical trial is most appropriate, at their discretion a patient can be referred to a civilian hospital," McCabe said. "That will bring VA facilities closer into the fabric of NCI clinical trials."

About 40 percent of NCI-designated clinical and comprehensive cancer centers have affiliations with VA facilities, and 48 VA medical centers participate in the cooperative groups as affiliate members. Six VA medical centers are part of the Community

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Clinical Oncology Program.

Of the 43,000 new cancers in 1994 in the VA system, there were 8,256 new prostate cancer, 7,266 new lung cancers, 2,400 new colorectal cancers and 1,500 new bladder cancers, NCI said.

Reaction to the agreement was positive in oncology. "I appreciate Dr. Klausner's leadership in expanding access to clinical trials," said James Armitage, president of the American Society of Clinical Oncology. "This is hopefully one of many examples that we will continue to see in this regard."

Under the agreement, the types of affiliations that would be established include:

—Enhanced linkages between the VA system and NCI cooperative groups. VA institutions would be considered for group membership, participation as a CCOP, or affiliate membership. All VA facilities providing oncology services will be allowed to apply for participation in the cooperative group program and will be reviewed according to the usual peer-review processes.

—For VA hospitals that are part of academic medical centers, more extensive participation in NCI's early clinical trials program. According to the agreement, the affiliations between VA institutions and the Univerisyt of Texas Health Sciences Center in San Antonio and the University of Wisconsin are models of the type of arrangements that could be extended to additional centers.

—Under special circumstances, such as trials of particular importance to the VA or trials of rare tumor types, eligible veterans may be offered access to NCI-sponsored trials in nearby civilian facilities participating in such studies. This option is to be defined by the VA in individual cases and implemented through the VA Comprehensive Cancer Centers and regionalized referral system.

—Closer linkages between the cancer planning activities in the VA Cooperative Studies Program and the NCI clinical trials program.

—Establish linkages between VA and NCI health services researchers to develop and initiate an agenda based on mutual research goals. This would likely include research on cost effectiveness.

Additional terms of the agreement include the following:

—NCI will provide to VA hospitals access to the Physician Data Query system for access to information about NCI-sponsored trials. PDQ will be enhanced to provide users with the ability to identify VA hospitals and list the specific trials in which they are participating.

—VA and NCI will jointly plan educational and promotional initiatives to inform veterans and VA physicians of the expanded opportunity to participate in NCI-sponsored studies.

NCI is continuing to negotiate a demonstration project with the Health Care Financing Administration.

1971-1996

National Cancer Act 25th Year

Three "Cancer Initiatives" Announced At White House

In a White House ceremony marking the 25th anniversary of the signing of the National Cancer Act, President Clinton announced three cancer research initiatives.

The initiatives include a $30 million increase in funding for research into the genetics of breast cancer, creation of an Internet web site on the disease and establishment of the Office of Cancer Survivorship at NCI.

"These steps help us to put science at the service of our families and say we will do whatever it takes to continue the fight until there is a cure for cancer," Clinton said at the Oct. 27 event. "I know about this from my own family's experience." Clinton's mother, Virginia Kelley, died of breast cancer in 1995.

The White House event, attended by top officials at HHS, NIH and NCI, as well as 200 cancer survivors, came about through the Friends of Cancer Research, a nonprofit group with the goal of bringing attention to funding needs for cancer research. The group is holding events around the U.S. to mark the 25th anniversary of the National Cancer Act, signed by President Nixon on December 23, 1971.

The event also provided the Administration the opportunity to point out its cancer-related initiatives over the past four years.

"Since I took office we have mounted a comprehensive campaign to prevent and treat cancer," Clinton said. "We are working to get tobacco out of our children's lives forever. We have accelerated FDA approval of cancer drugs and made it easier for patients to obtain promising therapies before they are formally approved.

"The Department of Health and Human Services, the Department of Defense, NASA and the CIA have all joined forces to develop cutting edge imaging technology for the early detection of cancer.

"Most important of all, we've increased spending on cancer research, treatment and prevention by some $400 million," Clinton said. "In the battle against breast cancer, we've increased funding for research and prevention by nearly 80 percent since 1993.

