THE CANCER LETTER

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CENTERS REVIEW BY PANEL, NCI LEADING TO CHANGES; HAMMER TELLS NCAB IT FACES "DIFFICULT DECISION"

The review of some of the nation's cancer centers by the President's Cancer Panel during the year, culminating with last month's meeting of the Panel at the Cancer Research Center of Hawaii, and the reappraisal of the Cancer Centers Program by NCI staff and their advisors, are leading to recommendations for significant changes in the program which most likely will be presented to the National

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In Brief

NIH BUDGET CUT BEING CONSIDERED, THREATENING NCI'S PLANS FOR REACHING YEAR 2000 GOALS

REAGAN ADMINISTRATION'S determination to reduce the federal deficit by slashing budgets could result in cutting the NIH request for the 1986 fiscal year by as much as $150 million or more, according to reports filtering out of the Office of Management & Budget. That would not bode well for NCI's hope of launching the drive to reduce cancer mortality 50 per cent by the Year 2000 with an increase of more than $300 million over the 1985 budget. High level discussions with the White House on the Year 2000 plan and the $1.45 billion bypass budget have been held; no official response yet has come down from OMB. The President's budget will go to Congress in late January, and as usual, it appears likely that any substantial increase in spending for the National Cancer Program will have to come from congressional initiative.... **NCI/NATIONAL** Toxicology Program archives have been moved from Bethesda to Research Triangle Park, N.C., where NTP is located as a component of the National Institute of Environmental Health Sciences. Seven vans, carrying 800 boxes of records and 5.5 million slides, were required for the move, which now completes transfer of all NTP personnel and activities to Research Triangle Park. The archives are maintained through a contract with Experimental Pathology Laboratories.... **WILLIAM BLOT** has been appointed chief of the Biostatistics Branch, a component of the Epidemiology & Biostatistics Program, in NCI's Div. of Cancer Etiology, DCE Director Richard Adamson announced. Blot has been chief of the Analytical Studies Section in the Environmental Epidemiology Branch.... **JOANN SCHELLENBACH**, acting director of press relations for the American Cancer Society since last September when Charles Dahle retired, has been officially appointed to the position, Irving Rimer, vice president for public information, announced. Schellenbach has been a science writer with ACS since 1980. Rimer also announced that Kristin White, medical journalist and author who has specialized in reporting on cancer research in recent years, has joined ACS as senior science writer, replacing Alton Blakeslee, who retired last year.

NEW GUIDELINES WOULD HELP CONSORTIUM CENTERS, CANCER CONTROL OUTREACH

(Continued from page 1)

Cancer Advisory Board in May. A committee of the Board of Scientific Counselors for the Div. of Cancer Prevention & Control was scheduled to meet this week in Chicago to work up a final draft of those recommendations which will go first to that Board, before presentation to the NCAB.

Primary thrust of the recommendations will be shaped around new guidelines for center core grants which will make available those grants for centers which emphasize cancer control outreach activities, or other activities which generally do not fare very well in peer review under the existing guidelines. They specifically will encourage development of consortium centers where appropriate (and would make it easier for the existing consortium centers to compete); they may permit funding of "overlay" centers, consortia including existing centers with their own core grants, to carry on cancer control outreach within their respective regions; and they may may make it somewhat easier for centers to be funded in more remote locations, such as Hawaii and Puerto Rico, which do not have strong basic research elements but are strong in ways that seem not to impress review committees under the present guidelines.

The DCPC committee will present its recommendations to the full Board in January. The NCAB meets the following week, probably too soon to fully consider the DCPC Board's action. Adoption of the new guidelines by the NCAB in May would permit their implementation for the 1986 fiscal year.

The situation in Hawaii greatly concerns NCI executives and their advisors. They feel it is very important that NCI support for the cancer center be continued. The state's population of one million Americans is too far from the mainland to be adequately served by other centers. The tremendous, unique opportunity for epidemiology studies is enhanced considerably by the existence of the center. And the state's congressional delegation can exert notable pressure when called upon.

