THE CANCER LETTER

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DCBDC Advisors Set Aside $2 Mil. For Research On The Microenvironment Of Breast Cancer

NCI advisors voted to set aside $2 million next fiscal year to fund grants for basic research in breast cancer in an ususual action that changed a proposed Program Announcement to a Request for Applications (RFA).

The Board of Scientific Counselors of the Div. of Cancer Biology, Diagnosis & Centers traditionally has not favored research initiatives presented as RFAs under the view that the money set aside for RFAs

(Continued to page 2)

In Brief

House Passes Appropriations Bill; Senate Markup In Late Summer; Kirschstein Acting NIH Director

FULL HOUSE last week passed the appropriations bill that contained no earmarks and gave NCI $2.1 billion, $102.9 million above FY 1993 and $40.9 million above the President's budget proposal. The NIH appropriation was $10.9 billion, $610 above FY 1993 and $269 million above the President's budget. **Each NIH institute** received at least a 5.2 percent increase, and the President's provision for $100.8 million in forward funding for breast cancer research was eliminated. (**The Cancer Letter**, July 2). The bill, approved by a 305-to-124 vote, contained appropriations for Labor, HHS and Education departments. **Senate markup** is expected to begin in late July, or, more likely, in September, Capitol Hill sources said. . . . **RUTH KIRSCHSTEIN** was named acting NIH director last week following **Bernadine Healy's** departure. Kirschstein has been director of the National Institute of General Medical Sciences for the past 20 years, and prior to that was director of FDA's old Bureau of Biologics. . . . **WENDY BALDWIN**, deputy director of the National Institute of Child Health & Human Development, was named NIH Acting Deputy Director for Extramural Affairs. She replaces **John Diggs**, who left for the Assn. of American Medical Colleges. . . . **RICHARD HODES** has been named director of the National Institute on Aging. Hodes, a cancer immunologist on NCI's staff since 1973, was senior investigator and chief of the Immune Regulation Section of NCI's Experimental Immunology Branch. . . . **CORRECTION: The Cancer Letter** inadvertently published in the June 18 issue a concept for an RFA proposed by the Div. of Cancer Treatment for "Positron Emission Tomography Diagnostic Oncology Group." The concept was withdrawn prior to the DCT Board of Scientific Counselors meeting and was not presented. The concept is tentatively scheduled for presentation at the board's next meeting in October. . . . **'IN BRIEF'** is continued to page 8.

DCBDC Advisors Ok Concepts For Breast Cancer RFAs, PA

(Continued from page 1)
depletes the funds available for investigator-initiated research. The board often changes such initiatives to Program Announcements.

At its meeting last month, the board took a concept for a Program Announcement on the microenvironment in breast and prostate cancer and insisted it be released as an RFA, with earmarked funds.

"The board has been dominated by outstanding scientists who have a long standing concern for the priority of investigator-initiated research," DCBDC Director Alan Rabson said to **The Cancer Letter.** "This shows the great concern among many scientists for doing the basic research in breast cancer."

The initiative was one of four breast cancer related concepts approved by the board in DCBDC's preparation for the possible infusion of money by Congress into breast cancer, and to a lesser extent, prostate cancer research, through the FY 1994 appropriations bill.

Two of the other three concepts were designated as RFAs, and the board approved all without changes.

"An Extremely Important Area"

Board member Margaret Kripke said the role of the microenvironment in breast and prostate cancer "is an extremely important area. But I'm disturbed by the fact that while we are going to talk about $10 million for construction later this meeting, there is no money set aside for this."

Noting that funds for those initiatives will come out of that designated for breast cancer research, Kripke asked if it would be possible to earmark some for the microenvironment effort as an RFA.

Rabson cited NCI policy of attempting to reduce the percentage of the Institute's budget going into RFAs, a policy reached in deference to wishes expressed at one time or another by members of all four NCI boards of scientific counselors as well as the National Cancer Advisory Board. "We had thought originally of this as an RFA, but the [NCI] Executive Committee felt that we could get enough high quality applications with a Program Announcement."

Board Chairman Albert Owens said he agreed with Kripke, and then asked whether "it is the sense of the board that this be given extra priority, with funds from the additional breast cancer money." The board voted unanimously that it was.

During the morning break, Owens told **The Cancer Letter** that it was his intention that the initiative be changed to an RFA. Rabson said he had not interpreted the discussion and vote that way, although agreeing that he would present the board's view to the Executive Committee (which must approve RFA proposals before they are submitted to BSCs for concept review).

