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DCT BOARD APPROVES REISSUING SURGICAL ONCOLOGY RFA FOR PLANNING, OKAYS NEW AND RECOMPETING PROJECTS

The Board of Scientific Counselors of NCI's Div. of Cancer Treatment last week gave concept approval to reissuing the request for applications for planning grants to develop surgical oncology research programs. In doing so, the Board backed DCT's policy of continuing certain initiatives aimed at stimulating interest in surgical oncology.

The Board gave concept approval to more than $5 million in grant and contract supported projects, including nearly $3 million for five

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In Brief

BARRY PIERCE NEW DCCP BOARD CHAIRMAN; ADAMSON SEEKS ADs FOR CHEMICAL, BIOLOGICAL CARCINOGENESIS

BARRY PIERCE, professor of pathology at the Univ. of Colorado and former member of the Board of Scientific Counselors of NCI's Div. of Cancer Cause & Prevention, will be the new chairman of that Board, replacing Peter Magee, whose term expired with last week's meeting. Other new members of the Board will be Louise Lombard, veterinary pathologist with Argonne National Laboratory; and Lee Wattenberg, an expert in chemical carcinogenesis at the Univ. of Minnesota. . . . **RICHARD ADAMSON**, DCCP director, announced that he intends to recruit associate directors for both the Biological and Chemical Carcinogenesis Programs. Each will have responsibility for extramural and intramural research within their respective programs. . . . **CORRECTION**: Gertrude Elion is the fourth woman elected president of the American Assn. for Cancer Research, not the third (***The Cancer Letter,*** June 3). Omitted was Elizabeth Miller, McArdle Laboratory, who was president in 1976-77. . . . **AN ACTING CHIEF** of the Clinical Trials Section is needed in the Biological Resources Branch of NCI's Biological Response Modifiers Program. The job entails planning and development of BRM clinical trials, both those conducted at the program's facility in Frederick, Md., and extramural trials at institutions with BRMP master agreements. The Senior Expert appointment pays from $41,277 to $53,661. Those interested should submit Personal Qualification Statement SF-171 with three references to Ms. Cynthia Kauff, Personnel Management Branch, NCI, Bldg. 31 Rm 3A23, Bethesda, Md. 20205. Applications must be postmarked by Aug. 15. Phone Kauff for further information at 301-496-6864. . . . **JOHN WEINER**, associate professor of medicine at the Univ. of Southern California, has been named administrative director of the Childrens Cancer Study Group. Weiner, a member of NCI's Cancer Clinical Investigation Review Committee, has worked part time with CCSG as a statistician since 1971. He replaces Richard Honour, who left for a position in industry.

DCT BOARD GIVES CONCEPT APPROVAL TO MORE THAN $5 MILLION IN PROJECTS

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RFA's (including the surgical oncology planning grants), and over $2 million in new and recompeting contracts. The Board also approved the concept of noncompetitive renewals for four contract supported projects costing almost $1 million.

All cost figures are staff estimates of first year awards.

DCT Director Bruce Chabner presented an update on the division's initiatives in surgical oncology. The RFA for P20 planning grants, originally issued in 1981, had 28 submissions of which only five were funded. "Many of the grants that were submitted were not planning grants in any real sense," Chabner said. "Some of the problems here were with applicants and some with NCI staff. The present version has been reworded for clarification concerning its purpose, which remains the planning of research proposals."

The new RFA, which will be released sometime this summer, will allocate $500,000 for the three year planning grants. The staff narrative describing the program:

Purpose of this grant is to plan and develop a program for research in surgical oncology. The treatment of cancer has evolved as a multidisciplinary effort involving (but not limited to) the disciplines of medical, pediatric, surgical and radiation oncology. The disciplines of medical, pediatric and radiation oncology have developed strong programs in clinical investigation, but academic development in surgical oncology has not kept pace. For most cancers, surgery is the keystone of primary treatment, which is the setting in which advances in multidisciplinary therapy are likely to occur. Since such advances are an important continued development of the multidisciplinary treatment of cancer and a long range objective of the Div. of Cancer Treatment, the attainment of this goal requires substantial strengthening of academic programs in surgical oncology.

Examples of proposals that NCI considers for support include:

—Planning the development of a research program in surgical oncology within the context of available staff and facilities.

—Feasibility studies that permit the applicant to gather data to determine the potential of developing such a program, and to explore the validity of various approaches to implementing the program.