"We launched a public awareness campaign to encourage older women to use Medicare to have mammograms," Clinton said. "And my balanced budget goes even further. It will guarantee free annual mammograms to Medicare beneficiaries, removing all financial barriers that prevent some women from obtaining this vitally important test.

"We are making progress," Clinton said. "The survival rate has gone up. Seven out of 10 children with cancer survive it. That's up from one out of 10 just 25 years ago. The death rate for breast cancer has gone down every year in the last seven, has dropped by nearly eight percent since 1990."

In attendance at the White House ceremony were HHS Secretary Donna Shalala, Susan Blumenthal, director of the Office of Women's Health; NIH Director Harold Varmus, NCI Director Richard Klausner, Assistant Secretary of Defense for Health Steven Joseph, and Jane Reese-Coulbourne, executive director of the National Breast Cancer Coalition.

The Three Initiatives

Under the genetics initiative, the Department of Defense breast cancer research fund will provide $20 million and NIH will provide $10 million to support a collaborative research program.

The funds will support "a broad range of investigations related to the role of genes in the development of breast cancer," according to a White House statement. "The Administration's objective is to move rapidly toward the goal of identifying high risk women and preventing breast cancer before it strikes."

The second initiative, a breast cancer web site, was established by the National Action Plan on Breast Cancer. The site provides answers to frequently asked questions about breast cancer, with links to other information sources on breast cancer clinical trials and research, breast cancer organizations, educational conferences, publications, and other resources, the White House said.

The web site location is: http://www.napbc.org.

The third initiative, the NCI Office of Cancer Survivorship, had been made public by the Institute several months ago. However, the White House event gave Clinton the opportunity to announce that NCI would officially open the office on Nov. 1.

"There's no greater proof of the progress we've made than the more than 10 million Americans who have survived cancer," Clinton said. "Many have special psychological, physical and health care counseling needs that we are only beginning to understand.

"Some face recurrence of their illness," Clinton said. "Some can't get health insurance. I'm proud to have passed landmark legislation to guarantee that cancer survivors will no longer live in fear of losing that health insurance just because they have a preexisting condition."

The office, in the Division of Cancer Treatment, Diagnosis and Centers, was formed to enhance NCI's research activities on the physical, psychological, and economic issues faced by cancer survivors.

The office is headed by Anna Meadows, a professor of pediatrics at the University of Pennsylvania Medical School and director of the Division of Oncology at Children's Hospital of Philadelphia. Meadows has been chairman of the Late Effects Study Group, an international consortium of 13 pediatric cancer centers, and is a member of the Children's Cancer Group.

Friends' Events

In related developments, the Friends of Cancer Research honored four congressmen and the wife of a fifth congressman for their work to support appropriations for cancer research.

Rep. John Porter (R-IL) received an award from the organization last week at an event in Chicago.

On Oct. 28, the Friends presented awards to Priscilla Mack, the wife of Sen. Connie Mack (R-FL), Reps. Michael Bilirakis (R-FL), C.W. "Bill" Young (R-FL), Dan Miller (R-FL), at an event at the Moffitt Cancer Center in Tampa, FL.

Friends of Cancer Research was begun by Ellen Sigal, a member of the National Cancer Advisory Board.

The group's board includes members of professional societies, advocacy organizations, industry and media.

Voluntary Organizations

American Cancer Society To Consider Targeting Funds For Prostate Cancer Research

The board of directors of the American Cancer Society next week is scheduled to vote on a proposal to target 10 percent of the society's research budget—about $7.5 million—to fund three new grant programs for prostate cancer research.

The funding set-asides would support grants in three major areas under the umbrella of prostate cancer: health policy and outcomes research; behavioral, psychosocial and quality of life research; and novel ideas in tumor cell biology.

The board is scheduled to consider the proposal at its meeting Nov. 4.

If approved, the proposal would represent the first such set-aside in the society's research budget, said Robert Young, president of Fox Chase Cancer Center and chairman of an ACS committee that selected the targeted areas.