When the board reconvened, Owens reopened the issue. Kripke insisted that the initiative should be an RFA. Owens conditioned his agreement on the availability of the additional breast cancer money.

Brian Kimes, director of the Centers, Training, & Resources Program, pointed out that although responses to RFAs are reviewed by special study sections and are funded from the earmarked money, when they come back for renewal they must do so as R01s and are funded from the R01 pool. That puts increasing pressure on the money available for traditional, investigator initiated research, Kimes noted.

The board then voted formally and specifically to change the initiative to an RFA and approved a maximum of $2 million a year which will fund from eight to 12 grants.

The other new RFAs in breast cancer approved by the board were:

▶ Planning and exploratory grants for development of breast cancer research in NCI designated centers. A total of $8.2 million was set aside to fund as many as 16 one-time awards to centers without existing breast cancer programs, and up to 12 awards of $150,000 each to centers with existing or developing formal breast cancer programs.

▶ Cancer education grants for breast cancer education initiatives, at a total first year cost of $1.6 million. This would fund 20 grants averaging $80,000 a year for three years.

The board approved a program announcement for enhancement of facilities for breast cancer research.

THE CANCER LETTER

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Although no money was earmarked, this represents a major boost to the prospects for NCI's extramural construction program. Kenneth Brow, chief of the Research Facilities Branch, said that NCI hoped to make as many as six awards, with applicants permitted to seek as much as $2 million each in direct costs.

However, these awards will require a 65-35 percentage ratio, with institutions asked to put up the larger amount. The split for construction grants has been 50-50 between NCI and awardees.

The board approved the concept of an RFA for development of AIDS related cancer programs in NCI designated cancer centers. Approximately $5 million in total costs will be earmarked for seven to 10 one time planning grants of up to $500,000 each over four years.

Contract recompetitions approved were:

▶ Biomedical computing software services in support of the Cancer Diagnosis Program. Information Management Inc. is the incumbent contractor. The five year renewal is estimated to total $100,000 a year.

▶ Feral mouse breeding colony. Hazleton Laboratories is the present contractor. The new contract will be for four years, with the estimated total cost at $150,000 a year.

The board approved expansion of the division's master agreement for cancer vaccine development. The additional cost is estimated at $400,000 a year for four years.

Following are the concept statements:

Role of the Microenvironment in Breast and Prostate Cancer. RFA, $2 million a year, eight-12 grants. Cancer Biology Branch, Extramural Research Program, Program director: Suresh Mohla.

The Cancer Biology Branch proposes to promote new research on molecular interactions among the cell populations of human breast and prostate cancer that contribute to malignant progression. These malignancies have a great number of characteristics in common; e.g. they are hormonally regulated by sex steroids during growth and differentiation of neonatal development and at the onset of puberty; these same hormones play an important role in modulating growth of these malignancies; and hormonal intervention remains a key component of treatment of both diseases. In addition, some association between the two neoplasms is suggested by epidemiological data of an increased risk of prostate cancer among relatives of women with breast cancer, as well as a significant increased risk of breast cancer in families with prostate cancer.

The hormonal regulation may be mediated in part by epithelial-stromal interactions during normal development and differentiation in both organs. More importantly, there is good evidence to indicate that aberrations in these interactions occur during the course of neoplastic progression and involve the same mechanisms and interactive phenomena that are observed in normal cells. Stromal components include fibroblasts, endothelial cells, macrophages, the extracellular matrix contributed by both epithelial and stromal cells, and in the case of breast tissue, adipocytes. Little is known of the contribution of this mosaic of cells to the malignant process and virtually nothing is understood at the molecular level. The aim of this initiative is to foster application of recent advances in molecular and cellular biology, using appropriate model systems, to study the effects of tumor cell-stroma interactions relevant to tumor development in human breast and prostatic tissues.

An association between the two diseases is suggested by epidemiological data. For example, a family history of prostate cancer can have a significant effect on increasing breast cancer risk. Similarly, a significantly higher frequency of prostate cancer in relatives of breast cancer patients than in relatives of control groups has been reported. Breast and prostatic carcinomas originate in epithelial cells; however, the growth and progression of the cancer is intimately related to it microenvironment, i.e. the stroma. Studies on embryological development of the mammary gland and the prostate have indicated that hormonally-induced ductal morphogenesis and epithelial growth is mediated by the interactions between stroma and epithelia. During this neonatal development the carefully timed acquisition of steroid hormone receptors by stromal cells may be responsible for these hormonally-induced events. Studies on the hormonal regulation of differentiation of the mammary gland in vitro indicate that the presence of stromal components can determine the extent and type of functional epithelial maturation. The biochemical interactions and molecular communications underlying these events are poorly understood.