Chabner said that current DCT initiatives toward support of surgical oncology "are along many fronts—increasing effectiveness of teaching at medical schools; training grants for young investigators; planning grants for medical school faculty members; program announcements to encourage submission of surgical oncology research grants by established investigators; a more activist approach by DCT advising applicants regarding revisions of unfundable grants; and assisting the Div. of Extramural Activities in selecting proper individuals to sit on review committees which consider surgical applications. We feel that these steps will, in time, have a positive measurable effect on the development of surgical oncology."

Chabner said the program announcement for surgical oncology R01s, first published in 1981, will be reissued periodically. "The present version has been revised somewhat to clarify some of the wording and to be less apparently restrictive than the original version. The changes in wording are minor. We feel that it is important to reissue this announcement periodically and plan to do so four times during the next year to increase awareness of it."

Chabner reviewed other DCT efforts in surgical oncology:

• Physician Investigator Development Awards (K08)—The announcement for this award was published last March as "Clinical Investigators Award." A specific review panel and dates for review are yet to be set. Funds from the Div. of Resources, Centers & Community Activities are to be supplemented by DCT monies as necessary in making awards to up to eight surgeons per year with meritorious applications. The awards will be for three years, to a maximum of $30,000 per year plus up to $10,000 for supplies. The stipulation is that the awardee will spend no less than 75 percent of his or her time in research. MDs and DOs will be eligible, unless they already have a PhD.

• R01 Review—The Experimental Therapeutics Study Section has been divided into a preclincal and a clinical part. Most of the clinical R01s submitted by surgeons will be reviewed by the clinical part of ET. The executive secretary of this committee was given a list of surgeons qualified to serve on this study section for the review of grants. It is not yet clear whether one or more of these individuals will be asked to serve as permanent members of this study section, or will be asked to serve in an ad hoc capacity when the specific need arises.

• Surgery as a Cancer "Activity"—The designation of surgery as an "activity" would allow for easier tracking of submitted grants by the head of the Surgery Section and would therefore be a significant administrative advantage. The NCI Executive Committee has discussed this issue and felt several months ago that the draft of the guidelines describing surgical oncology was too broad to be useful. A revised version of these guidelines is in its final stages and this matter will be discussed again with the Executive Committee as soon as a final version has been drawn up.

• Professional Oncology Education Programs (R25)—These are grants to schools of medicine, dentistry, public health and nursing to increase emphasis in certain areas of health science. The money pays for salaries for individuals engaged in these efforts, which primarily involve teaching, course development, etc. Surgical oncology has been added to the

list of targeted areas, which included epidemiology, nutrition, prevention, cancer control, and radiation oncology. "We feel that this is a potentially fruitful way of capturing the imagination of medical students at a time when their ideas about career choices are still very much in flux," Chabner said.

Philip DiSaia, who is retiring as chairman of the Board's Surgical Oncology Research Development Subcommittee since his term on the Board has expired, applauded the division's efforts and said that for the most part SORDS' recommendations had been carried out. "Now we need some long range planning." William Shingleton, a member of SORDS, agreed.

The Board gave concept approval to other new major RFAs, for the Developmental Therapeutics Program, Radiation Research Program, and Biological Response Modifiers Program.

Discovery and characterization of multidrug resistant human and other mammalian tumor cell lines. A total of $500,000 will be set aside for first year awards, with an anticipated project period of three years. Developmental Therapeutics Director John Driscoll said the amount probably would fund four grants. Staff description:

The development of drug resistance in tumor cell populations treated with chemotherapeutic agents has been recognized as a major problem in cancer treatment. Detailed studies in Chinese hamster and murine cell systems have shown that under some selective conditions, e.g. colchicine, vincristine, or adriamycin treatment, cell populations demonstrating a pleiotropic or multidrug resistant phenotype emerge. In many of these cells, broad spectrum resistance to multiple agents of different modes of action is associated with reduced intracellular accumulation of drug and the appearance of a membrane glycoprotein marker. Recently, laboratory evidence has been presented that multidrug resistant cells occur in human tumor cell populations. This latter evidence is consistent with clinical experience, particularly with previously treated patients, wherein resistance to multiple agents of different modes of action is observed.

While some potentially important collateral sensitivities have been observed among mammalian cell types showing the multidrug resistant phenotype, it seems likely that additional new agents specifically useful in treating these resistant cells will be needed. In order to establish an evaluation program to identify such agents, NCI will require well characterized multidrug resistant human tumor cell lines in which new agents can be studied. This is an RFA for grants which propose to discover and characterize multidrug resistant human and other mammalian tumor cell lines that have potential for this purpose.

