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DCE Board Approves Two New Grant Programs, New Contract, Recompetitions Totaling $22 Mil.

The Div. of Cancer Etiology Board of Scientific Counselors has approved concept statements for two new grant programs, one on mechanisms of hormonal carcinogenesis, and the other on AIDS-associated neoplasia, voting unanimously to commit $1 million in first

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In Brief

Sharp Won't Take MIT Presidency; Brow Returns To NCI; Goldman Succeeds Lawrence At MCV

PHILLIP SHARP has decided not to accept appointment as president of Massachusetts Institute of Technology (**The Cancer Letter**, Feb. 23). After first indicating he would take the job, leading MIT to make such an announcement, "I stepped back and looked at it and couldn't picture myself doing full time administrative work," Sharp told **The Cancer Letter**. "I decided I could not give up research. I apologized to the institute for not being more decisive". . . . **KEN BROW**, former deputy chief of NCI's Research Facilities Branch, has returned to the institute as chief of the branch. He replaces his former boss of 13 years, Donald Fox, who retired last fall. Brow left NCI over four years ago to join the Public Health Service Div. of Facilities Planning, and later moved to the NIH Div. of Engineering Services. Brow, like Fox, is an engineer. He said, "It's good to be back." . . . **DAVID GOLDMAN**, chief of hematology/oncology at the Medical College of Virginia, has succeeded **Walter Lawrence** as director of the MCV Cancer Center. He will continue to head hematology/oncology, and Lawrence continues as chief of surgical oncology. . . . **JAMES WILLSON** has been appointed associate director for clinical programs at Case Western Reserve Univ. Cancer Research Center. Willson trained at Johns Hopkins and NCI and was a staff member at the Wisconsin Comprehensive Cancer Center before moving to Cleveland. . . . **FLORIDA PEDIATRIC** CCOP is likely in the funding range for the "CCOP 3" recompetition, bringing to 42 the number of CCOPs reported in the funding range. James Talbert is the PI. . . . **FOUR REQUESTS** for Proposals (RFPs) have been cancelled in their entirety by NCI. They are: NCI-CM-07326-14 Preparation of Bulk Chemicals and Drugs for Phase 2 & 3 Clinical Trials, NCI-CM-07328-28 Synthesis of Compounds for Preclinical Toxicology and Phase 1 Clinical Studies, NCI-CM-07342-14 Preparation of Bulk Chemical and Drugs for Phase 2 & 3 Clinical Trials for Small Business and NCI-CM-07343-28 Synthesis of Compounds for Preclinical Toxicology and Phase 1 Clinical Studies for Small Business.

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DCE Board OK's New RFA Concepts, Recompetitions Totaling $22 Mil.

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year funding to each five-year program. Approximately five to seven grants would be funded under the proposed grant program, "New Approaches for Understanding the Mechanisms of Hormonal Carcinogenesis." Five or six grants would be funded under the proposed grant program, "Mechanisms of Viral-Induced AIDS-Associated Neoplasia."

At its meeting last week, the board agreed to commit more than $22 million in funding for competitive contracts or grants. Among those approved was a concept statement for a new, four-year contract to provide logistical support for the annual meeting of the Laboratory of Tumor Cell Biology. The proposed first year award is $100,000.

The board also unanimously approved recompetition of a contract for the provision of purified AIDS virus proteins and subhuman primate facilities, currently held by Bionetics Research Inc., for a total of $4,985,251 over four years. The concept statement is published in the March 9 issue of **AIDS update.**

Also approved was $475,000 in additional funding for a case-control study of cutaneous malignant melanoma that the board had approved in October 1988. The extra funding for the $3.3 million study was necessary because NCI estimates of salaries for professionals carrying out the study were lower than the best and final offers, according to NCI staff.

In addition, the board approved two interagency agreeements with the National Institute of Occupational Safety & Health, titled "Task Order for a Feasibility Assessment for Inorganic Acid Aerosols," $50,000 for 12 months, and "Biological Markers of Occupational Bladder Cancer," $700,000 over four years. The latter is a study of worker populations with established exposure to aromatic amine bladder carcinogens.

Concept statements for the new procurements follow. All were approved by unanimous vote. Other concept statements will be published in next week's issue of **The Cancer Letter.**

New approaches for understanding the mechanisms of hormonal carcinogenesis. Proposed first year funding $1 million, approximately five to seven grants to be awarded for up to five years.