The Hawaii core grant is up for renewal this year, and was approved but with a priority score about 30 points beyond the next lowest score (15 core grants are being recompeted this year). The core grant budget of $83.9 million would permit funding them all, but only with some reductions from the recommended budgets and from the budgets of the noncompeting grants. The tentative funding plan now is for the competing renewals to be funded at about 95 per cent of the recommended budgets, and for the noncompeting renewals to take cuts as much as 15 per cent from the recommended levels. Those renewals had to accept funding 85 per cent of the recommended budgets last year and had hoped to get full funding this year. That seems possible now only if one or two of the competing grants goes unfunded.

Chairman Armand Hammer of the President's Cancer Panel advised the NCAB last month that it would have to "face the difficult decision on whether to fund" the Hawaii grant. Hammer missed the Hawaii meeting, the first he has not attended since becoming chairman nearly four years ago. He noted that it is "a small center, with unique problems."

The NCAB will consider the center core grants in closed session at its Feb. 4-6 meeting.

Marvin Anderson, chancellor of the Univ. of Hawaii, opened the Panel meeting in Honolulu by promising to increase the university's commitment to the cancer center. "The center has been productive, especially in research on the role of diet and nutrition. We recognize that a further commitment is needed from the university, to further develop cancer research and control programs, especially clinical research. That will require more funds from the university, and I want to assure NCI that we will do it."

NCI Director Vincent DeVita told the packed room of about 80 cancer professionals, scientists and others interested in the cancer program, "Here's how we see you from Bethesda. This is a heavenly state, with a diverse population. You have 1,300 cancer deaths a year. The majority of the population has a generally low incidence of cancer (although native Hawaiians have the highest incidence of any U.S. ethnic group). There is a great opportunity here for research on impact of diet on cancer. You have a piece of each of NCI's network (center, CCOP). We hear you are having trouble putting it all together. We're here to see how we can help."

DeVita said native Hawaiians have a high incidence of lung cancer "not entirely explained by smoking." Native Hawaiians have a high fat, high fiber diet, with increased incidence of some cancers associated with high fat except for a low incidence of colon cancer, another intriguing opportunity for research, DeVita said.

Lawrence Piette, director of the cancer center, described its relationship to the university. "Our success depends on our ability to negotiate agreements with other departments and divisions. That is not always easy because of turf problems and personalities, but I feel we have succeeded to some extent."

Piette cited "our very strong epidemiology program, with our unique data base," and mentioned efforts to improve the basic science program and the emphasis on clinical research. In cancer control, "we've been trying to keep up with the changing mandates from NCI and have been trying to develop

cancer control research." Opportunities for research include the obivous, "to fund epidemiology based studies, and to exploit the (university's) medical school to develop clinical research programs."

Piette noted that the medical school is one "without walls, that uses all the resources available." The university does not have its own hospitals, but has formal arrangements with local community hospitals.

A group of community physicians not affiliated with the cancer center successfully competed for a Community Clinical Oncology Program award, Piette noted. "Although we felt that a CCOP here could detract from the cancer center's ability to carry out clinical trials, we recognized the independence of the community physicians. We had hoped for full interaction with the CCOP, and still hope eventually we will."

That referred to what NCI executives consider one of the major problems of the cancer center—that it is carrying out clinical trials, affiliated with the Southwest Oncology Group, while the Honolulu CCOP works completely independently of the center and is affiliated with the Eastern Cooperative Oncology Group.

Piette said that before the center came into existence, there were only two board certified oncologists in Hawaii; now there are 13, "some as a direct result of the center's education program." There was no radiologic physics program; "now we have one, with the full support of radiotherapists throughout the state." Other laboratory programs developed in the center are being transferred into the community, including hyperthermia.

"Before, many cancer patients here felt they had to go to the mainland to receive optimal treatment," Piette said. "That is not the case today."

Thomas Hall, director of the center's Div. of Cancer Control, Education & Outreach, related the history of cancer control efforts in Hawaii. Honolulu had one of the now-maligned Community Based Cancer Control Programs, an NCI supported effort of the mid-1970s now considered a failure. Hall said that many elements of the Hawaii CBCCP are still in place long after NCI funding ended, including smoking cessation, breast cancer screening, nurse training, and rehabilitation and continuing care efforts. "This residue is a large number of programs intact and continuing, which can serve as a resource for cancer control research," Hall said.