Multidrug resistant tumor cell lines either may be selected in vitro using the techniques developed in mammalian cell culture systems or they may be established directly from patients shown to be clinically resistant to chemotherapy. Characterization of the cell lines must include: verification of the human origin of the cells, demonstration of tumorigenicity in suitable animal hosts, detailed evaluation of the relative drug resistance of the cells in vitro, and evaluation of the mechanism of resistance for each cell line. Particular attention should be paid to the stability of the drug resistant phenotype.

Applicants will be requested to provide samples of each cell line discovered to the NCI Tumor Bank and to provide detailed information to NCI on the discovery and characterization of these cell lines.

Basic research in factors influencing NMR relaxation times. A total of $1 million will be set aside for first year awards, with an anticipated project period of three years. Radiation Research Director David Pistenmaa said that amount probably would support six grants. Staff description:

Nuclear magnetic resonance imaging provides not only anatomical cross sectional images but also characteristic T_1 and T_2 paramagnetic relaxation times. T_1 is the time it takes the sample to become polarized, i.e., for the magnetic spins of the nuclei in the sample to line up with the strong external magnetic field of the imaging system. It is also the time constant of return of these spins to equilibrium after being stimulated by the radio frequency pulse. It is affected by the surrounding environment in the tissue and by the vibrations of the molecules in the neighborhood. Typically, T_1 is longer for more liquified samples and for pathological tissues (including edema) than for normal solid tissues. T_2, on the other hand, is a measure of the time it takes the magnetic nuclear spins to get out of phase with each other after being magnetized because of the interactions of the local spins on each other.

When T_1 and T_2 are both measured, the combined result can be found to be characteristic of bone, muscle, fat, blood, abscess, or tumor, for example, depending on the values. Such information has already been used to color code the tissues to distinguish their distributions in the NMR tomograph in both animals and humans. It is hoped that noninvasive differential diagnosis of normal vs. pathological tissue may one day be made possible through these relaxation time measurements.

However, more basic research is needed to understand the biophysical and biochemical factors which influence the T_1 and T_2 parameters as a basis for this capability. In vivo relaxation times are the result of complex contributions from water, lipids, and blood flow, among others. In vivo studies in animals and humans are required as well as in vitro studies of excised tissues to correlate NMR findings with histopathology. Fundamental studies in tissue culture may also be helpful.

Many other research programs in NMR imaging and MNR spectroscopy are being supported for their growing applications in medical imaging and in analytical research. Knowledge about the conditions which determine T_1 and T_2 will contribute to the fundamental understanding of the differences between normal and abnormal tissues and will enhance the value of these other NMR activities.

Chabner said that the division's current budget for FY 1984 does not include money for this project. However, NCI Director Vincent DeVita has assured him that if NCI receives a final appropriation above the President's request, the project would be funded.

Board member Theodore Phillips said this project "is critical in the development of NMR. There are 30 units going in around the country this year. One million dollars is not much. It is urgent that money be made available to help us evaluate these images."

Discovery of strategies for the in vitro and in vivo preclinical testing of monoclonal antibodies and their immunoconjugates for biologic and therapeutic effectiveness. A total of $500,000 will be set aside for first year awards, which will be three year cooperative agreements. Staff description:

Monoclonal antibody and immunoconjugate therapy have demonstrated antitumor effectiveness in both animal models and human situations. The potential number of antibodies and immunoconjugates that can be produced is enormous. The ability to predict in vivo efficacy of these agents in humans by a preclinical testing mechanism would be of significant value in the process of developing the best monoclonal antibody reagents for utilization in cancer treatment.

Current techniques available for the preclinical evaluation of the effects of monoclonal antibodies and immunoconjugates on tumor cells include in vitro cytotoxicity studies, soft agar cloning assays, Winn assays, rodent xenografts, and the subrenal capsule assays. Evaluation of monoclonal antibodies and immunoconjugates in each of these assays has not been extensive and it remains to be determined which will be helpful and effective in defining, elucidating, or predicting mechanisms of activity and/or clinical effectiveness. Proposals are sought that will define the predictive capability of these assays or develop new assays with the ability to predict antitumor efficacy of monoclonal antibodies and immunoconjugates. A further goal of the studies should be to provide information relevant to understanding the mode of action and biological mechanisms by which effective antitumor monoclonal antibodies or immunoconjugates exert their effects in cancer treatment.

