THE CANCER NEWSLETTER

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NCAB APPROVES NEW PANCREATIC CANCER PROJECT, HEARS FAVORABLE REPORT ON ORGAN SITE PROGRAMS

The National Cancer Advisory Board approved at a spirited closed-door session last week the establishment of a National Pancreatic Cancer Project, the fourth such organ site program to be organized by NCI. Like the others (large bowel, bladder and prostate), the pancreas project will be grant-supported with planning and management centered at a "headquarters" institution rather than NCI.

Approval did not come without a fight. Some members have objected to the targeted approach inherent in organ site programs, arguing that such efforts drain funds and investigators from basic research.

(Continued to page 2)

In Brief

CONFEREES OK NCI APPROPRIATIONS AT $691.7 MILLION; FINAL AMOUNT AVAILABLE WON'T BE SET UNTIL SPRING

NCI APPROPRIATIONS for 1975 fiscal year came out of the House-Senate conference as reported (*The Cancer Newsletter*, Oct. 4), $691.7 million. That's $91 million more than the Nixon Administration had asked, $102 million more than NCI got last year, but $112 million less than NCI had originally sought. NIH received $2.04 billion, up from the 1974 figure of $1.8 billion. President Ford probably will sign the $33 billion Labor-HEW appropriations bill since it trimmed the budget request by $485 million, with most of the cut coming from welfare funds. Conferees invited the President, should mandatory welfare grants exceed their estimate, to make up for it by using his authority under the new budget act to make cuts elsewhere in Labor and HEW programs. NCI probably won't be sure of how much it will get until next spring. . . . **GERALD MURPHY**, director of Roswell Park and member of the National Cancer Advisory Board, has been appointed secretary-general of the International Union Against Cancer (UICC). The four-year term will carry through UICC's next congress, scheduled for Buenos Aires in 1978. . . . **AMERICAN CANCER** Society board of directors has approved in principle a $100,000 grant to M.D. Anderson to study use of a continuous application device for ambulatory cancer patients receiving chemotherapy. The device was developed by Alza Corp.; limited commercial prospects made the financial assistance necessary. . . . **NCAB REFUSED** to overturn an adverse decision on a grant application by D.R. Grasseti, Berkeley, to study metastatis prevention by cell surface modification. Grasseti had appealed the decision in letters to various NCAB members, and Chairman Jonathan Rhoads asked Gerald Murphy and Irving London to take another look at it. They reported that after reviewing study section and NCI staff actions, they concluded Grasseti had had a "full and fair review". . . . **CHAIRMAN** of the new biomedical research panel may be Franklin Murphy, board chairman of the Times-Mirror Co. and former UCLA chancellor.

PROSTATIC CANCER TRIALS FINDING ENCOURAGING RESPONSE TO DRUGS

(Continued from page 1)

Others don't like the administrative structure, in which most decisions and initial grant review are made at the headquarters institutions.

Consideration of the pancreas project, however, came after a subcommitee headed by former board member Arnold Brown, charged with reviewing the organ site programs, recommended that they be continued. That, and perhaps an encouraging report on the prostatic cancer project by Gerald Murphy helped overcome the opposition.

Isadore Cohn, Louisiana State, reported on planning for the pancreas project. Cohn noted that cancer of the pancreas is the fourth greatest cause of cancer death, behind lung, large bowel and breast, killing 20,000 Americans a year. Incidence has increased 25% in the last 20 years, during which time stomach cancer has decreased by 25%. There is no effective treatment; of the 449 cases followed in New Orleans, there were only 10 three-year survivors.

One of the first tasks will be selection of a scientific director of the project. Cohn said that person would be an MD, not a surgeon, and someone familiar with the grant program and NCI policy.

Areas of interest will be distributed widely, Cohn said. "We want to attract the best basic scientists who are not working on disease-oriented projects."

Priority areas will include identification of etiologic agents and epidemiology studies in prevention; use of new techniques in diagnosis; and surgery, chemotherapy and radiotherapy in treatment.

Factors that will rate high in scoring grant applications include urgency, uniqueness, payoff prospects, probability of success, and follow-up capability, Cohn said.

The Brown subcommittee offered a series of recommendations, the first of which was that the national organ site program should be continued. Initiation of new such projects should be on a highly selective basis, however, the report said. And criteria should be developed for terminating individual projects and returning their grants to the usual funding mechanisms.