"What is needed for further cancer control development?" Hall asked. "From NCI, we need planning and developmental funds; cancer control funds in our core grant; a better paced issuance of RFAs and RFPs; and more time to respond to RFAs and RFPs. From the Cancer Research Center of Hawaii, we need equal access to grant and overhead funds. From the Univ. of Hawaii, we need stability of the School of Public Health faculty. I'm pleased to say that we are achieving that."

Hall said that the concept of a consortium grant "is one that might well be worth considering."

DeVita described his concerns about the lack of a relationship between the cancer center and the CCOP. "We had to stretch to fund the CCOP (it scored well above the cutoff but was funded anyway because of NCI's determination to get a better geographic distribution of CCOPs). The issue may be whether we should continue it. I think we mucked that up."

"I'm not suggesting that you discontinue the CCOP," Piette said. "I would like to see their program and ours continue together. As it is, there is much duplication. It is our hope that the CCOP will make SWOG rather than ECOG its research base. I hope that we may find some way to merge (the center's clinical research) with them, into one big CCOP."

"Would you recommend that we not allow the CCOP to continue its affiliation with ECOG?" DeVita asked.

"My preference is that, yes, it would be better for the CCOP and center to relate to one group. But the CCOP would maintain its autonomy and independence."

"The CCOP grew out of a grass roots movement in this area," Hall said. "The people who are part of the CCOP were not related to the center, and had not contributed patients to clinical trials. They are contributing patients now, with no loss of patients to the center... Wiping out the CCOP would put us back where we were before. Those people contributing patients now would stop contributing them." Hall said the CCOP physicians had their own reasons for affiliating with ECOG; "it's not that they are anti-SWOG."

Noboru Oishi, director of the center's Clinical Science Program, noted that the center is a fully funded member of three cooperative groups—SWOG, Pediatric Oncology Group and the National Surgical Advjuvant Breast & Bowel Project.

Clifford Straehley, professor of surgery at the School of Medicine and director of medical education at the Kaiser Foundation Hospital, cited lung cancer treatment as an example of "how the center has impinged on the management of cancer, particularly at Kaiser Hospital. We had major help from the cancer center in getting our tumor registry set up. Of 490 lung cancer patients for which I participated in their care, 40 per cent were resectable. Of the stage 1 and 2 patients, 63 per cent survived at least three years free of disease. Our education program was built around the tumor board. Eighty nine per cent of the patients were smokers. The center helped establish stop smoking clinics."

CANCER LETTER FINAL ISSUE OF 1984; NEXT WILL BE PUBLISHED JAN. 4

This issue of **The Cancer Letter**, Vol. 10 No. 48, is the final issue of 1984. The next issue, Vol. 11 No. 1, will be published Jan. 4, 1985.

The Cancer Letter office will remain open most of the time during the holidays, with intermittent closing when the staff is getting into the spirit of the season, or is just goofing off. We'll put the tape machine on when we are gone, and your message will be answered when we return. We'll be back on the job full time Wednesday, Jan. 2.

DCBD BOARD APPROVES CONCEPT FOR CYTOGENETICS SOLID TUMOR DIAGNOSIS

The Board of Scientific Counselors of NCI's Div. of Cancer Biology & Diagnosis approved at the Board's recent meeting the concept of a grant supported program for research on solid tumor cytogenetics in the diagnosis of cancer. DCBD staff recommended that $750,000 a year be earmarked for the program; the Board approved that figure but final approval still must come from the NCI Executive Committee.

A unique feature of this program is that the request for applications (RFA) will be written to stimulate applications for support through three grant mechanisms—RO1s, new investigator awards and supplements to existing grants. DCBD staff estimated that the amount recommended might support as many as three to four awards in each of those categories.

The Board also approved the concept for a contract to be awarded competitively for maintenance of a feral mouse breeding colony. Total estimated cost over the three year period of the award was $375,000.