Sex hormones, both natural and synthetic, have been implicated in carcinogenesis for more than half a century. In humans, causality with use of these agents has been shown with endometrial, vaginal, cervical, liver and possibly breast cancer. In experimental models, sex hormones used individually or in combination have yielded high tumor incidence in a variety of organ sites, including kidney, uterus, pituitary, mammary gland and testis. In these examples, it is clear that hormones can play a fundamental role in promoting the propagation of the transformed cells. The precise changes that take place in the transformation or the molecular nature of the hormone's involvement in these responses is unclear. Nevertheless, expanding knowledge of chemical carcinogenesis mechanisms and the nature of the genetic changes that account for the malignant state of cells suggest that the time is right for further research.

A workshop sponsored by the Chemical & Physical Carcinogenesis Branch last September concluded that more work in several areas is necessary to elucidate the mechanisms of hormonal carcinogenesis:

1. There is a need to karyotype the malignancies which arise out of existing experimental hormonally induced tumor models. Also, oncogene expression in such malignancies should be assessed and their dependency on or production of known growth factors determined.

2. There is a need to develop systems in which one can readily go from the intact animal to the in vitro environment of tissue culture. Such systems would facilitate the elucidation of a hormone's role in tumor initiation and promotion, and normal and tumor cell selective growth in the overall process.

3. New approaches and new technology must be developed to analyze the different aspects of hormonal carcinogenesis. For example, better systems are needed to test for the role of hormones as direct or indirect carcinogens. In addition, development of better systems for genetically dissecting the problem of hormonal carcinogenesis, i.e., transgenetically modified animals and cells systems with genetically altered expression and dependencies on growth factors and their receptors.

Research funded under the proposed RFA would seek to elucidate basic mechanisms of steroid hormone action that relate to the possible roles of hormones as carcinogens, regulators of cell differentiation states, and coordinators of growth factor production and interactions. The purpose of this initiative will be to provide a means to enhance multidisciplinary investigations on the mechanism of hormonal carcinogenesis in experimental animal systems in vitro and in vivo and with human tissues in vitro and in vivo through the issuance of an RFA for principal investigator initiated research grants.

Examples of studies that might be supported by this funding mechanism are: 1) studies of the hormonal metabolites that lead specifically to genetic damage or chromosomal malfunction, 2) studies of karyotype and cytogenetic/cytoskeletal changes in

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models of hormonal carcinogenesis, 3) studies on the role of natural and anabolic androgens, and progestins in hormonal carcinogenesis in organ sites such as the liver and mammary gland, 4) establishment of new in vitro experimental models for studying hormonal carcinogenesis in various understudies organ sites such as pituitary, testis, prostate, uterus and liver, 5) study of the roles of specific hormones in the oncogenic process by the use of transgenic animals or gene transfected cells.

Multidisciplinary studies, including consortial arrangements, under an RO1 application will be encouraged as well as individual projects that would contribute to our understanding of the mechanisms of hormonal carcinogenesis.

Mechanisms of viral-induced AIDS-associated neoplasia. Proposed first year funding $1 million, approximately five to six grants to be awarded for up to five years.

Patients infected with HIV, already at high risk for the development of a broad spectrum of opportunistic infections, are also at risk for developing a variety of neoplasms. The number and kind of such AIDS-associated malignancies is increasing. While the immunocompromised status of AIDS patients must play a significant role in the development of cancer, the possible viral etiology of some of these cancers also should be considered. Several mechanisms of oncogenesis involving viruses are possible. Thus, HIV or one of its genes could cause neoplasia directly; alternatively, HIV or one of its genes might interact with one of several DNA viruses, such as cytomegalovirus (CMV) or hepatitis B virus (HBV), etc., with which many AIDS patients are latently infected, or the HIV induced immunosuppression may result in the reactivation of a latent virus, such as Epstein-Barr virus (EBV), which then may cause B-cell lymphomas directly.

To assess the role of HIV in viral oncogenesis, the Biological Carcinogenesis Branch sponsored a workshop last November on "The Role of Human Immunodeficiency Virus and Other Viruses in AIDS Associated Malignancies." The workshop participants indicated the role of HIV regulatory genes and proteins in viral pathogenesis and disease progression to oncogenesis could be assessed in transgenic animals; they noted that mating transgenic mice containing different HIV gene constructs may have the potential of producing a complex animal model that could prove useful in these investigations. The severe combined immunodeficiency disease (SCID) mouse reconstituted with component of the human immune system may provide a model in which these individual components and their role in HIV pathogenesis and neoplasia can be investigated.