The Biological Response Modifiers Program, through a contract, has a number of monoclonal antibodies and antibody-toxin conjugates available for study. The program has the desire and the need to explore and develop strategies for preclinical testing and to correlate these with ongoing clinical and animal model trials. BRMP also has an ongoing preclinical common tract screen which evaluates for biological response modification in assays of T and B cell function, NK cell activity and macrophage cytotoxicity. Plans are under way to develop a specific tract screen for such agents as monoclonal antibodies, for which the common tract screen would be inappropriate. Cooperative agreement holders would be required to interdigitate with the activities of both screens. A substantial amount of federal involvement will be required to accomplish this goal. Because of this, we propose the use of the cooperative agreement mechanism.

Discovery of new biological evaluation models for the Drug Development Program. A total of $425,000 will be set aside for first year awards, with an anticipated project period of three years. Staff description:

There is a need to discover new models to identify better anticancer agents. Despite remarkable advances in the surgical and radiological treatment of primary neoplasms and the use of aggressive adjuvant therapies, most cancer patients die of metastatic disease. Although considerable progress has been made in finding agents to treat and even cure some forms of cancer, there remains a critical demand for effective therapies for the major solid tumors, including those of the breast, colon and lung. The current strategy of the drug development program is to screen 10,000 carefully selected materials in an in vivo P388 leukemia prescreen followed by an evaluation of about 250 compounds in a screen consisting of a panel of four in vivo tumor models (L1210 leukemia, B16 melanoma, MX-1 human mammary xenograft and the M5076 tumor). Other tumor models, such as the CD8F1 mammary or Colon 38, are used for special studies, such as the evaluation of closely related structures to determine the one with the most desirable properties for clinical development. The in vitro human tumor colony forming assay also is being evaluated as a parallel screening system.

NCI is interested in discovering new in vitro and in vivo models for drug evaluation at either the prescreen or screening levels. Proposed projects must address relevance to the cancer problem and potential for use as an evaluation system for new anticancer agents. Reproducibility, labor, material and equipment requirements should be considered. Recent advances in our knowledge concerning the identification of oncogenes, the processes associated with cellular differentiation, novel assays for tissue specific cytotoxins, the growth of genetic mutant cell cultures, and the growth of human tumors which metastasize in nude mice provide some examples of research areas which offer opportunities for the development of new methods or tumor models for application in the drug development program. NCI will provide a number of suitable compounds for evaluation in the proposed assays. Because of the anticipated substantial involvement of NCI in the development of protocols for the proposed models and drug supply, the cooperative agreement mechanism is proposed.

"How does this differ from the Drug Discovery Program?" Phillips asked. "This money might better be spent by adding to that, funds for which are inadequate."

(The new initiative, in which NCI will help establish multidisciplinary Drug Discovery Groups, will get under way with issuance of the RFA in July. The DCT Board approved the concept of that program last year.)

"This program will develop models, not drugs," Driscoll said. "There is a continuing need for new models."

"If we don't have new models, we'll come out with the same things over and over," Board member Paul Calabresi said.

The Board approved two new concepts which will be funded by contracts.

Development of an in vitro screening system using human tumor cell lines. Proposed first year award, $200,000, three and a half years.

In vitro screening methods offer several potential advantages over screening in animal models. These include: lower cost, shorter assay time, easier laboratory control and assay standardization, and the requirement for very small amounts of test compound. Additionally, in vitro models based on the use of human tumor cells can be readily developed.

Recent drug screening trials with a human tumor colony forming assay (clonogenic assay) have identified a number of active compounds, including novel structural leads, which were negative and relatively nontoxic in the murine P388 leukemia prescreen. This result suggests that either the cell culture system is more senstive than the current prescreen or that it is identifying a different class of agents. Further in vivo testing of these agents is currently under way which should clarify this situation. In either case, such in vitro testing would seem to be an effective way of identifying compounds which would otherwise be lost to the screening program. Because of the technical complexity and associated cost of the colony forming assay, it is not feasible to test all of the P388 prescreen negative, nontoxic compounds (currently about 8,500 per year) in this system. The purpose of this project is to develop and evaluate a simpler in vitro screening system based on the use of human tumor cell lines which may be used on a large scale to screen these compounds.