"ACS has never targeted a particular portion of the research budget into a specific area before," Young said to **The Cancer Letter**. "The concept has been controversial, but there was a strong feeling on the part of the committee and ACS leadership that it is an experiment, there clearly were areas of high priority that were relatively underfunded, and we would see if this mechanism would stimulate an expansion in these critical areas.

"It is very different from earmarking in that it doesn't set up a separate bureaucracy with a separate set of ideas, it uses the already established peer review mechanism," Young said. "These grants have to compete in a conventional review. We're not going to fund bad science."

The concept for targeting a portion of the research budget grew out of a review of the society's research portfolio last year by the ACS Blue Ribbon Advisory Committee, Young said. The committee decided to commit 10 percent of the $75 million research budget on research that is high priority or underserved nationally. Earlier this year, the committee appointed an advisory group to select the high priority areas.

The Research Evaluation and Targeting Advisory Group, which Young chaired, sent more than 700 surveys to leaders of ACS and its divisions, NCI-designated cancer centers, professional societies, ACS donors, and others for suggestions on targeting research funds. The survey generated ideas for funding 17 broad areas and 41 separate targets.

The group sifted through the ideas for three months, Young said.

"We decided to look for opportunities where ACS research funding could fill an important underserved niche," Young said. "Above all, it would have to fund excellent science and use the existing peer review structure."

The group decided that four general areas of research represented opportunities for ACS to make an impact: psychosocial, behavioral and quality of life research; outcomes and health policy research; "novel ideas" grants to help investigators to test risky hypotheses; and prostate cancer research.

"What the group decided to do was include all of the areas of targeting under the umbrella of prostate cancer," Young said. "Prostate cancer would be the overall disease focus, but within that we would focus on psychosocial, behavioral and quality of life research, outcomes and health policy research, and novel ideas grants."

Many scientists and clinicians believe there are opportunities for progress in treatment and control of prostate cancer, Young said. "ACS was putting a very small amount of money—about $4 million—into prostate cancer, which is the most commonly diagnosed noncutaneous malignancy in the U.S.," Young said.

ACS spent about $800 in research funds for every case of childhood cancer in the US, $69 per case of breast cancer, and $13 per case of prostate cancer, Young said.

"While there are efforts in NCI and the Department of Defense to expand funding for prostate cancer, there is no major push by either of those groups to fund within prostate cancer the areas of psychosocial, quality of life, health outcomes, or novel ideas," Young said. "None of those techniques or concepts are receiving wide national attention."

Three Requests for Applications, which describe the grant programs, will be released following the ACS board's decision.

The RFAs for psychosocial/quality of life and health outcomes/policy research each set aside $3 million per year for three years for funding approximately four grants in each area per year, at a cost of $250,000 each. Funds could be shifted

between these two areas depending on the quality of applications. Unspent funds would roll over to the support these areas in the next fiscal year, and would not go to the general ACS research pool.

The RFA for novel ideas in prostate cancer cell biology would set aside $1.5 million each year to fund approximately eight grants for $65,000 per year. Any unspent funds would roll over to this RFA the next fiscal year.

In contrast to the society's regular research project grant program, which is limited to beginning investigators, the targeted RFAs would be open to investigators at any stage in their careers.

"The rationale for this is, if an area is underserved, then you shouldn't put further constraints on investigators by limiting the number of people who can apply," Young said.

In addition, the other 90 percent of the ACS research budget would not exclude prostate cancer research proposals, Young said.

Young said his committee plans to re-evaluate the program over the next three years.

Cancer Meetings Listed For Next Three Months

November

New Developments in the Multidisciplinary Management of Thoracic Malignancies—Nov. 1, Cleveland, OH. Contact Ireland Cancer Center, tel: 216-844-5878.

Chemotherapy Foundation Symposium—Nov. 6-8, New York City. Contact Jaclyn Silverman, Mount Sinai School of Medicine, tel: 212-241-6772, fax: 212-996-5787.

Oncology Nursing Society Fall Institute—Nov. 8-10, Phoenix, AZ. Contact ONS, tel: 412-921-7373, ext. 553.