Studies are needed to determine whether the immunocompromised status of AIDS patients allows for the selection of viral variants which have increased or altered pathogenesis or oncogenic potential. Models need to be developed to assess the complex paracrine effects which could occur in individuals coinfected with different viruses each having immunomodulating capabilities. Information correlating the degree and type of immune dysfunction with the pathogenesis of the various oncogenic viruses coinfecting individual patients needs to be obtained.

The goal of this RFA concept is to stimulate research on the molecular mechanisms of AIDS associated neoplasia in which viruses or viral genes have a role. EBV, CMV, HBV, human papilloma virus and human T-lymphotropic viruses 1 and 2 are among the suspected oncogenic viruses having potential for interaction with HIV. Studies can focus on oncogenic viruses functioning as cofactors in the context of HIV infection or on HIV serving as a cofactor in the context of oncogenic virus infections.

The areas of proposed investigation include:

1. Investigations of the possibility that the AIDS immunosuppressed state allows for the selection of virus variants of EBV, CMV, HPV, HBV, HTLV-1, HTLV-2 and HIV which exhibit differences in virulence, tissue tropism, oncogenic potential, etc.

2. Investigations of the molecular interactions between viral and cellular genes or viral and cellular proteins which could be involved in the initiation and progression of AIDS associated malignancies.

3. Investigations of direct and indirect processes, such as autocrine and paracrine effects, by which multiple viral coinfections play a role in AIDS associated neoplasias, e.g., the HTLV-1 tax gene transactivates cellular genes, such as IL-2 and GM-CSF, which could then act upon HIV infected cells and lead to increased levels of HIV.

4. The development and use of small animal models to investigate the molecular basis of virus induced AIDS associated neoplasia, e.g. transgenic mice could be used to study the roles and interaction of various viral genes in the development of neoplasias; SCID mice reconstituted with components of the human immune system could be used to investigate the roles of these various components in immunosurveillance and destruction of virus transformed cells.

5. Investigations of the alteration of virus pathogenesis and oncogenesis as a consequence of the immune status of the patient, e.g., correlates could be sought between oncogenic viral pathogenesis in AIDS patients with varying levels of immune function or between AIDS patients and individuals with other types of immunosuppression such as organ transplant recipients.

Logistical support for the annual meeting of the Laboratory of Tumor Cell Biology. Proposed first year award $100,000, estimated total funding $400,000, four years. This is a concept for a new competitive contract.

The annual meeting of the Laboratory of Tumor Cell Biology has been held since 1972. This meeting began as a small gathering of scientists of the laboratory and was gradually extended to include a few close collaborators. The purpose of the meeting was to discuss ideas for future directions of research based on the accomplishments of the previous year. During the initial years, this gathering was very informal. However, with the discovery of the first human retroviruses in the early 1980s, and the discovery of HIV as the cause of AIDS in the mid 1980s, the interest in this meeting has increased exponentially and its size has grown from 20-40 attendees to several hundred. It has now become an internationally recognized meeting. The support for this meeting will be covered by the royalty money from patent No. 4,520,113.

Considering the high cost factor, the next meeting will be limited to 500 participants and the meeting cost is budgeted to $100,000 a year. To handle a meeting of this size, the laboratory is requesting procurement of support services for the planning and implementation of the 1990 and the future annual meetings.

The major objectives of this contract are to: 1) Select and arrange suitable conference facilities, 2) arrange master account at conference site and facilitate post-conference account reconciliation and payment, 3) based on laboratory approval, prepare, reproduce and distribute initial and follow up mailings according to lists provided by the laboratory, 4) make hotel reservations for all out of town participants, 5) provide project officer weekly status reports regarding participant confirmations, 6) receive camera ready copy of conference book, 7) coordinate with project officer for the audiovisual equipment requirements, 8) prepare and assemble conference books and kits, 9) provide on-site logistics for the conference, 10) assist the laboratory with post-conference activities and complete administrative reports for conference support.

Proceedings of this meeting will be published every year.

Center Directors To Rewrite Five Year Plan, With Minimum Staff Help

The National Cancer Advisory Board Centers Committee rejected the draft proposed for the Cancer Centers Program five year plan (**The Cancer Letter**, Feb. 2) and handed the job of writing a new proposal to a new ad hoc group dominated by center directors.