Investigators will be requested to develop three to five human cell lines for use as an in vitro screening panel. A large number of well characterized human tumor cell lines are currently available through the NCI Tumor Bank as well as commercial and private collections. Many of these retain differentiated characteristics in vitro and therefore offer the potential for evaluation of the effects of active agents on differentiation in a secondary level of testing. Various human tumor cell lines and normal human fibroblast lines demonstrate significant differences in sensitivity to established agents. These differences have been related to differences in DNA repair phenotype as well as numerous other cellular properties. Detailed protocols for measurement of drug effects based on inhibition of colony formation, or an endpoint of comparable sensitivity, will be required for each cell line

considered for inclusion in the cell line panel. Protocols will include provision for metabolic activation in at least one element of the cell line panel, for example, a continuous human hepatoma cell line has recently become available which demonstrates broad ability to activate procarcinogens and anticancer drugs such as cyclophosphamide. This cell line offers a unique opportunity to provide human cell mediated metabolic activation in a very practical way.

A drug sensitivity profile will be established for each candidate cell line based on response to a battery of standard anticancer drugs. Cell lines will then be selected for inclusion in the final screening panel based on sensitivity and reproducibility of response to the standard agents.

Production of a liposome pharmaceutical for the delivery of agents capable of activating pulmonary macrophages and the development of liposomes capable of delivery to the liver. Proposed first year award, $250,000, two years.

Liposomes (phospholipid vesicles) are effective biological carriers of agents. Dried phopholipids swell, upon rehydration, to form multilamellar structures into which a variety of agents may be incorporated. Depending on charge and composition, liposomes may be targeted to and incorporated by a variety of internal cellular components.

Liposomes may be prepared from a variety of phospholipids but the major components are usually phosphatidylcholine, cholesterol and charged cell lipids. Variations in lipid composition, membrane charge, and carbohydrate determinants on the vesicle surface can affect in vivo tissue distribution. Multilamellar vesicles of defined composition and charge have been developed and targeted to the alveolar macrophage. These liposomes, containing macrophage activating factor, muramyl dipeptide, or muramyl tripeptide phosphatidylethanolamine, are effective in activating murine alveolar macrophages in vitro or in vivo and are therapeutically effective in reducing pulmonary metastases in murine models. Component A of this RFP will be directed towards the procurement of a pharmaceutical for clinical trials consisting of a liposome preparation containing an agent capable of activating human alveolar macrophages.

Methods exist for varying surface composition for targeting liposome delivery to liver and spleen although, in general, the reticuloendothelial system in these organs is the system responsible for lipsome removal. Experiments aimed at demonstrating therapeutic effectiveness with hepatic metastases have not been performed. Component B of this RFP will support experiments aimed at the development of liposome preparations with proven efficacy in the activation of hepatic macrophages. The relationship of the situation (versus activation of blood monocytes) in the treatment of hepatic metastases can then be explored.

Recompetitions and noncompetitive procurements approved by the Board will be published next week in *The Cancer Letter.*

CONCEPT REVIEW FIGURES ARE ESTIMATES ONLY: RFPs, RFAs NOT YET AVAILABLE

The dollar estimates with each concept review brought before the various boards of scientific counselors are not intended to represent maximum or exact amounts which will be spent on those projects. They are intended only as guides for board members to help in determining the value of the projects in relation to resources available to the entire program or division. Responses should be based on the workscope and description of goals and methods included in the RFPs (contracts) and RFAs (grants and cooperative agreements). Availability of RFPs and RFAs will be announced when the Institute is ready to release them.

FREI, FREIREICH SHARE ONE GM AWARD; AMES, ERIKSON WIN THE OTHER TWO

Four scientists were named this week as winners of the 1983 General Motors Cancer Research Foundation Awards. Each of the awards offers a gold medal, $100,000 in cash, plus $30,000 to support a workshop.

Emil (Tom) Frei and Emil (Jay) Freireich, who together developed the first cure for leukemia and whose studies profoundly affected modern cancer chemotherapy, were named winners of the Charles F. Kettering Prize for the most outstanding recent contribution to the diagnosis or treatment of cancer. They will share the $100,000 prize.

Bruce Ames, who developed the world's most widely used test to determine whether a chemical damages DNA and therefore may cause cancer, won the Charles S. Mott Award for the most outstanding recent contribution to the causes and ultimate prevention of human cancer.

Raymond Erikson, the first scientist to identify a chemical made by a cancer gene, won the Alfred P. Sloan Award for the most outstanding recent basic science contribution to cancer.

Frei is director and physician in chief of the Dana-Farber Cancer Institute and professor of medicine at Harvard Univ. School of Medicine. Freireich is professor of developmental therapeutics and chairman of the Dept. of Developmental Therapeutics at the Univ. of Texas System Cancer Center/M.D. Anderson Hospital & Tumor Institute. He is also professor of medicine at the Univ. of Texas Medical School.