Staff descriptions of the concepts follow:

Title: Solid tumor cytogenetics and cancer diagnosis. Sheila Taube, DCBD Diagnosis Branch who will be program director, presented the concept: ---The aim of this potential program initiative would be to encourage studies that will expand our understranding of cytogenetic changes in solid tumors. Chromosome analysis has been shown to be extremely useful and important in the diagnosis and evaluation of hematopoietic tumors. There are insufficient data, at present, to determine whether cytogenetic analysis of solid tumors will be equally informative. In order to collect the necessary data, existing technology must be improved and more scientists must be trained to use these specialized techniques. This program initiative would be designed to address current needs in this area.

There has been continuing discussion in the scientific literature concerning the potential importance of chromosome analsysis in cancer detection, diagnosis and prognosis. Attempts are being made to correlate observed chromosome alterations with the stage of a tumor or with the presence of a particular tumor type. For example, there is growing evidence that cytogenetic abnormalities have prognostic importance in some leukemias. Similarities have been observed among the karyotypes of melanocytic lesions at different stages. To date most studies have been small and many more cases need to be examined. In addition, many more tumor types must be examined to determine whether cytogenetic changes occur uniquely or generally. Uniqueness would be important for distinguishing subtypes of a given kind of cancer (e.g. the different types of lung cancer) or establishing the origin of metastatic tumors. However, it is also possible that some alterations are common to the early stages of progression of a number of different kinds of tumors and although these alterations may not be unique to a particular tumor, they may still be of value in grading the degree of malignancy.

In order to facilitate karyotype analysis, the ability to grow tumor tissue in vitro must be improved. A major problem in the collection of karyotype data from solid tumors has been the inability to obtain sufficient suitable metaphases from these tumors. It is also necessary to develop methods which assure that the population of cells dividing in culture is either representative of the population within the original tumor or representative of a critical population within the tumor. Further research is required to address these problems.

Energetic collection of karyotype data is currently limited by the availability of trained personnel. Recent developments in molecular biology, rather than eliminating the need for cytogenetics, have caused renewed interest in the field. A decline in the number of cytogenetics laboratories has led to reduced training opportunities in this area. Thus, another purpose for encouraging research in this area would be to train more professionals who can develop viable independent research programs of their own.

The growing body of data indicating that there may be consistent karyotypic alterations in the cells of solid tumors and that these changes may be useful in diagnosis and prognosis have prompted the Diagnosis Program to investigate the research needs in this area. A Cytogenetics Working Group, composed of experts in the fields of cytogenetics and culture of normal and tumor tissues, concluded that more information about the cytogenetics of solid tumors is needed and research in this field should be stimulated. Areas of emphasis should include collaborative development of culture techniques and assessment of different cytogenetic techniques as well as encouragement of young investigators and new people to enter the field. It was agreed that an initiative of this sort would be successful in encouraging new laboratories and laboratories working in peripheral areas to focus research programs on these important problems.

Title: Feral mouse breeding colony. Robert Callahan, chief of the Oncogenetics Section of the Laboratory

of Tumor Immunology & Biology in DCBD, presented the concept:

This contract is to provide for the maintenance and housing of a feral mouse breeding colony. The colony represents a major resource for the Oncogenetics Section, LTIB, and plays an integral part in a study on the role of mouse mammary tumor virus (MMTV) in the etiology of murine mammary gland neoplasia. This contract, in addition, provides mice and tissue samples upon request to other investigators at NIH and other research facilities around the world. We propose to make these strains of mice available to the successful offeror of a competitive contract.

Research on the role of MMTV in the etiology of murine mammary gland neoplasia has been restricted almost entirely to a limited number of laboratory strains of MMTV and inbred strains of Mus musculus domesticus. In earlier work, we expanded this effort to feral breeding populations derived from different geographical locations (U.S., Europe, North Africa, Asia). This led to the development of two pedigreed outbred colonies of mice: M.m. musculus (designated Czech II) and M. cervicolor popaeus (designated MCPT), which have unique characteristics pertinent to studies of murine mammary tumorigenesis. The Czech II mice unlike inbred mouse strains lack MMTV proviral sequences in their germline. These mice do, however, contain a congenitally transmitted feral MMTV. The genome of this virus is readily distinguishable from laboratory strains of MMTV by restriction enzyme analysis. We have now completed a preliminary study of the effect of the chemical carcinogen dimethylbenzanthracene (DMBA) on the incidence of mammary gland neoplasia in Czech II mice. Seven per cent of the untreated breeding females have developed mammary tumors whereas no tumors have been observed in virgin females up to two years of age. Treatment of the mice with DMBA significantly increased the frequency of tumors (30-50 per cent of the treated mice) and decreased latency in tumor development (average 11 months). Most of the chemically induced and all of the spontaneous mammary tumors were type A adenocarcinomas. The MCPT colony is derived from mice trapped in Thailand. This species of Mus is infertile with inbred strains of mice. MCPT mice express a MMTV related virus in lactating mammary glands. This virus is also clearly distinguishable from laboratory strains of MMTV by immunological and restriction enzyme analysis. The MCPT colony has a 50 per cent incidence of mammary tumors. Most of these tumors contain a MMTV like virus. The unique characteristic of these tumors is that a significant number are histologically different from MMTV induced mammary tumors of inbred mice.