The draft had come out of a series of meetings between an ad hoc committee of center directors, elected by the centers, and an 11 member NCI staff group, chaired by NCI Deputy Director Maryann Roper.

The centers committee included Walter Eckhardt, director of the Armand Hammer Center for Cancer Biology at Salk Institute; Shirley Lansky, director of the Illinois Cancer Council; Albert Owens, director of the Johns Hopkins Oncology Center; Alan Sartorelli, director of Yale Comprehensive Cancer Center; Phillip Sharp, director of the Center for Cancer Research at MIT; and John Ultmann, director of the Univ. of Chicago Cancer Research Center. Sydney Salmon, current president of the Assn. of American Cancer Institutes, also participated in those meetings.

The NCAB committee met last week with Eckhardt, Lansky, and Owens from the ad hoc centers committee; NCAB Chairman David Korn; and NCI staff members to consider the draft in light of comments received from 21 centers, along with concerns of NCAB members.

Their conclusion: the draft proposal was a useful start on development of a five year plan, but it included so many elements found objectionable by NCAB members and center directors that a complete rewrite is necessary.

It quickly became obvious that a rewrite could be accomplished faster and better by a smaller group. At Roper's suggestion, the six member ad hoc centers committee was given the job, with the addition of Korn and three NCI staff members: Brian Kimes, director of the Centers, Training, & Resources Program in the Div. of Cancer Biology, Diagnosis & Centers; Judith Whalen, planning officer in the Office of Program Operations & Planning; and a third staff member to be selected by NCI Director Samuel Broder. Owens agreed to chair the group.

An effort will be made to have the new draft ready for presentation to the NCAB at its May meeting, and also for discussion by Broder with center directors at the annual meeting of the American Society of Clinical Oncology in Washington in May and the annual AACI meeting at the Mayo Clinic in June.

Kimes presented a summary of comments received from center directors on the proposed draft, noting that while "some center directors largely embraced the plan with numerous positive comments, there clearly remain a number of areas of concern." Those were:

General Concerns

* The plan outlines numerous new activities for centers but makes no provisions for the budget increases needed to accomplish new objectives and goals. These new activities for the most part are not allowable expenses on P30 core grants. Without a clear budget statement, the plan is contradictory to the current trends of reduced funding available for research, research resources, and training. There is a consistent view that without additional money, centers would have to dilute their current efforts and strengths in order to accommodate new efforts and requirements. There is no reference to the fact that centers cannot accomplish current goals and objectives with the reduced funding available. New programs (e.g., control research and diagnostics) must be linked to new dollars not at the expense of activities currently funded through RO1s and PO1s.

* The plan is perceived by many center directors as being too prescriptive and focused on centralized planning by NCI personnel. There should be an emphasis on the individuality and diversity of centers and their ability to take advantage of local creativity and local opportunities. The plan appears to see all centers as homogenous entities in the future. The plan has a directive/prescriptive tone rather than a facilitative/collaborative tone.

* The plan often gives the impression that there is a major shift in the cancer centers program from emphasizing basic and clinical research to cancer control and prevention research.

* The plan must be careful to distinguish between capabilities of academic based institutions vs. free standing institutions. The plan may be missing out on major opportunities to promote rational organization of private, city, county, state, and federal resources to accomplish broad goals.

* The plan is a mixture of specific goals and larger policy issues that could be distinguished from each other in a final document. The plan often reads like guidelines rather than a plan.

* The plan should be shorter and state goals unequivocally but leave specific methods of implementation to the centers to work out with NCI staff. Using examples to illustrate ways to deal with specific problems is more helpful and less directive.

* Each center should formulate its own plans relative to the five year plan that take advantage of current capabilities and strengths to the maximum and that provide for development of additional

activities that require longer term considerations.

* The plan seems to attach the entire burden of the National Cancer Program to the cancer centers program where there are other larger programs with more funding and with specific funding mechanisms to meet these goals.

* Minority training goals are laudable but NCI must recognize the difficulty of finding suitable candidates and should stress organized efforts to identify suitable candidates rather than specific accomplishments.

* The plan attempts to address too many forums.

Networking

* Collaborations among centers should not be a forced process but a facilitative one that benefits the research of individual scientists.

* Networking should not be used to create a central authority or more bureaucracy.

* Networking should recognized the inherent competition among cancer centers.

Basic Research

* Requesting additional training and recruitment of minorities is not possible without additional financial support.