Familial clustering of breast cancer indicates that there is a genetic component predisposing individuals to breast cancer. Although it is the epithelial cell which is designated as cancerous, several reports have indicated that skin fibroblasts derived from breast cancer patients may also be altered and exhibit characteristics associated with a transformed and/or fetal phenotype. More than 90% of patients with familial breast cancer, 67% of their clinically unaffected first-degree relatives and 50% of the patients with sporadic disease also had fibroblasts of this phenotype. Furthermore, these characteristics of fibroblasts may precede the detection of breast cancer.

Many growth factors including bFGF, aFGF and TGFa may be made available to epithelial cells from the adjacent mammary stroma. Human breast fibroblasts can also produce IL-6; IL-6 can stimulate 17-beta oxidoreductase activity in tumor cells which in turn increases the availability of 17-beta estradiol to enhance estrogen-dependent growth of breast carcinomas. Other important epithelial mitogens are the IGF's. Recent data indicate that the primary source of IGF expression is the breast stroma. Analysis of fibroblasts from benign breast lesions showed the production of IGF-I mRNA while fibroblasts from malignant lesions expressed IGF-II mRNA, suggesting a correlation with disease progression.

Fibroblast stroma has also been shown to produce extracellular matrix molecules such as fibronectin and tenascin which influence cell proliferation and adhesion. Tenascin is known to reduce epithelial cell adhesiveness. It is absent in normal breast, its distribution being restricted to embryonic and malignant tissues.

A new gene coding for the metalloproteinase enzyme stromelysin-3 (ST-3), has been identified that is expressed specifically in stromal cells surrounding invasive breast carcinomas. ST-3, which degrades the extracellular matrix, is postulated to play an important role in progression of breast cancer.

Androgens regulate the early growth and morphogenesis of the prostatic epithelium indirectly by their effects on mesenchymal (stromal) tissues. Other data raise the possibility that stromal-epithelial interactions also play a role in tumorigenesis or act as a determinant of some of the biological properties of carcinoma cells. A major growth stimulatory factor for prostatic epithelial cells produced by stromal cells appears to be fibroblast growth factor (FGF). FGF-7 or keratinocyte growth factor, produced by the stromal cells in the Dunning rat prostate tumor by androgen treatment, is a mitogen for these tumor cells which harbor FGF-7 receptors. Chung et al., using LNCaP cells to study the effects of stroma on the induction of tumorigenicity in nude mice, showed the pivotal role of bone- or prostate-derived fibroblasts in this process.

Differences in tumor incidence in different mouse strains or in rat models may also result from characteristics of the stromal compartment. Recent observations indicate that mesenchymal or stromal inductors can impose strong control over the growth of transformed epithelial cells. In the human prostate, the regulation of epithelium by stroma may be even more relevant than in other organs because the epithelial to stromal ratio is about 1 to 1; in the mature rat prostate, it is 5 to 1.

There is a lack of availability of appropriate model systems that take into consideration cell-cell communication and the tumor microenvironment. It is critical to begin to dissect genetic pathways involved in stromal-epithelial interactions, yet studies in this area require stringent controls and optimal biological milieu.

In animal models, a number of chemicals (environmental carcinogens and synthetic chemicals) have been implicated as potential breast and prostate carcinogens but virtually nothing is known about the interaction of such carcinogens with stromal components in normal or malignant breast and prostatic tissues. It is possible that environmental carcinogens play an especially important role in breast cancer since the fat component of breast stroma is a reservoir for carcinogen storage. Continued exposure to these chemicals might induce progressive changes in the adjacent epithelium which could be detected experimentally. The role of environmental factors, e.g., hormonal status, diet, and concomitant exposure to naturally occurring estrogenic compounds, in modulation of epithelial-stromal interactions is yet to be determined.

The preliminary observations about stromal-epithelial interaction suggest many intriguing features which are common to these malignancies. However, most of the information obtained so far has been phenomenological. This initiative is intended to encourage research projects to elucidate the mechanisms of these interactions. It may include multi-disciplinary collaborations among basic and clinical scientists and should embrace an array of molecular and cellular approaches.

Development of Breast Cancer Research Programs in NCI-Designated Cancer Centers. RFA, total $8.2 million, up to 16 awards. Cancer Centers Branch.