MMTV does not appear to contain its own oncogene, instead it seems to induce tumor development by insertion mutation of host cellular genes. Recently two genetic loci have been identified in inbred mice (designated Int-1 and Int-2) which represent two domains of the tumor cellular genome which are frequently occupied by an integrated MMTV proviral genome. When this MMTV genome is inserted in either of these loci the respective host flanking cellular sequences are uniquely expressed. It has been speculated that their expression is involved in the initiation or progression of mammary tumor development. This work stimulated us to determine whether these or other Int-loci are similarly affected in the feral Czech II and MCPT mouse mammary tumors. Analysis of Czech II tumor cellular DNA revealed the presence of MMTV proviral DNA in many but not all mammary tumors. The corresponding liver cellular DNA from MMTV positive tumor bearing mice lacked MMTV proviral DNA. Four out of 18 virus positive mammary tumor DNAs containing common host viral junction fragments were examined for the presence of MMTV proviral DNA within either Int-1 or Int-2. In each case the Int-1 and Int-2 MMTV common integration regions were unoccupied. Int-1 was occupied by an MMTV genome in one of the other virus positive tumor cellular DNAs examined. Int-2 was unoccupied in all of these tumors. Similar results were obtained with MCPT mammary tumor cellular DNA, suggesting that the Int-1 and Int-2 loci are infrequently occupied in these tumors. Recently we have obtained recombinant DNA clones of the Czech II common host viral junction fragment. Using a unique host flanking cellular DNA sequence as a probe we have identified four of six spontaneous virus positive tumors having viral insertions in this region of the cellular genome.

Future efforts involving the Czech II and MCPT colonies will address the following: (1) defining the genetic organization of the new common insertion region or Int locus and determine whether flanking host cellular sequences are expressed uniquely in Czech II mammary tumors; (2) determining the frequency of insertion at the new Int locus in Czech II mammary tumors induced by laboratory strains of MMTV and the MCPT virus; (3) determining whether chemical carcinogens in the presence and absence of MMTV affect the expression or integrity of the new common insertion region; (4) determining whether there are new common insertion sites in MCPT mammary tumors and the frequency of viral insertion into the new Int locus.

To successfully answer these questions we need a standing colony of 2,000 mice. This will allow us to obtain a sufficient number of viral and carcinogen induced tumors for analysis. The Czech II mice, although not inbred, are genetically homogenous enough to permit transplantation of mammary tumors. Additional mice will allow us to increase the amount of selected tumors available for study after transplantation. To analyze the frequency with which the laboratory strains MMTV (C3H) and MMTV (GR) as well as the feral MMTV (MCPT) integrate into the new Int locus it will be necessary to develop a virus free Czech II subline into which these other viruses can be introduced.

The contractor will provide proper facilities and technical support for the maintenance and breeding of the indicated species of mice (total 2,000). This will include technical help experienced in the handling and husbandry of feral mice, breeding of

feral mice and knowledge of requirements for maintenance of outbred colonies; milking mice, observation of mice for early tumor development; surgery and dissection, injections and preparation of tissue for histology. Analysis of all tissue samples and specimens will be performed by the Oncogenetics Section. Protocols for the injection of chemical carcinogens and virus as well as for the breeding of new mouse sublines will be provided by the Oncogenetics Section.