* Networking is not a substitute for individual scientists developing spontaneous collaborations.

Prevention and Control Research

* It is not appropriate to force clinical cancer centers to assume sizeable responsibilities in cancer control and prevention. This is the responsibility of comprehensive cancer centers, and requiring this for all clinical centers would be a disaster for some.

* Specifying dollar levels for comprehensive and clinical centers is unrealistic and unfair and possibly counterproductive.

* Medical school curricula are already over-burdened and center directors are not likely to have the authority to implement these goals. These goals should be elective and not mandatory.

Diagnosis and Treatment Research

* Training more MDs in research is not practical considering that fewer young physicians are interested in research careers.

* Minimum dollar levels placed on diagnosis research should not be required. All language should stress "strive for" goals. Diagnosis research is not heavily supported by available resources.

* Targeting clinical activities to the community is not possible for some very specialized centers.

* Giving comprehensive centers more access to new treatment agents is counterproductive when clinical centers can and do use these agents as effectively.

* There are enormous forces (e.g., third party payers) that are aimed at reducing health care costs and which are affecting the ability of cancer centers to achieve many of the current objectives in treatment and diagnosis. The plan does not recognize this as a problem to deal with.

Education, Training, & Information Dissemination

* If a center has a CIS there is no problem, but centers should be able to meet this goal without CIS.

* Developing personnel plans, especially for matrix centers, is not realistically under the control of cancer center directors.

Administrative Strategies

* Redefining the core grant should be a major type of discussion for the future (e.g., guidelines).

* Finding ways to distribute funds more equitably based on levels of peer reviewed support is important to pursue.

* Creating more administrative burdens (e.g, reporting all publications places an undue administrative burden on centers) takes key center staff time away from efforts in education, communication, programmatic development, and fund raising.

* Providing comparative information to peer reviewers on how other centers use their budgets goes against the idea that centers are diverse and have individual strengths and promotes homogeneity and standardization of center operations.

* A staff investigator line is very important to some centers and should be re-evaluated carefully.

Evaluation

* Building in peer review criteria for compliance to the five year plan is not the role of peer reviewers.

NCAB Centers Committee Chairman John Durant suggested that the new draft include in a preamble the statement that "funding for the entire National Cancer Institute is too thin, and that redistribution of money [taking money from other programs for the centers program] is not part of the plan. We need more money for all of NCI."

Roper said that if that statement were to come from NCI, it could be considered "budget busting" and could land staff members in hot water. Korn noted that the NCI bypass budget is a legal process which requires NCI to state the optimal needs for each program. "There is good rhetoric in the bypass budget."

"Either you have a new plan, or you take the old plan and add to it," NCAB committee member Helene Brown said.

"The new plan should be looked at as what the needs are now. Maybe cancer control has come far enough to be included. That doesn't mean you can

take the 1971 plan and add dollars to it. We need a new plan."

John Niederhuber, chairman of the Div. of Cancer Treatment Board of Scientific Counselors, suggested "we go back to square one and start over. This draft is too much like guidelines. It will have to be completely rewritten." Lansky agreed.

Korn objected to the history of cancer centers included in the draft. Owens and NCAB committee member Walter Lawrence suggested that the history be omitted from the new draft.

Roper asked if the group wanted NCI staff to write a new draft, "culling" from comments by center directors and members of the group.

"That would be unfair on our part to throw out ideas and suggestions and then ask staff to put it together," NCAB committee member Enrico Mihich said. He mentioned the process in which he participated in the late 1970s in developing a plan for the Biological Response Modifiers Program. A group including some members of the DCT Board of Scientific Counselors, with no NCI staff involvement, met for a year and a half. "If we really want a document that reflects the scientific community's views, the committee could meet once a month for six months, and then submit a document for NCI to work on."

"The BRMP plan had some major weaknesses because there was no NCI staff involvement," Kimes said. "It was a good plan, but it had a major problem."

"The concept was not incorrect," Mihich said. "We can prepare a draft and then you can do what you want with it."

Roper agreed that "that is not a bad idea," and after further discussions of what the plan should and should not include, the group went along. The new draft will be written by the six center directors, with assistance from three NCI staff members.

Korn was added to lend some balance. Lawrence noted that the Institute of Medicine report which solidly backed the centers program had been criticized as "self serving," although center representatives were a minority of those who wrote the report. Mihich noted that Korn "has gained a reputation as being anticenters, perhaps unfairly, because of representations to Congress, probably because he's a dean [of Stanford Medical School]."