Objective is to stimulate, through competitively awarded P20 Planning and Exploratory Grants, the development and establishment of breast cancer research programs in NCI-designated cancer centers. A breast cancer research program thus established would be expected to become an integral part of the research portfolio of the individual cancer center and to be sustained thereafter through the various resources of the cancer center. With this Planning and Exploratory award, the successful applicant would be expected to accomplish the following:

1. To establish a formal research program in breast cancer research within the cancer center, drawing together all investigators from within the center to plan and develop the program and to begin the process of discussing novel approaches to the problem of breast cancer.

2. The planned program would be expected primarily to engage multiple research approaches to breast cancer involving basic research and clinical research, and to explore opportunities for prevention and control research when appropriate as well. The plans for the program should have sufficient breadth and depth in the topic area and should be undergirded by a well-thought-out conceptual basis for creating a focused, cohesive program with a variety of discipline to be brought to bear on the problem of breast cancer.

Sub-components of the plans for development of a program in breast cancer research can also include the following:

--Focus on breast cancer in elderly women, collaborating when possible with other organizations and institutions near the cancer center which have an interest and focus on geriatrics, e.g., National Institute on Aging supported Geriatric research centers, and VA-supported Geriatric Research Education and Geriatric Research Education and Clinical Centers.

--Focus on environmental influences on breast cancer, collaborating when possible with National Institute for Environmental Health Sciences supported centers at the same institution or with major NIEHS grant holders at the same institution.

3. Plans should be included for recruiting new investigators to the cancer center in order to strengthen the program in weak areas, to increase the breadth of the program and/or to bring in investigators with a special expertise or talent, all of which are aimed at creating a vital, interactive research environment. In recruiting new scientists, particular attention should be given to the possibility of drawing individuals from other disciplines into the breast cancer research arena in order to bring new and innovative approaches to bear on the problem.

4. The funds requested could support:

a. partial salary of the Program Development Leader.

b. funds for special retreats for the purpose of breast cancer program development and to stimulate cross disciplinary collaborations among investigators particularly those bridging basic science with clinical research.

c. the establishment of shared resources specifically oriented to breast cancer research.

d. recruitment of new scientists to the institution who wish to engage in cancer research, and as a means by which the program is strengthened and/or broadened.

e. pilot projects for feasibility studies that will stimulate

collaborative research, that will move basic research discoveries into the clinical research arena, and that will help to build the research base in support of the breast cancer research endeavor through competitive funding sources.

Support would be through competitive award of Planning and Exploratory Grants (P20s) for no more than four years.

The National Institute on Aging and the NCI Cancer Centers Branch are discussing potential collaborative projects focused on cancer in the elderly. A sub-component of this initiative, potentially co-sponsorable by the two Institutes, could focus specifically on breast cancer in elderly women involving collaborations with investigators with NIA-supported Geriatric research centers or with VA-supported GRECCs.

The National Institute of Environmental Health Sciences is encouraging its centers to engage in research on the environmental factors involved in breast cancer and has expressed to the Cancer Centers Program an interest in cross-center collaborations. A sub-component of this initiative could be focused on environmental factors of breast cancer involving collaborations with investigators in NIEHS-supported centers or with groups of investigators with substantial research grant support from NIEHS.

Exclusions: Cancer Centers which are already supporting substantially developed or fully established formal programs in breast cancer research are precluded from applying for this initiative in terms of its primary objectives. However, such cancer centers would be permitted to apply for limited funds to augment their existing program with the special subcomponents noted above. Thus, centers with substantially developed or fully established breast cancer research programs can apply for funds to add subcomponents involving:

--breast cancer in elderly women, with collaborations with investigator with NIA-supported Geriatric research centers or with VA-supported GRECCs.

--environmental factors of breast cancer, with collaborations with investigators in NIEHS-supported centers or with groups investigators with substantial research grant support from NIEHS.

Cancer Centers without existing breast cancer programs could apply for up to $400,000 total costs. A total of $6.4 million would be dedicated to this part, permitting up to 16 awards to be made. Cancer Centers with developing or existing formal breast cancer programs could apply for one or both sub-components targeting environmental factors in breast cancer and/or breast cancer in elderly women, for up to $150,000 total costs each. A total of $1.8 million would be dedicated to this part, permitting to 12 sub-components to be awarded.

Breast Cancer Education Initiatives. RFA, $1.6 million first-year funding, 20 grants. Cancer Training Branch, Program director: Vincent Cairoli.

The Cancer Training Branch proposes to invite grant applications to create new educational programs aimed at reducing the mortality and morbidity of breast cancer.

NCI is interested in supporting innovative educational proposals which would disseminate what is professionally known about the prevention, early detection, and treatment of breast cancer to primary care physicians, other health professionals, and the lay community with special attention to minority and other underserved populations.