Intersection of Pathology and Genetics on Hereditary Nonpolyposis Colon Cancer—Nov. 11-12, Bethesda, MD. Contact NCI Early Detection Branch, Dr. Sudhir Srivastava or Barbara Bonaparte, tel: 301-402-6480 or Dr. Miguel Rodriguez-Bigas, tel: 716-845-5815.

Cytokines and Growth Factors in Hematology and Oncology—Nov. 14-16, Atlanta, GA. Contact Imedex USA, tel: 770-751-7332, fax: 770-751-7334.

Recent Advances in Melanoma and Soft Tissue Sarcoma—Nov. 21-22, New York City. Contact Memorial Sloan-Kettering Cancer Center, Jean Campbell, tel: 212-639-3511, fax: 212-639-3535.

December

International Conference on Mechanisms of Antimutagenesis and Anticarcinogenesis—Dec. 2-6, Okayama, Japan. Contact Dr. H. Hayatsu, Faculty of Pharmaceutical Sciences, Okayama Univ., Okayama 700, Japan, tel: 81-086-251-7945, fax: 81-086-254-2129, e-mail: hayatsu@ph2ews1.okayama-u.ac.jp

Pittsburgh Cancer Conference: Innovations in Cancer Care—Dec. 3-4, Pittsburgh, PA. Contact University of Pittsburgh Medical Center, Diane Applegate, tel: 412-647-8263, fax: 412-647-8222.

San Antonio Breast Cancer Symposium—Dec. 11-14, San Antonio, TX. Contact Lois Dunnington, tel: 210-567-4745, fax: 210-567-4822, e-mail: lois_dunnington@oncology.uthscsa.edu

January

AACR/ASCO Joint Conference: Basic and Clinical Aspects of Lymphoma—Jan. 10-14, Palm Springs, CA. Contact AACR, tel: 215-440-9300, fax: 215-440-9313.

Arizona Cancer Center 7th International Workshop on Chromosomes in Solid Tumors—Jan. 20-22, Tucson, AZ. Contact Patty Sundberg, tel: 520-626-2276, fax: 520-626-2284.

Marrow Transplantation in Children: Current Results and Controversies—Jan. 23-25, Ft. Lauderdale, FL. Contact Dr. Michael Trigg, Univ. of Iowa, tel: 319-356-1608, fax: 319-356-7659.

National Conference on Cancer Nursing Research—Jan. 23-25, Panama City, FL. Contact American Cancer Society, tel: 404-329-7616.

Future Meetings

Radiation Therapy Oncology Group Semi-Annual Meeting—Feb. 20-23, Houston, TX. Contact Nancy Smith, RTOG, tel: 215-574-3205, fax: 215-928-0153, email: nsmith@acr.org.

Skeletal Complications of Malignancy—April 19-20, NIH Natcher Conference Center, Bethesda, MD. Contact The Paget Foundation, tel: 212-229-1582, fax: 212-229-1502, email: pagetfdn@aol.com.

Critical Issues in Tumor Microcirculation, Angiogenesis and Metastasis—June 2-6, Boston, MA. Contact Carol Lyons, Massachusetts General Hospital, tel; 617-726-4083, fax: 617-726-4172.

World Conference on Lung Cancer—Aug. 10-15, 1997. Contact Secretariat, tel: 353-1-8306795, fax: 353-1-8309090.

Funding Opportunities

NCI RFPs Available

RFP NCI-CM-77020-10

Title: **Development And Production Of Parenteral Dosage Forms For Clinical Studies**

Develop and produce pharmaceutically acceptable parenteral dosage forms of promising new agents with activity against cancer or the HIV virus. Certain agents selected by the NCI, DCTDC, Cancer and AIDS operating committees will be assigned for development and production as parenteral products (primarily sterile freeze dried products). Batch sizes will range from small development batches (less than 100) to intermediate size batches to be used in Phase I and II trials; however, escalation to large batch size (10-30,000 or more) for Phase III/IV trials and Group C distribution is possible. It is estimated that the successful offerors must be prepared to supply more than five-hundred thousand parenteral dosage units each year. The capability to develop and manufacture other pharmaceutical dosage form (i.e., large volumes parenteral, sterile emulsions, micro-dispersions, etc.) is desirable but not essential. Data obtained from the contract will: 1) be used to support IND applications submitted by the NCI to the U.S. Food and Drug Administration, 2) be provided to other NCI contractors engaged in large scale dosage form manufacture and analytical evaluation of these dosage forms and 3) be provided to physicians, pharmacists, and nurses and other medical personnel handling these products in a clinical setting. It is anticipated that two cost reimbursement, completion type contracts will be awarded for a base period of three years with two one-year options for each contract. The offeror must be registered with the FDA as a pharmaceutical manufacturing facility for sterile products at the time of proposal submission.