Korn was out of the room during that discussion. When he returned, he was informed that he had been added to the committee of center directors who would write the new draft.

"You mean me and the center directors? Boy, that will be jolly," he quipped.

NCAB Centers Committee member Roswell Boutwell was quoted in the Feb. 2 issue of **The Cancer Letter** as saying: "We're (McArdle Laboratory) at a plateau in our physical capacity to expand training." **The Cancer Letter** related that comment to a proposed requirement in the draft of the five year plan to increase training of minority scientists.

In fact, Boutwell was referring to McArdle's capacity for training all students, minorities and otherwise. "I strongly support expanding training of minority scientists," Boutwell told **The Cancer Letter** last week. "We must bring minorities into the mainstream of science, and all of American life for that matter. For our survival, we can't have an underclass of citizens."

NCI Channels More Money To CIS, Funds 17; Three Others Continue

Thanks to reprogramming of about $3 million a year from NCI divisions, the Cancer Information Service has been renewed for three more years with the addition of one more fully funded office. CIS operates the 1-800-4-CANCER phone service, providing responses to questions about cancer from more than 400,000 callers a year. CIS offices also distribute pamphlets and other literature in response to public queries.

During the previous contract period, NCI funded 16 CIS offices and provided literature and other services to eight unfunded, or independent, offices. In preparing for recompetition of the contracts, NCI staff had proposed that a cost sharing formula be adopted which would reduce funds available for each office and make it possible to give financial support to more of them.

Negative reaction from the funded offices eventually convinced NCI executives to abandon that plan. However, a near level budget of a little less than $5 million a year was all that was available in the NCI budget. With increased costs of inflation and some expansion of services, that would have reduced the number of funded offices to 10 or less.

NCI Director Samuel Broder agreed that the program was too valuable to cut back and authorized division directors to reprogram funds to the Office of Cancer Communications, provided OCC could convince them of the merits of CIS. OCC did just that, and the new contracts will total $7.95 million a year for three years.

Seventeen offices are now funded; three more have agreed to continue as independents. Three others, which had been funded previously but which lost out in the recompetition, will continue as independents if

they can generate local financial support. The funded offices and areas they cover (states or phone area codes) are:

Johns Hopkins Univ. Cancer Center (MD); Mary Babb Randolph Cancer Center (WV, VA); Fox Chase Cancer Center (PA, DE, So. NJ); M.D. Anderson Cancer Center (TX, LA); Memorial Sloan Kettering Cancer Center (New York City, Long Island, No. NJ); Yale Comprehensive Cancer Center (CT, RI); UCLA (California area codes 818, 805, 707, 415, 408, 209); Lucille Parker Markey Cancer Center (KY); Fred Hutchinson Cancer Center (WA, OR); Dana-Farber Cancer Center (MA, ME, NH, VT); Roswell Park Memorial Institute (New York area codes 518, 315, 914, 716, 607); Ohio State Univ. (OH); Duke Univ. Medical Center (NC, SC); Sylvester Comprehensive Cancer Center (FL, GA, PR); Penrose Hospital (CO, NM, WY); Utah Regional Cancer Center (UT, ID, MT, NV); Illinois Comprehensive Cancer Center (IL).

The Alabama Comprehensive Cancer Center, Univ. of Kansas Medical Center, and Thompson Cancer Survival Center in Tennessee have agreed to serve their respective states as independent offices.

The Univ. of Wisconsin, Michigan Cancer Foundation, and Univ. of Hawaii, all of which were funded in the previous contract period, were not successful in the recompetition. Their continuation as independents hinges on obtaining other support.

Utah presently is funded only for serving that state. Addition of Idaho, Montana, and Nevada is conditional on future funding availability.

The Univ. of Southern California had the CIS contract in Los Angeles previously, with UCLA as a subcontractor. UCLA submitted its own proposal in the recompetition, as did USC; UCLA prevailed. USC is not considering continuing as an independent.

Those areas of the country not covered by a CIS office are served by the national CIS. Callers to the 1-800-4-CANCER number automatically are channeled to the national service, operated by Biospherics Inc. under a separate contract with NCI.

Kate Duffy of OCC is chief of the Cancer Information Service.

RFPs Available

Requests for proposals described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. 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 announcements from other agencies will include the complete mailing address at the end of each.