Since it is essential that any educational strategies rest on a knowledge base derived from the best current research findings, NCI proposes that cancer centers and other organizations with appropriate breast cancer expertise collaborate with educational specialists and other professional and lay groups, particularly those with access to underserved populations, to design and implement programs to achieve the objectives of this initiative.

Responses to this initiative can be directed toward a number of target populations such as: primary care physicians, health professional students, women's groups, minority and other underserved groups, and employer-based groups.

Breast cancer patients, once diagnosed, will need data, perspectives, and risk/benefit analyses to enable them to communicate and make choices with their physicians about their own treatment and about the future course of their lives. Lay groups may need basic introductions to breast cancer. For example, most women know what a mammogram is or have heard of it, but they are less aware of the unique benefits of periodic screening mammograms, may be unduly concerned about radiation risk, or may be deterred by insensitive techniques on the part of the technologist.

Health care professionals who have contact with women in a health maintenance setting or who treat breast cancer patients in a community setting must have their knowledge and skills constantly updated and expanded in order to provide better care and comfort to these women. For example, primary care physicians may need current information concerning breast cancer risk evaluation for different age populations, the formal range of current breast cancer screening guidelines, how to conduct proper physical breast examinations, and how to follow up on an abnormal physical finding or mammogram.

Health professional students could be given a comprehensive orientation to a range of breast cancer issues, especially the importance and impact of clinical trials, early in their career training. An essential component of all these educational programs should focus on the knowledge and attitudes of both professional and lay audiences concerning the rationale, selection criteria, and referral procedures for treatment and prevention clinical trials for breast cancer.

NCI encourages innovative programs using the most appropriate educational techniques and media for given target groups to disseminate this information. These educational programs should also include information and hands-on experience when appropriate with the NCI PDQ and Cancer FAX databases.

Careful evaluations of any proposed program to ascertain the most effective methods of reaching these target audiences in the future will be required.

Support will be through the Cancer Education Grant Program (R25) mechanism, a curriculum-driven program aimed at developing and sustaining innovative and unique educational approaches that ultimately will have an impact on reducing cancer incidence, mortality, and morbidity, as well as on improving the quality-of-life of cancer patients.

It is expected that 20 grants averaging $80,000 total cost will be awarded and that each grant will continue for three years. Indirect costs are to be limited to actual costs or eight percent of total direct costs, depending upon which sum is smaller. Any tuition or equipment costs are to be excluded from the direct cost base for the computation of the indirect cost amount.

Enhancement of facilities for breast cancer research. Program announcement. Research Facilities Branch.

The Research Facilities Branch proposes to issue a Program Announcement for construction grant awards in FY 1994 that will enhance the nation's efforts in breast cancer research. Emphasis will be on facilities for improving early detection, prevention, diagnosis, prognosis, and treatment of human breast cancer.

Applications may be submitted from institutions which have a critical mass of high quality ongoing basic to clinical breast cancer research and a breast cancer patient population of appropriate size to sustain an innovative breast cancer research program or institutions that clearly have the potential to develop quality innovative breast cancer efforts. The institution must agree to a matching fund ratio of 35 percent from the NCI and 65 percent from the institution.

Applications will be accepted for new construction, renovation and completion of "shelled" space that will be dedicated to breast cancer research and achieve one or all of the following:

1. Provide the facilities for specialized resources critical for breast cancer research in early detection, prevention, diagnosis, prognosis, and treatment of breast cancer.

2. Provide a spacial configuration to: (1) consolidate breast cancer researchers; (2) stimulate clinical research; (3) encourage multidisciplinary interactions.

3. Provide a spacial configuration that will increase basic/clinical research interactions and promote translational research objectives.

The established C06 grant mechanism will be used. Applications may be submitted for up to $2,000,000 in direct costs. No indirect costs are involved.

Development of AIDS-related Cancer Programs in NCI-designated Cancer Centers. RFA, total $5 million, seven to 10 planning grants. Cancer Centers Branch.

To stimulate and sustain basic and clinical research in AIDS malignancies in NCI-designated cancer centers, competitive planning grants would be awarded to achieve the following:

1. The development of a formal program for AIDS malignancies within the cancer center involving cancer researchers and AIDS researchers. When the institution receives support from a CCSG, a Center for AIDS Research (CFAR) and/or an AIDS Clinical Treatment Unit (ACTU), the infrastructure of the program should encompass participants in these three areas in a way that takes maximum advantage of research opportunities and research resources.