It is proposed that this be a contract that is incrementally funded for four years. The estimated total direct and indirect costs for these four years are $171,120, $185,487, $201,072, and $217,964. However, the Board voted to reduce the award period to three years and to limit total costs to $125,000 a year.

RFPs AVAILABLE

Requests for proposal 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 Blair building room number shown, National Cancer Institute, NIH, Bethesda, MD. 20205. Proposals may be hand delivered to the Blair building, 8300 Colesville Rd., Silver Spring, Md., but the U.S. Postal Service will not deliver there. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CM-57692-16
Title: Fungal fermentation
Deadline: Approximately Feb. 10

The Div. of Cancer Treatment is interested in receiving contract proposals from offerors with the capability to provide and operate a microbiological and small extraction laboratory to ferment various genera of the fungal world for use by NCI in the systematic evaluation of its ability to produce antineoplastic agents. The ultimate goal is to provide NCI with potential antineoplastic agents of novel structural types from fungal origin for use in the treatment of cancer in man.

The specific objectives of this project are to: (1) ferment approximately 1,500 fungal cultures under various conditions and/or using many different substrates; (2) optimize and scale up certain cultures in 10-20 liter volumes as may be required by NCI; and (3) filter sterilize and lyophilize broths and concentrate mycelial extracts.

The successful offeror will be expected to ferment approximately 1,500 fungal species over a period of three years. Approximately 500 cultures are expected to be available during the first contract year. Isolation of an additional 1,000 cultures may be conducted in house or be acquired from other institutions. If isolation is done in house, the successful offeror should use his ingenuity in the use of isolation techniques and selected media. Taxonomy is fundamental to all branches of biology and is of utmost importance when working with fungi. It is essential to know what organisms are being fermented. It shall be essential to have mucor and aspergillus species evaluated. In addition, many phycomycetes, basidiomycetes, etc., should be included in these studies. No trichothecene producers nor producers of known antitumor agents should be included.

The successful offeror will use ingenuity in selecting suitable media and conditions. To encourage production of novel agents, media should be varied to the maximum from the standard growth media. The chemical composition of the media and the physical environment for fungal growth, such as temperature, pH, aeration, etc., shall be varied.

It is anticipated that NCI would require refermentation of 5-10 cultures per year. Accurate and detailed documentation of the cultures being fermented, including source, growth parameters, fermentation conditions and scale up, including media ingredients, Ph, temperature, aeration, agitation, length of fermentation, harvest times, method of harvest, cell/broth ratio, volume of filter sterilized broth, weight of lyophyl/sample bottle, extractants and pertinent observations, and culture preservation.

When deemed necessary by NCI, optimized conditions for the growth of the cultures must be determined. The successful offeror will be expected to establish optimum fermentation parameters in laboratory bench type or microfermentors of at least 5-14 liter capacity to produce sufficient quantities of materials for NCI. This may include studies of inoculum buildup, nutrient selection, temperature, aeration, agitation, time of addition of any precursor needed, harvest time and pH controls to optimize yields of the active principle.

The government anticipates one award. It is anticipated that the resulting contract will be awarded on an incrementally funded basis for a three year period, beginning on or about July 15, 1985. Each increment will be for a one year period.
Contract Specialist: Patricia Shifflett
RCB Blair Bldg Rm 228
301-427-8737

RFP NO1-CM-57718-15
Title: Chemical coupling of cytotoxic agents to tumor reactive monoclonal antibody
Deadline: Feb. 4

The Biological Response Modifiers Program seeks a contractor with the chemical expertise to conjugate or chemically couple several cytotoxic agents to monoclonal antibodies directed against antigens found on human tumor cells. Examples of cytotoxic agents include the whole toxins ricin and abrin or their A chain subunits, gelonin, pokeweed antiviral protein and diphtheria toxin A chain or fragments or drugs such as chlorambucil, methotrexate, daunomycin and alpha amanitin, or radioisotopes (alpha and beta as well as gamma emitters). The choice of monoclonal antobodies and cytotoxic agents to be coupled will be made by the NCI project officer or can be proposed by the respondent.