Ames is professor of biochemistry at the Univ. of California (Berkeley). Erikson is professor of cellular and developmental biology at Harvard.

"There are more than 10,000 American children alive today who, born at any other time in history, would have died of leukemia," the GM Foundation said in a news release. "Their cures are dramatic proof of the significant improvements that have come to the treatment of childhood leukemia in the past few decades. Much of the pioneering research that led to this achievement was the work of Frei and Freireich. These researchers, working together for 17 years, developed the first treatment for leukemia that truly cured patients. In the process, they established nearly all the principles of scientific chemotherapy trials for cancers of all kinds.

"The type of therapy they devised—using many drugs in combination—virtually revolutionized cancer medicine and is now one of the mainstays of treatment for most types of cancer. Combination therapy for leukemia 'has saved the lives of more cancer patients than any other advance over the past 25 years,' commented Charles Moertel, head of oncology at the Mayo Clinic.

"Frei and Freireich began their scientific careers at NCI. 'They made a fascinating team to watch,'

said Gordon Zubrod, who hired them then and who was, at the time, NCI's clinical director. 'Their interactions and collaborations were so combined that the research arose from the two of them. It was truly a synergistic association. Their contributions are important not only in curing acute lymphocytic leukemia, but because they profoundly influenced the chemotherapy of Hodgkin's disease and the whole of present day chemotherapy.'

"The life and death of minute bacteria living in tiny petri dishes in a laboratory in Berkeley has triggered a worldwide revolution in environmental health," the GM release continued. "High powered legal battles, nationwide health legislation and billion dollar industry cleanups to remove possible environmental carcinogens from food, clothing and other common products have turned on the seemingly uneventful lives of these one celled microbes.

"The special bacteria were genetically engineered by Ames, who used them to develop a test that has become the world's most widely employed screen for determining whether a chemical is likely to cause cancer. The test measures mutations in bacteria. The Ames test is usually the first in a series of evaluations of a chemical which are used to estimate its cancer causing potential to man. Tests in mice and other animals as well as epidemiological studies in man are necessary also.

"Ames work 'has formed the foremost current approach to the screening of environmental factors and chemicals and has represented a major contribution to human health and basic understanding of the etiology of cancer,' said Thomas Edgington, professor of immunology at the Scripps Institute. In addition to developing the screening test, Ames established the relationship between a chemical's ability to cause mutations and its potential for causing cancer. He also helped clarify how mutations of DNA occur and, recently, began to identify naturally occurring anticancer substances.

"The Ames test is currently used in more than 3,000 government, industry and university laboratories throughout the world as an early warning system for detecting mutagens and possible carcinogens. In the 12 years since its developing, more than 5,000 chemicals have been screened with the Ames test.

"Scientists are on the brink of understanding how cancer begins," the GM release continued. "A number of startling discoveries in the past few years have revealed what seems to be a common biochemical change in the cell that triggers the first steps toward malignancy. An understanding of this process may eventually help cancer specialists develop new ways to diagnose, treat and even prevent cancer.

"The excitement felt by many biologists is reflected in the awarding of the Alfred P. Sloan Prize to Erikson. A leader in the emerging field of cancer genes, Erickson is the first scientist to identify the chemical made by such a gene, uncover its unique biological properties and show that it could alter cell metabolism, producing changes associated with cancer.

"Erikson's research has been a systematic attack on the problem of identifying exactly what happens in a cell when a cancer gene is switched on. 'Unquestionably, Dr. Erikson's group has made the major advance in basic cancer research in the past five years,' said William Rawls, professor of pathology at McMaster Univ. in Hamilton, Ontario. 'He has made an important breakthrough in the understanding of the precise molecular mechanism of oncogenesis.'

"Erikson's work is a recent discovery, but it has already stimulated a new field of study investigating the biochemical ways normal cells become cancerous. Since his initial report in 1977, other researchers have discovered several additional chemicals made by cancer genes, most of which affect cells in the same unique way. This is an important conceptual advance for cancer specialists. They have long suspected that, though there are more than 100 types of cancer, a single mechanism would be found by which all cancers arise. Though it isn't certain yet that this is the case, evidence suggests that one or a few biochemical changes may be characteristic of most cancers."

AACI, ASCO, ACCC HOLD "USEFUL" MEETING WITH HCFA ON DRG ISSUE

Representatives of the Assn. of American Cancer Institutes, American Society of Clinical Oncologists and Assn. of Community Cancer Centers met with officials of the Health Care Finance Administration last week to express their concerns over DRG reimbursement for cancer treatment.