2. The creation of a co-program leadership responsibility involving an established cancer researcher and an established AIDS researcher. These individuals would be responsible for developing the program and establishing the means through which scientific interactions and collaborations would be achieved.

3. The recruitment to the program of basic and clinical cancer and AIDS researchers within the institution who have successful track records in receiving external peer-reviewed support and/or strong publication records in scientific journals.

4. The funds requested could be used for:

a. salaries of the program leaders;

b. funds for retreats/special meetings for the purpose of stimulating and sustaining an intensive cross-disciplinary planning and implementation process;

c. the establishment of research resources specifically needed to pursue AIDS-related cancer research;

d. recruitment of new scientists to the institution who wish to pursue AIDS-related cancer research;

e. pilot projects for feasibility studies that will encourage collaboration between cancer researchers and AIDS researchers, that will encourage the movement of basic research discoveries into more applied research with patients, and that will build the research base (e.g., more R01s) of the center in AIDS malignancies.

Support would be through competitive award of planning grants (P20s) for four years and would be non-renewable.

Biomedical computing software services in support of the Cancer Diagnosis Program. Recompetition of a contract held by Information Management Inc., total $100,000 per year for five years. Project Officer: Gladys Glenn.

The purpose of this solicitation is to continue computerized data support services to the Cancer Diagnosis Branch. Biomedical computing support services have been provided under various contracts for the past sixteen years to manage data from diagnostic and prognostic marker resource and research projects. This support has included analysis and programming services for two serum banks and for research projects developed by the Branch. The current scope of work continues the support of the serum banks including maintaining information about the inventory, keeping records of clinical data for the samples in the breast cancer serum collection, formulating coded serum panels at the direction of the project officer, providing analyses for the NCI of data submitted by panel recipients, and providing programming and data analysis support for special project developed by the branch. The current contract will end June 14, 1994.

Feral Mouse Breeding Colony. Recompetition of a contract held by Hazleton Laboratories, $150,000 per year, four years. Laboratory of Tumor Immunology and Biology, Principal Investigator Robert Callahan.

The Oncogenetics Section, LTIB, is requesting concept approval to recompete its current contract for the maintenance and housing of a feral mouse breeding colony. This contract represents a major resource for the Oncogenetics Section and plays an integral role in the research of Drs. Robert Callahan, Gilbert Smith, Dan Gallahan, Edith Kordon, and Shukichi Myasaki on the identification and characterization of mutations relevant to the etiology of mammary gland neoplasia. Their studies have focused primarily on three feral mouse strains which have unique characteristics pertinent to the study of mouse mammary tumorigenesis.

Current contract provides facilities and technical support for housing, breeding, and maintenance of 1000 feral and inbred mice. This includes technical help experienced in the handling and husbandry of feral mice, breeding of feral mice, knowledge of requirements of outbred colonies, milking mice, observation of mice for early tumor development, surgery, dissection, injections, and preparation of tissues for histology. The colony is composed of approximately 700 mice that are held long-term (2 years) for tumor development and 300 mice as a breeding nucleus.

Master agreement for cancer vaccine development. Master Agreements, total cost per year $400,000. Laboratory of Tumor

Immunology and Biology, Project Officer: Kathleen Siler.

The objective of the Master Agreement is to make available to NCI, clinical grade recombinant vaccines, baculovirus derived proteins, peptides and monoclonal antibodies to be used in clinical protocols to elicit specific active immunotherapy responses in carcinoma patients. This agreement would enable NCI to identify a pool of institutions and/or organizations capable of providing or testing FDA approved GLP and/or GMP clinical grade reagents.

The Master Agreement will be composed of six tasks to support the development, production and testing of clinical grade recombinant anti-cancer vaccines as broadly described above.

Task A would provide for the development of clinical grade recombinant vaccinia, other pox viruses, Salmonella, polio, adenovirus, and/or BCG with inserted tumor associated genes and/or cytokine genes.

Task B would provide for the development of clinical grade recombinant baculoviruses and protein products using inserted tumor associated genes and/or cytokine genes.

Task C would provide for the development of clinical grade anti-idiotype and anti-tumor antigen monoclonal antibodies.

Task D would provide for the production of peptides reflecting sequences of tumor associated genes and/or cytokine genes.

Task E would provide for testing of the recombinant constructs, peptides and anti-idiotype monoclonal antibodies for immunogenicity and anti-tumor activity in rodents. Task F would provide for testing the recombinant constructs, peptides and monoclonal antibodies for immunogenicity in non-human primates.