RFP NIH-ES-90-05

Title: In vitro transformation of oncogene primed cells by genotoxic chemicals

Deadline: Approximately April 6

The National Institute of Environmental Health Sciences is soliciting proposals for a project to study in vitro transformation induced by chemicals in cells that are engineered to express cellular oncogenes or other genes likely to be involved in neoplastic processes.

The conceptual framework for this project is the hypothesized cooperation between experimentally activated oncogenes and chemically induced genetic effects where neither event alone is sufficient to cause transformation. The genetic manipulation is directed to the activation of proto-oncogenes, inappropriate expression or transcriptional activation, rather than somatic mutation in coding sequences. Proto-oncogenes that are cloned into retroviral derived vectors and introduced into recipient cells will provide the method for generating target cell populations.

The project will include the following tasks: Task 1--Recombinant DNA cloning, construction of proto-oncogene recombinants and generation of retroviral construction of proto-oncogene recombinants and generation of retroviral vectors for nonmutated mouse proto-oncogenes. Task 2--Introduction of vectored oncogenes into test cells and characterization of cellular phenotypes. Task 3--Characterization of vectored subclones exposed to selected chemicals.

A three year contract is anticipated. The government estimates the project will require approximately 1.5 professional person years, 1.5 technical person years and .25 administrative person years of effort per year.

Requests should reference the RFP number and should be sent to NIEHS, Contracts and Procurement Management Branch, OM, ATTN: Mary Armstead, Contracting Officer, 79 T.W. Alexander Dr., 4401 Building, PO Box 12874, Research Triangle Park, NC 27709.

RFP NIH-ES-90-08

Title: A study of tumor suppressor genes

Deadline: April 27

The National Institute of Environmental Health Sciences is soliciting proposals for a project designed to identify and ultimately clone tumor suppressor genes in rodents. The primary strain of mice to be examined is the B6C3F1 mouse, though other heterozygous rodent strains also may be considered.

The contractor will be required to 1) identify polymorphic probes in the B6C3F1 mouse using new or previously described probes that have been mapped to chromosomes in the mouse or other species (probes shall be made available to laboratories as designated by the project officer), 2) if necessary, map these probes to specific chromosomes in the mouse and the human, 3) identify mouse chromosomes that show loss of heterozygosity in specific tumor tissue DNAs using these FPLP probes, 4) when chromosomes that show loss of heterozygosity in tumors are identified, regionally localize relevant FRFLP probes in these chromosomes, and 5) reprobe membranes with selected oncogene probes to determine if certain oncogenes are amplified in tumors studies.

A five year contract is anticipated. The government estimates that the project will require approximately 1.5 professional person years and 1.5 technical person years per contract year. All responsible sources may submit a proposal which shall be considered.

Requests should reference the RFP number and should be

forwarded to: NIEHS, James Doyle, Contract Specialist, Contracts and Procurement Management Branch, OM, 79 TW Alexander Dr., 4401 Research Commons Bldg., P.O. Box 12874, Research Triangle Park, NC 27709.

RFP NCI-CO-03881
Title: Booklet printing
Deadline: April 23

Single award for a fixed price contract for delivery 45 days after award of contract. Production area, assumed 125 mile radius of zero milestone, Columbia, MD. Bidders outside area must furnish documentation of their ability to meet schedule. Inspection of source materials will be April 5-6, 8 a.m.-5 p.m. at NIH Bldg. 31 Rm 10A30, 9000 Rockville Pike, Bethesda, MD. For an appointment contact Erin Lange one week prior to source review. Booklet. 500,000 copies of 16 pages with separate wraparound cover. Printed in four-color process, 1 PMS, plus varnish on cover; 2 PMS colors on text pages. Operations include saddle stitch, trim, printing, folding, negatives, packaging, mailing and f.o.b. destination to Columbia, MD. Contractor furnish paper. Quality attributes level II for printing and finishing. Bid request on Standard Form 26. Phone, telegraph, fax request not acceptable.
Contract Specialist: Erin Lange
RCB Executive Plaza South Rm 608B
301/496-8628

RFAs Available

RFA 90-CA-10
Title: Human T-cell lymphotropic viruses in human neoplasia
Letter of Intent Receipt Date: June 4
Application Receipt Date: Aug. 3

Little is known about the viral and host factors involved in HTLV pathogenesis which result in cancer induction vs. those which result in neurotropic damage. An elucidation of the overall pathogenic mechanisms of HTLV is needed. The goals of this RFA are to stimulate research on the role of HTLV-1-like viruses in human neoplasia and other diseases with suspected retroviral etiology and the development of animal models to delineate the mechanisms of disease pathogenesis.