Francis McKay, associate director for administration and finance of Fox Chase Cancer Center, represented AACI; John Potter, director of the Vincent Lombardi Cancer Research Center at Georgetown Univ., represented ASCO; and Robert Enck, director of oncology at Our Lady of Lourdes Hospital in Binghamton, N.Y., represented ACCC.

The three met with Michael Maher, director of the HCFA Office of Reimbursement Policy, which is in the process of developing guidelines for implementing DRG regulations, including the exceptions which the HHS secretary may by law make for certain institutions.

Participants agreed it was a "very useful" meeting. They explained how DRG can unfairly impact cancer care providers, especially those with patients on research protocols and the centers with a high percentage of tertiary care patients.

"I'm confident HCFA will make some accommo-

dation," McKay said following the meeting. "It's too early to tell if that will be acceptable, however."

On another Washington front, the House committee report on the Health Research Extension Act of 1983, the Waxman bill which among other things extends the National Cancer Act, called attention to the fact that the budget resolution recently passed by the House for FY 1984 "includes, at the recommendation of the Committee, sufficient funds to preclude the elimination of support for 16 cancer centers."

The report deals with an authorization, not an appropriation, bill, but it does demonstrate the support in the House for additional NCI funds above the President's budget to restore money cut from the center core grant budget.

The Waxman bill provides a line item authorization for center core grants, a provision opposed by the Administration. The attempt to drastically cut core grant funds supported the case of those who have argued for the line item.

"The specific authorization of appropriations for cancer research and demonstration centers indicates the Committee's strong support for the cancer center core grant program," the report said. "The Committee believes that cancer center core grants are essential to the National Cancer Program and should, during periods of fiscal restraint, not incur program reductions disproportionate to other institute activities."

The Senate Appropriations Committee, in a 1983 supplemental appropriations bill, has added $9.4 million to the NIH budget for research on AIDS, including $3.3 million for NCI. The committee report on the bill noted that the extra money would permit NCI to fund 73 percent of approved AIDS-related grants. "The research grants would include studies on the nature of the defective regulators of immunity in AIDS, cause and reasons for loss of disease fighting capabilities of AIDS patients, and herpes viruses and immune responses in male homosexuals," the report said. "Intramural research efforts would be expanded to isolate a causative virus from AIDS patients. In addition, facilities would be modified to provide the proper isolated research environment."

The committee also expressed concern about high cancer rates among Hawaiians. "The committee has recently learned that peoples of Hawaiian ancestry have the highest incidence of cancer in our nation. The rate of cancer cases among Hawaiian men is reported to be 465 per 100,000 and that for Hawaiian women 408.5 per 100,000. This compares to 371.6 for caucasian men and 301.2 for caucasian women. The committee was very concerned to learn of these statistics and urges the National Cancer Institute to give greater attention to this native Hawaiian population. The committee also directs NCI to review its efforts to address the unique needs of all native American peoples in the Pacific basin region, in light of the native Hawaiian data."

DCCP BOARD GIVES CONCEPT APPROVAL TO 18 NONCOMPETITIVE CONTRACTS

Noncompetitive contracts receiving concept approval last week from the Board of Scientific Counselors of NCI's Div. of Cancer Cause & Prevention totaled 18, with first year costs estimated at $2 million and the total for the lives of the projects at $6.8 million.

Five of the concepts were for new procurements:

- U.S. cancer mortality rates and trends, 1950-79. Environmental Protection Agency Health Effects Research Laboratory, $110,000, one year.
- Epidemiologic studies of cancer in China. Chinese Cancer Institute, $325,000 first year, total $975,000, three years.
- Comparison of mechanisms of carcinogenesis by radiation and chemical agents. A three day workshop-symposium cosponsored with the Div. of Cancer Treatment, to cost each division an estimated $25,000.
- Third NCI/EPA/NIOSH collaborative workshop: Progress on joint environmental and occupational cancer studies. Cost estimate, $25,000.
- Procurement of byproduct human specimens from normal surgical and clinical procedures and pathology data from patients with primary hepatocellular carcinoma and chronic active hepatitis. First year estimatee cost, $130,000, total $520,000 for four years.

This material will be made available to grantees and others on a payback basis. Because much of this material is in short supply, it will not be competed in the usual sense. Institutions where it is available will be invited to submit proposals which will be reviewed by technical review committees.