RFPs Available

Requests for proposals described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Executive Plaza South room number shown, National Cancer Institute, Bethesda MD 20892. Proposals may be hand delivered to the Executive Plaza South Building, 6130 Executive Blvd., Rockville MD.

RFP NCI-CP-40511-21

Title: Cancer risk following evaluation and treatment for infertility (coordinating center)

Deadline: Approximately Aug. 23

The Environmental Studies Section, Environmental Epidemiology Branch, of NCI, is seeking a contractor to perform the above named project. This proposed contract will create a coordinating center to assist the NCI project officers in monitoring the work of a number of clinical centers and to assist in essential data collection elements of this project. This project will involve the accumulated of a large cohort of women evaluated and treated for infertility at a number of major medical centers. The interest in the study will be to assess subsequent cancer risks associated with both the underlying causes of infertility and different treatment regimens used for infertility. It is anticipated that approximately five clinical centers will be necessary to accumulate the large cohort (approximately 10,000) needed. It is further anticipated that the majority of the subjects accumulated for the project will have been evaluated for infertility around the mid-1960s, when they were in their mid-twenties. The types of support to be provided by the coordinating center contractor in the conduct of the study include: assisting in the identification of infertility patients, training field staff (including abstractors and interviewers), abstracting medical records, tracing subjects in a manner that minimizes losses to the follow-up, determining vital status and collecting death certificates for deceased subjects, approaching alive subjects in a manner that achieves high rates of participation to a questionnaire, validating reported medical events, coding data, developing appropriate data bases to achieve study objectives, and assuring quality control for all aspects of the study. It is expected that the proposed contract will be a cost-reimbursement, completion type for a 48-month period of performance. The proposed contract is to be a 100% small business set-aside. The SIC code is 7379 with a size standard of $14.5 million. Award is anticipated by April 15, 1994.

Contract specialist: Barbara Shadrick, RCB Executive Plaza South Rm 620, Tel. 301/496-8611.

RFP NCI-CP-40513-21

Title: Cancer risk following evaluation and treatment for infertility (clinical centers)

Deadline: Approximately Aug. 23

The Environmental Studies Section, Environmental Epidemiology Branch, of NCI, is seeking a contractor to perform the above named project. This proposed acquisition is for the award of approximately five clinical center contracts for the purpose of identifying the types and number of patients required to test the hypothesis of interest for this study. Investigators from these clinical centers will assist in identifying the types of data that should be collected in order to classify types of infertility and treatment utilized. This project will involve the accumulation of a large cohort of women evaluated and treated for infertility at a number of major medical centers. The interest in the study will be to assess subsequent cancer risks associated with both the underlying causes of infertility and different treatment regimens used for infertility. It is anticipated that approximately five field centers will be necessary to accumulate the large cohort (approximately 10,000) needed. It is further anticipated that the majority of the subjects accumulated for the project will have been evaluated for infertility around the mid-1960s, when they were in their mid-twenties. The types of support to be provided by the clinical center contractors in the conduct of the study include: identification of infertility patients, assessing the completeness of the ascertainment processes, defining methods of categorizing various causes of infertility and treatment regimens, assisting in patient location efforts, approaching study subjects to assure a high rate of participation, assisting in retrieval of medical records to validate reported medical events, and ensuring patients' confidentiality. It is expected that the contracts will be cost-reimbursement, completion types for a 48 month period of performance. Award is anticipated by April 15, 1994.

Contract specialist: Barbara Shadrick, RCB Executive Plaza South Rm 620, Tel. 301/496-8611.

RFP NCI-CP-40514-21

Title: Biomedical computing--design and implementation

Deadline: Date not available (see below)

The Epidemiology & Biostatistics Program in NCI's Div. of Cancer Etiology seeks computer-related support for its biostatisticians, epidemiologists, computer professionals and others within the program in the form of data management and analysis of large sets of biomedical data. This computer related support falls into three main categories: 1) data management activities, consisting of keying, formatting, and editing data collected from field studies, 2 systems design and development, consisting of defining technical specification requirements and developing the program language code required to implement automated solutions, and 3) statistical analysis and modeling, consisting of using standard software packages and specialized

software to carry out analyses under the general guidance of the EBP investigators.