The principal investigator should possess an MD or PhD with extensive experience (minimum of five years) in immunology, immunochemistry or biochemistry and devote a minimum of 25 per cent of his/her time annually. In addition he/she should have recent experience in (a) the development of methodology related to chemical coupling of a variety of drugs, toxins and radioisotopes, to immunoglobulins; (b) experimental immunology including radioimmune assays and in vitro assays to measure antibody activity; and (c) protein purification.

In addition to the principal investigator, an immunologist/immunochemist at the doctoral level should be assigned for a majority of his/her time to the project and must have recent experience in chemical coupling reactions, cellular immunology, and immunoassays. The qualifications of the support team should give expertise to chemical coupling, in vitro assays, protein purification, radiolabeling of proteins, in vivo animal studies, and pharmacokinetics.

The level of effort for this project is estimated at 5.5 person years annually.

Contract Specialist: Jeaneen Monk
RCB Blair Bldg Rm 212
301-427-8767

RFP NO1-CM-57717-15
Title: Development of screening procedures for testing the potential antitumor efficacy of human lymphokines on human cells
Deadline: Feb. 19

The Biological Response Modifiers Program seeks a contractor to develop and operate a specific track preclinical screen for human lymphokines. The contractor shall receive from the government lymphokine preparations that are to be evaluated. The contractor shall quantitate, evaluate and perform biological assays which will indicate the relative potency of human lymphokine preparations in modifying human immune effector mechanisms that might prove to be beneficial to cancer patients.

Assays that measure direct effects of lymphokines on a variety of cultured human tumor types, both unmanipulated or pretreated with a noncytotoxic concentration of a chemotherapeutic drug. The assays to be utilized should be grouped into core assays and additional assays.

It is anticipated that the BRMP will require testing of approximately six different lymphokine sets each year and that a set will consist of one or several preparations or formulations of each lymphokine supplied at the same time for comparative purposes. Such assays may involve measuring effector mononuclear cells with cytotoxic potential for tumor cells. Assays involving recognition and proliferation in response to foreign cellular elements, especially tumor related antigens, are also desirable assays for the evaluation of lymphokines. Assays are restricted to utilization of human normal and malignant tissues.

It is expected that approximately 10 assays will be performed on each set of lymphokine and that, for comparative purposes, all preparations or formulations within a set must be simultaneously tested within each required assay.

The principal investigator should possess an MD or PhD with at least five years experience in immunology and cell biology and must devote at least 35 per cent of his/her time annually to this effort. It is expected that an incrementally funded cost reimbursement level of effort type contract will be awarded for a period of three years.

Contract Specialist: Jeaneen Monk
RCB Blair Bldg Rm 212
301-427-8767

RFP NO1-CM-57720-15
Title: Production of hybridomas secreting antibodies reactive specifically with cytokines
Deadline: Feb. 4

The Biological Response Modifiers Program seeks a contractor with the expertise necessary to produce monoclonal antibodies reactive with various human, primate, and rodent cytokines. It is expected that three to five cytokines will be available annually for development of hybridomas by the contractor. In most cases, the cytokines will be provided by the BRMP and the contractor will provide BRMP with anticytokine secreting hybridomas. In some cases, the contractor may have available cytokines that are of interest to BRMP that will be developed on the contract. In a few instances, the contractor will be required to perform some cytokine purification prior to immunization.

The principal investigator should possess an MD or PhD with at least five years experience in immunology and cell biology and must devote at least 25 per cent of her/his time annually to this effort. In addition she/he should have recent experience in the development of monoclonal antibodies to cytokines, radioimmune binding assays and cytokine assays. It would be very desirable if the principal investigator can document recent hands on experience in the production and isolation of both monoclonal antibodies and cytokines.

The qualifications of the overall team should have expertise in rodent handling and experimentation, cell culture (large scale production), biochemistry (protein purification), and immunoassays.

The level of effort for this project is estimated at three person years annually.

Contract Specialist: Jeaneen Monk
RCB Blair Bldg Rm 212
301-427-8767

RFP NO1-CM-57719-15
Title: Preclinical assessment of monoclonal antibodies
Deadline: Feb. 19

The Biological Response Modifiers Program seeks a contractor to develop a coordinated program for uniform preclinical testing and evaluation of monoclonal antibodies and immunoconjugates (drugs, toxins, radioisotopes) in several test systems prior to entry into clinical trials.