Inquiries: Therese Dick, RCB NCI, 6120 Executive Blvrd Rm 603-MSC 7220, Bethesda, MD 20892-7220, tel: 301-496-8620

RFP NCI-CM-77027-30

Title: **Pathology And Veterinary Support Services**

The NCI Division of Cancer Treatment, Diagnosis and Centers, Developmental Therapeutics Program anticipates the award of one cost-reimbursement contract, for a five year period, beginning on or about July 30, 1997. As a minimum requirement, the contractors must comply with the FDA's current Good Laboratory Practice Regulations. The proposed awarded contract will be administrated on a work assignment managed basis. Work assignments will be issued under the proposed, level of effort, contract resulting from this solicitation. DTP is seeking organizations to perform a variety of pathology and veterinary services to support the DTP preclinical toxicology and pharmacology program for anticancer and anti-AIDS drug development. The organization should have the facilities and staff to carry out the requested efforts and the management expertise to respond to the diverse and changing needs of this project. Specifically, the work assignments to be issued will involve the following: operation of a repository to hold the pathology materials and raw data generated in past and future toxicology studies; storage of data on optical medium; performance of an independent verification (peer review) of the pathological findings by the study pathologist especially with respect to individual diagnoses, drug-relatedness, nomenclature and slide quality; provide a pathology support program to prepare blocks and slides and conduct histopathological evaluation of tissues; perform the site visits to conduct necropsies, slide preparation or to assist the Project Officer in project evaluation. This includes providing expertise in special techniques to assess cardiotoxicity, neurotoxicity, nephrotoxicity, etc.; storage, maintenance and shipment of Government infusion equipment to other DTP contractors; development and implementation of a new surgical or other procedures for drug administration or sampling; instruction in these procedures; or performance of these procedures in actual animal studies; conduct site visits to the DTP toxicology contractor laboratories to evaluate pathology laboratories, animal care programs or to investigate pathology or animal care problems; and to support the Toxicology and Pharmacology Branch toxicology efforts required through the preparation of study protocols, study monitoring and report evaluation. The Principal Investigator should be a board certified veterinary pathologist or veterinarian with at least three years experience with similar programs. This is recompetition of a contract performing these activities.

Inquiries: Elsa Carlton, RCB NCI, 6120 Executive Blvrd Rm 603-MSC 7220, Bethesda, MD 20892-7220, tel: 301-496-8620.

RFP NCI-CM-77028-30

Title: **Preclinical Toxicology And Pharmacology Of Drugs Developed For Cancer, Aids And Aids-Related Illnesses**

The NCI Division of Cancer Treatment, Diagnosis and Centers, Developmental Therapeutics Program, anticipates the award of five cost-reimbursement contracts, for a five year period beginning Aug. 30, 1997. As a minimum requirement, the contractors must perform all toxicology studies in accordance with the FDA's current Good Laboratory Practice. Contractors must also indicate their willingness to sign a confidentiality of information statement. The proposed awarded contracts will be administered on a work assignment managed basis.