A single RFP is being issued to initiate recompetition of three contracts all currently being performed by Information Management Services Inc. to provide research support for the EBP. This proposed contract will be a cost-reimbursement type contract with a requirement of 294,400 total direct labor hours to be provided over a four-year period. The previous contracts have provided computer related services for over 100 studies per month. The proposed contract will be a 100% small business set-aside, SIC Code 7374, with a size standard of $14.5 million. All responsible sources capable of providing this support and meeting these requirements are encouraged to submit an offer and will be considered. A Delegation for Procurement Authority clearance by the Department [of Health & Human Services] is pending. The RFP package will not be issued until such time as final DPA clearance is received. Proposals will be due approximately 30 days after the actual release data of the RFP package. Award is anticipated by April 15, 1994.

Contract specialist: Barbara Shadrick, RCB Executive Plaza South Rm 620, Tel. 301/496-8611.

RFAs Available

RFA CA-93-030

Title: **Native American Women's Cancer Initiative**

Letter of Intent Receipt Date: July 30

Application Receipt Date: Oct. 13

The Special Populations Studies Branch of NCI's Div. of Cancer Prevention and Control invites grant applications to conduct research to develop and determine the effectiveness of cancer control and prevention intervention strategies in Native American women, including American Indian, Alaska Native, Native Hawaiian, and/or American Samoan women. The long range goals of this initiative are to improve cancer survival rates and reduce cancer mortality rates among Native American women through cancer prevention and control efforts.

Applications may be submitted by public and private, for-profit and non-profit organizations serving the indigenous female community in a specified geographic area such as Native American health clinics (e.g., P.L. 93-638 clinics); voluntary Native American organizations; Native American research centers or consortia; hospitals that serve large numbers of Native American women; consortia of female health providers; and/or Federal (e.g., the Indian Health Service), State or local governments. Teams of applicants are encouraged, but one organization must be identified as the lead institution to assume responsibility for the conduct of the project.

Support mechanism: NIH research project grant (R01). Total project period may not exceed four years. Anticipated award date: May 1, 1994. Range of the amounts of the direct cost will vary from $130,000 to $320,000 per year. Approximately $1.5 million in total costs per year for four years will be committed to fund grants. It is anticipated that up to five awards will be made, at least one from each option noted below.

This RFA has three options. Option A focuses on common/disproportionate cancer rates and barriers to early detection services. These projects will develop, implement, and evaluate interventions that are designed to overcome the barriers that Native American women experience in accessing culturally appropriate quality cancer control services including screening, appropriate follow-up, diagnostic, treatment, and rehabilitation programs. Option B emphasizes reduction of risk factors among the Native American female population. Projects will develop, implement and assess cancer prevention and control interventions that are designed to reduce risk factors of this population in regions of the country where the cancer control needs have been increasing and data are sparse. Option C stresses research capacity development in which workshops will be designed to provide technical assistance to increase the research application and scientific skills of Native American women. The applicant must specify which option is the focus in the application and it is recommended that only one option be the focus of any application.

The aim is to support studies in four or five different geographic regions of the U.S. Although every attempt will be made to provide regional representation, the possibility exists that applications may not be awarded for all geographic regions and/or Native American populations.

These studies will have three phases within the four years. Phase I--A planning phase; Phase II--an intervention and evaluation plan implementation phase; and Phase III--data analysis, report preparation and dissemination among both lay and professional Native Americans and non-Natives.

Inquiries may be directed to: Dr. Linda Burhansstipanov, Div. of Cancer Prevention and Control, NCI, Executive Plaza North Rm 240, Bethesda, MD 20892; Tel. 301/496-8589.

In Brief

Fox Chase Awarded $1 Mil. Grant To Fund Five Young Investigators

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. . . **PEW CHARITABLE** Trusts have awarded Fox Chase Cancer Center a $1 million grant to establish a young investigators program in biomedical research. The program will support work by five scientists who recently established laboratories at the center: **Oded Gonen, Dietmar Kappes, Yoshihiro Matsumoto, Andre Rogatko,** and **Randy Strich.** Their labs will receive $100,000 a year for two years. . . . **U.S. CIGARETTE TAX** of 56 cents per pack is among the lowest in industrialized countries, according to a study by the Worldwatch Institute. Only Spain's tax is lower at 37 cents per pack. More countries are raising cigarette taxes to compensate for smoking-related health costs and to discourage smoking, the Washington, D.C.-based environmental think-tank said. Denmark, Norway and Canada levy taxes exceeding $3 per pack. Smoking costs the U.S. $65 billion a year, estimates the congressional Office of Technology Assessment. Employers lose $43 billion in productivity from missed workdays. The report, "Vital Signs Brief #7: More Countries Raising Cigarette Taxes to Cut Health Care Costs," is available from the Worldwatch Institute, 1776 Massachusetts Ave. NW, 8th Floor, Washington, D.C. 20036, phone 202/452-1999.