It is anticipated that 20-30 monoclonal antibody

preparations will be evaluated annually by immunofluorescent and/or immunoperoxidase histochemistry and other relevant in vivo and in vitro tests.

The principal investigator should possess an MD or PhD with extensive experience (minimum five years) in immunology, immunochemistry, and cell biology and should devote at least 25 per cent of her/his time annually to this effort. Also, an immunologist at the doctoral level, or with equivalent experience, should be assigned for a majority of her/his level of effort to the project and must have recent experience in vitro and in vivo assays for monoclonal antibody specificity and cytotoxicity, and in immunoassays. Adequate facilities must be available to handle radioisotopes and toxins conjugated to monoclonal antibodies and attention must be given to handling of animals used for experimentation.

It is anticipated that an incrementally funded cost reimbursement level of effort type contract will be awarded for a period of three years.

Contract Specialist: Jeaneen Monk
RCB Blair Bldg Rm 212
301-427-8767

RFP NCI-CP-EB-51018-60
Title: Support services for occupational studies
Deadline: Feb. 28

The Environmental Epidemiology Branch of NCI's Div. of Cancer Etiology is seeking an organization highly experienced in providing technical support for all phases of occupational health studies including the design of data collection documents; hiring and training of interviewers and abstractors; collecting, keying, editing, updating, and recording data; tracing individuals; evaluating workplace exposures; and creating and manipulating data files.

Key personnel to be provided by this contract include a project manager, two data collection managers, three senior computer programmer/analysts, four computer programmers, one secretary, one questionnaire specialist, and one industrial hygienist. Other temporary personnel to be hired as needed include abstractors, interviewers, keyers, and other field labor.

The project manager should be experienced: (1) in supervising the conduct and management of epidemiologic studies; (2) in training interviewers and abstractors; (3) in coordinating other aspects of field studies such as obtaining death certificates and medical records; and (4) in tracing study subjects to determine their vital status. Data collection managers should have experience in training abstractors and interviewers, in coordinating field aspects of epidemiologic studies, and in monitoring data collection and manipulating. Computer programmers should be experienced and skilled in manipulating large data sets and in developing edit programs. The industrial hygienist should be board certified and experienced in conducting walk through surveys in various industries. The questionnaire specialist should be experienced in developing and testing questionnaires used in mail, telephone, and in person interviews.

Frequent face to face meetings between NCI and project and coproject officers and key contractor personnel are necessary to monitor activities of the studies being simultaneously conducted under this contract. The face to face meetings are crucial to the conduct of the studies to ensure that study protocols are being carefully followed and to make adjustments when problems develop. Inability to hold such meetings would seriously compromise the scientific quality of the studies. Since many studies (15-30) are being conducted simultaneously under this contract, face to face meetings occur on a daily basis between NCI investigators and key contract personnel. To assure the offeror's availability for attendance at these meetings, a mandatory qualification criteria shall be included in the RFP requiring the offeror to demonstrate how they will accomplish this task.

Contract Specialist: Thomas Porter
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301-427-8888

NCI CONTRACT AWARDS

TITLE: Conduct of research on occupational carcinogenesis.
CONTRACTOR: National Institute of Occupational Safety & Health, $63,000.

TITLE: Epidemiology of human T-cell leukemia/lymphoma virus in Jamaica.
CONTRACTOR: Univ. of West Indies, $244,854.

TITLE: Hepatitis B virus and liver cancer in Army veterans of WWII
CONTRACTOR: National Academy of Sciences, $75,000.

TITLE: Cancer risk in women irradiated for benign gynecologic disorders
CONTRACTORS: Harvard College, $413,776, and Health Research Inc., Buffalo, $25,000.

TITLE: Cancer risk in patients irradiated for peptic ulcer
CONTRACTOR: Univ. of Chicago, $276,355.

TITLE: Tracing through other sources to confirm addresses of x-ray technologists
CONTRACTOR: Hooper Technologists, #69,800.

TITLE: Tracing through other sources for former Connecticut hospital patients
CONTRACTOR: Johns Holding Co., $5,111.

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