Offerors are required to proposed levels of effort for both levels: Level A: 46,875 labor hours, and Level B: 93,750 labor hours over a five year period. DTP is seeking organizations to carry out pharmacology and toxicology studies, the data from which must be suitable for filing with the FDA as part of Investigational New Drug Applications Offerors should have the facilities and staff to carry out such studies and the management expertise to analyze and evaluate the data. Work assignments are estimated to involve two or three chemical agents annually per contract. The objectives of the assignments in relative order of importance are: (1) assessment or acute and subacute toxicity in rodents and dogs including determination of a maximum tolerated dose (MTD), of dose limiting toxicities (DLT), schedule-dependent toxicity, of the reversibility of adverse effects and of a safe clinical starting dose; (2) validation of analytical methodology to quantitate plasma drug levels in preclinical animal models and to measure plasma drug levels in rodents, dogs, and/or non-human primates treated with the agents under study, (3) determination of bioavailability of drug after parenteral and/or oral administration if efficacious drug levels can be attained in plasma in vivo and is the drug crosses the blood-brain barrier, (4) the use of pharmacokinetic information to permit extrapolation of toxic effects across species by relating plasma drug levels to the time of appearance and severity of toxicity, and to establish the safety of potentially efficacious doses. The Principal Investigator should have a doctoral degree in pharmacology/toxicology plus at least five years experience in directing, implementing and evaluating drug toxicity studies in experimental animals. The pathologist, pharmacokinetics and analytical chemist should likewise have credentials which illustrate their competence and accomplishment in service as critical team members in the conduct of such studies.

This is a recompetition of a group of 5 contractors currently performing these activities.

Inquiries: Elsa Carlton, RCB NCI, 6120 Executive Blvrd Rm 603-MSC 7220, Bethesda, MD 20892-7220, tel: 301-496-8620.

NCI Program Announcement

PA-97-004

Title: **Molecular And Genetic Studies In Pancreatitis And Pancreatic Cancer**

The National Institute of Diabetes and Digestive and Kidney Diseases and the National Cancer Institute wish to encourage experienced and new investigators to pursue basic and clinical investigations into the molecular genetics of acute and chronic pancreatitis as well as the "preneoplastic" genetic changes that occur and predispose individuals to adenocarcinoma of the pancreas. Basic studies include the generation of transgenic animal models of pancreatitis which show inherited forms of pancreatitis. Particularly, organ-specific transgenic mice are sought that exhibit acute or chronic pancreatitis. Alternatively, for pancreatic cancer, the fifth most common cause of death from cancer, basic science studies are sought which identify the numerous genetic alterations that are involved in this form of carcinogenesis. Such studies could utilize transgenic mice or gene knock-out mice to systematically determine pancreatic preneoplastic genetic events.

Clinical studies are also sought that increase our knowledge in the early detection and diagnosis, prognostication, prevention and treatment of pancreatitis and pancreatic cancer. These studies could utilize the recent advances in the field that identify a genetic locus on human chromosome 7 that exhibits linkage to hereditary pancreatitis as well as the recent observation of allelic loss of tumor suppressor gene(s) on human chromosome 18 as a early event in human pancreatic carcinogenesis.

Support for this program announcement will be through the NIH research project grant (R01) award, the FIRST (R29) award and the small grants (R03) award.

Inquiries: Thomas Kresina, Division of Digestive Diseases and Nutrition, NIDDKD, 45 Center Drive, MSC 6600, Bethesda, MD 20892-6600, tel: 301/594-8871, fax: 301/480-8300, email: tk13v@nih.gov.

NCI Contract Awards

Title: Phase I single and multiple-dose safety, pharmacokinetic and efficacy clinical study of genistein in prostate neoplasia. Contractor: University of North Carolina at Chapel Hill, $789,187.

Title: Phase I multiple-dose safety and efficacy clinical study of nonsteroidal anti-inflamatory based regimens in adenomatous polyposis coli patients. Contractor: M.D. Anderson Cancer Center, $1,682,630.

Title: Cancer in patients with ataxia-telangiectasia and in their relatives. Contractor: Danish Cancer Society, Copenhagen, Denmark, $302,939.

Title: Biological specimen repository for patients at high risk for cancer. Contractor: Biological Research Faculty & Facility Inc., Maryland, $1,916,349.

Title: Preclinical evaluation of intermediate endpoints and their modulation by chemoprevention, workstatement #24. Contractor: American Health Foundation, Valhalla, NY, $626,432.

Title: Preclinical evaluation of intermediate endpoints and their modulation by chemoprevention, workstatement #26. Contractor: University of Illinois, Chicago, IL, $508,415.