Other recommendations were:

–Basic research (oncogenic viruses, immunology, carcinogenesis) done under an organ site project should be unique or of particular relevance to the project rather than to cancer in general.

–Mechanisms must be established to insure adequate communication between organ site programs and other components of NCI concerning planning and operations in areas of common interest.

–Advisory committees overseeing establishment of the programs should be replaced by a review committee appointed by NCAB, chaired by an NCAB member and including other members and appropriate consultants. This committee should report regularly to NCAB with an assessment of the progress of each organ site project and recommend an annual budget ceiling.

–Consideration by NCAB of actions by the working cadres on individual grants should be on the basis of summary sheets similar to those made available from study section reviews.

–New organ site projects should be established on the basis of the following criteria:

A. Existence of a high incidence of mortality and morbidity for the organ site in question.

B. Existence of promising scientific leads that could be exploited by an organized and coordinated effort joining scientists and clinicians of different disciplines and professional fields who can be expected to make valuable contributions to the solution of cancer in that organ.

C. Development of a rational plan for such an organized effort.

D. Paucity of research related to the specific organ site cancer despite promising leads.

E. Reasonable expectations of success in achieving major progress within several years.

F. The availability of the needed manpower or the existence of programs for the training and education of this manpower.

–A mechanism should be established for selecting the national project directors on the basis of their scientific and clinical eminence and their administrative competence rather than by self-selection through the process of submitting exploratory grant requests.

–Periodic reports should be made to NCAB by investigators involved in each of the organ site projects.

–Sufficient administrative flexibility should be retained by each organ site project to allow easy adaptation to new developments and trials of innovative administrative techniques.

The report noted that each national project is a comprehensive program of research in which an NCI program director shares much of the responsibility for planning and implementation with a national project director from an institution other than NCI. The national project director is assisted by an administrative staff in his own institution, the headquarters institution. He is also assisted by a multidisciplinary working cadre of scientists which he organizes and which he recruits from institutions throughout the nation.

Ad advisory committee, advisory to NCI and to NCAB, provides an initial review by evaluating a detailed and comprehensive overall plan of research developed by the national project director and the working cadre. NCAB, acting upon a recommendation from the advisory committee, provides a second review of the plan. If NCAB favors implementing the plan, it recommends an upper level of funds it feels is adequate for national project. The project director

announces the areas of high priority interest and solicits applications to meet the requirements of the approved plan. The working cadre reviews research proposals for scientific merit and for importance and adherence to the approved plan.

The report evaluated the three organ site projects in operation and offered some criticism of each.

NATIONAL LARGE BOWEL CANCER PROJECT

M.D. Anderson is the headquarters institution. Murray Copeland is project director and Rulon Rawson is associate director and chairman of the working cadre. John Speer is assistant director for science. The budget was $4 million in fiscal 1973, $4.2 million in 1974 and $4.6 million this year.

Investigators submitted 359 letters of interest and 96 applications, of which 43 were approved. Grant funds were distributed as follows – carcinogenesis, $395,000; immunology, $399,000; cell kinetics, $286,000; genetics, $257,500; detection, $157,000; epidemiology, $56,500.

"It appears that not enough support has been given to chemotherapy and to detection," the report said. "This is partly the result of the thinking of the working cadre that there is considerable activity in these areas in other programs at NCI and the fact that many applications in the detection area have not been considered worthy of support."

Implementation of the working cadre decision to emphasize pharmacology, drug metabolism and pharmokinetics in an effort to develop more rational approaches to chemotherapy has been slow, the report said. A major problem has been difficulty encountered in remaining informed of other NCI activities relating to the colon and rectum.

NATIONAL BLADDER CANCER PROJECT

St. Vincent's Hospital, Worcester, Mass., is the headquarters institution. Gilbert Friedell is project director, and Robert Greenfield is his deputy. The budget was $2.5 million in 1973, $4.6 million in 1974 and $4.4 million this year. The working cadre reviewed 72 applications, approved 40, disapproved 19, and 13 were either withdrawn or are pending review.

Grant funds were distributed as follows – experimental biology, $434,000; carcinogenesis, $445,331; diagnosis, $380,368; and treatment, $334,122.

The only criticism offered by the Brown subcommittee was that efforts to publicize the program initially were restricted to personal contacts by Friedell, his staff and members of the working cadre. This has been corrected to include announcements in various publications. This group also has complained of a lack of communcation with NCI on other bladder cancer activities.