Studies will be invited in, but not limited to the following areas:

1) Systematic laboratory studies to define the possible retroviral etiology of diseases whose clinical features suggest a retroviral role, including diverse hematologic and solid tissue malignancies.

2) Exploration, through laboratory studies, of HTLV-2 disease pathogenesis and its role in human cancer.

3) Studies to address the basis for the differing pathogenic potentials of the HTLV isolates, i.e. molecular mechanisms for the leukemogenic vs. neurotropic behavior of the virus, including the comparison of genomic sequences of HTLV isolates from leukemia patients, IV drug abusers and TSP patients, and comparison of virus-target cell interactions of HTLV infections which result in neoplasia vs. those that result in neurotropic damage.

4) Laboratory studies to determine the role of cofactors (genetic, viral, bacterial) in the triggering of disease expression associated specifically with HTLV-1 infections.

5) Identification of host and viral factors responsible for the repressed state of HTLV-1 genome in vivo.

6) Development of animal/tissue culture models of human lymphoproliferative and neurologic diseases, including the use of mutant retroviruses with altered pathogenic properties and transgenic mice.

The RFA would support studies that seek to answer what mechanisms are involved in conferring the HTLV viruses with differing pathogenic potentials, such as cancer induction and neuropathogenicity, but would not support extramural studies which primarily involve the isolation and demonstration of retroviruses in neurological diseases. Where appropriate, collaborative arrangements to facilitate the achievement of research goals should be considered. Applications should contain as goals both methodological development and application to a specific area of HTLV oncogenesis/pathogenesis.

Approximately $800,000 in total costs per year for five years will be committed to specifically fund applications that are submitted in response to this RFA. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. The total project period for applications submitted in response to the present RFA should not exceed five years. The earliest feasible start date for the initial awards will be April 1, 1991. Although this program is provided for in the financial plans of NCI, award of grants pursuant to this RFA is also contingent upon the availability of funds for this purpose. Nonprofit and for profit institutions are eligible to apply. Foreign as well as domestic institutions are eligible.

Copies of the complete RFA may be obtained from Dr. Padman Sarma, Program Director, RNA Virus Studies I, Biological Carcinogenesis Branch, Div. of Cancer Etiology, NCI, Executive Plaza North Rm 540, Bethesda, MD 20892, phone 301/496-9734.

RFA 90-CA-12
Title: Clinical diagnostic studies of brain tumor using pet and other imaging modalities
Application Receipt Date: May 18

The Radiation Research Program in NCI's Div. of Cancer Treatment announces the availability of an RFA to advance diagnostic clinical research using PET and other imaging modalities in evaluating essential features of brain tumor metabolism to improve knowledge of tumor growth, patient therapy, patient prognosis and management.

Advances in the last decade in imaging and imaging related technology have permitted more precise anatomic/pathologic diagnosis and also are providing functional information. These advances potentially extend the capacity of imaging method from its customary role of anatomic diagnosis with inferred function to direct observation of physiologic and pathophysiologic phenomena and are the direct result of the technological development and clinical use of PET, magnetic resonance spectroscopy, radiolabeled monoclonal antibodies and other imaging modalities. In view of successes of PET, MRS and other modalities in providing significant functional information about normal and malignant tissues in vivo, clinical study of brain tumor metabolism has become not only possible but timely.

The overall objective of this RFA is to advance the use of PET, MRS, radiolabeled monoclonal antibodies and other modalities to evaluate essential features of brain tumor metabolism, improve our knowledge of tumor growth, determine effects of therapy and follow patients prognosis and management. In other words, the aim of this RFA is to improve our understanding of pathophysiology of brain function in patients with primary brain tumors using PET and other radiographic methods at diagnosis and during the course of therapy.

Where feasible and appropriate, applications for the proposed clinical studies should include a suitable representation of minorities and women. If the applicant cannot comply, a clear rationale for their exclusion must be provided.

It is anticipated that approximately three or possibly four scientifically meritorious applications can be funded.

Requests for copies of the complete RFA may be addressed to Dr. Matti Al-Aish, Acting Chief, Diagnostic Imaging Research Branch, Radiation Research Program, NCI, NIH, Executive Plaza North Suite 800, Bethesda, MD 20892, phone 301/496-9531.