Noncompetitive renewals of ongoing projects were given concept approval, as follows:

- Study of human health consequences of polybrominated biphenyls contamination of farms in Michigan. Centers for Disease Control, $165,000 first year cost estimate, total $530,000, three years.
- Studies of radiation induced chromosome damage in humans. Dept. of Energy, $100,000 first year. Staff had asked for three years at that rate which would have expanded the study to more population groups. The Board asked for a more detailed justification for expanding the study, to be presented at its September meeting.
- Radiation dosimetry for epidemiologic studies. Univ. of Texas/M.D. Anderson, $80,000 first year, $400,000 total, five years.
- Radiation risk estimation in Israeli children irradiated for tinea capitis. Chaim-Sheba Medical Center, $115,000, one year.
- Immunologic studies of high risk groups. Uni-

formed Services Univ. of Health Sciences, $505,000 first year estimate, $2.525 million total, five years.

- Epidemiologic studies of cancer in Alaskan natives. Centers for Disease Control, $60,000 first year, total $120,000, two years. Staff had asked for five years and $330,000.
- Study of DuPont chemical workers bladder cancer screening program. E.I. DuPont, $20,000, one year.
- Support services for a mortality study of workers exposed to formaldehyde. Westat Inc., $150,000.
- Chemical carcinogen reference standard repository. IIT Research Institute. This involves a memo of understanding with the Coordinating Research Council, a nonprofit corporation supported by the American Petroleum Institute and Society of Automotive Engineers. CRC will provide 20-25 nitro-PAHs a year to the repository operated for NCI by IIT Research Institute. The compounds will be made available to investigators on a payback basis.
- Epidemiologic study of mesothelioma risk factors utilizing population based tumor registries. Univ. of Southern California, $50,000, one year.
- Epidemiologic study of mesothelioma risk factors utilizing population based tumor registries. New York State Dept. of Health, one year, no additional cost.
- Services for a case control study utilizing VA files–mesothelioma and employment. Veterans Administration, one year, $160,000.
- Mesothelioma and employment: Utilization of SSA quarterly earnings file. Social Security Administration. $11,200, one year.

Pathology review for the mesothelioma studies will cost an estimated $100,000.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP, citing the RFP number. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs to the individual named, the Blair building room number shown, National Cancer Institute, 8300 Colesville Rd., Silver Spring, Md. 20910. RFP announcements from other agencies reported here will include the complete mailing address at the end of each.

RFP C1-83-0336

Title: *Carcinogenic testing in the sencar and strain "A" mice*

Deadline: *Not available*

The use of sencar (sensitive to carcinomas) and strain A mouse models in the past five years in EPA laboratories have shown considerable promise in allowing EPA to evaluate the carcinogenic potential of organic concentrates of water samples taken from potable water supplies, water concentrate fractions using alternate disinfectants, samples for testing efficacy of gac filtration, humic substances, and coal tar and asphaltic paints.

In this project the carcinogenic potency of water related environmental samples will be studied using the sencar and strain A mice. In the sencar mice, the samples will be tested in one or all of three types of tumor studies. They are (1) initiation/promotion study, (2) promoting potential study, and (3) a complete carcinogenicity study.

For both the sencar and strain A studies positive control and vehicle control groups will be included in each study. Appropriate doses of the test samples are administered either topically, subcutaneously or orally (for sencars) and either orally or interperitoneally (for strain A) depending on the nature of the test substance. Tumor incidence is charted from weekly observation of the sencar animals. Lung adenoma counts are made in the strain A mice following sacrifice of the animals at 9 months.

The total exposure period for sencars including the initiator and promotor applications will be 20 to 30 weeks. Approximately seven months thereafter the mice are sacrificed and complete gross and selected histopathological examinations are made. The endpoints for sencar studies include (1) number of mice with tumors, (2) number of tumors per mouse, (3) time to first tumor, (4) characterization of tumors, and (5) histopathological diagnosis of tumors.

Strain A mice are exposed three doses per week for eight weeks. They are sacrificed at nine months of age and lung adenoma counts are made. Endpoints for strain A studies include: (1) number of tumors per per animal, (2) number of tumors, and (3) histopathological evaluation of tumors.

Interested sources are invited to submit a written request for a copy of the RFP. This procurement shall be screened for a possible small business set aside. All prospective offerors shall include in their response their company SBA classification when requesting an RFP. Further screening shall be done for a possible labor surplus area set aside.

Contracts Management Div.
Contracts Branch A
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