NATIONAL PROSTATIC CANCER PROJECT

Roswell Park is the headquarters institution. Gerald Murphy is project director, and Jack Saroff is assistant director. The budget was $2.8 million in 1974 and $3 million this year.

The emphasis in the first two years has been in clinical studies, which will account for $981,000 in fiscal 1974. Etiology and prevention will receive $562,400, and detection and diagnosis $466,000.

"Early problems in the delegation of responsibility have been solved so that at present the administrative apparatus is working well," was the only criticism suggested by the Brown subcommittee.

The report concluded that, "based on our review of the three organ site programs, we have no doubt they are performing well and fulfilling the purposes for which they were established. . . . Research activity in each of the areas has increased significantly, both by persons already active in studies of each cancer site, but, more importantly, by persons new to the areas and some new to cancer research.

"The quality of the individual grants supported varies from mediocre to first rate. The less impressive studies are largely those dealing with the more mundane aspects of cancer in the three organ sites, such as simple histologic classification."

Murphy presented a separate report to NCAB on progress being made in the prostatic cancer project. He was particularly encouraged by the study comparing standard treatment with 5FU and cytoxan on patients with advanced metastatic prostatic cancer.

With standard therapy, patient responses at the end of 12 weeks of treatment resulted in none with partial regression, six stabilized and 14 with progression of the disease.

With 5FU, one of 18 in the study had partial regression, 10 were stable and 11 progressed.

But with cytoxan, three of 25 had partial regression, 10 were stable and 12 progressed.

"We've had some in remission for 10 to 12 months," Murphy said. "This is rather startling. We've never seen a response rate like this. We've waited far too long to apply chemotherapy to prostatic cancer."

Murphy plans to continue the studies aggressively, using other drugs and drug combinations.

Top priority projects to be implemented in the program are:

Etiology/prevention – comparison of Japanese and American men with and without prostatic cancer; cultivation of prostatic tissue in an organ culture system and study of its hormone dependence; comparison of populations with different frequencies of prostatic cancer with respect to risk indicators; and Gs antigen in prostatic cancer.

Detection/diagnosis – detection of circulating prostate specific antigen; blocking factors in prostatic cancers; immunochemical assay for detection of prostate cancer.

Treatment – evaluation of elective radiotherapy of axial skeleton in patients with stage C carcinoma of the prostate; phase II studies of chemotherapeutic agents in prostatic carcinoma.

ACCC PLANS "STRAIGHT TALK" MEETING IN D.C. ON COMMUNITY CANCER PROGRAMS

"Developing a Community Cancer Program" will be the topic of a meeting in Washington Feb. 1 and 2 sponsored by the Assn. of Community Cancer Centers for community physicians and other health providers.

"This meeting will be two days of hard, straight talk about the problems encountered in building a community cancer program and how, working together, we can solve some of these problems," said James Donovan, ACCC president.

The meeting includes six workshops for participants:

–Cancer care in your community – is it good enough?
–Money for cancer programs – where is it?
–Establishing your community cancer program – could you use help?
–Does your hospital understand quality cancer care – why not?
–Does your tumor registry help you – why not?
–Can a comprehensive center help you – how?

"We intend to make this meeting productive," said Donovan. "We're holding it in Washington to give our members the opportunity to tell Congress, NCI and other key health leaders about the vast amount of work not yet started where it really counts, at the community level–where one out of every four people will be victims of this disease."

Donovan said this meeting, like ACCC's other efforts, was aimed at helping the formation of these programs through self-efforts. He said that community cancer programs cannot count on total assistance from federal government sources and must be built on that premise.

"The meeting is just the first of several major efforts by the association to provide open, continuing two-way communications for individuals involved in community cancer care," Donovan said. "Other efforts will include the development of an ongoing assistance program to new and established community cancer groups and programs, and a mechanism for insuring rapid translation of new technology and a form useful in community care.

"Our program is designed to give the individual who sees a need for a cancer program in his or her community the opportunity to discuss the experiences and problems others have had in trying to develop a community program. We will try to provide new programs with as much direct assistance as the association can afford. Right now we are the only source they can turn to," said Donovan.

Registration forms for the meeting may be obtained by writing to ACCC, P.O. Box 30279, Bethesda, Md. 20014, or by calling ACCC executive secretary, Lee Mortenson at 301-656-3987. The meeting will be held at the Key Bridge Marriott hotel.

NCAB GIVES PRESIDENT FORD EVIDENCE BACKING LIMITS ON TAR AND NICOTINE

President Ford now has in his possession what NCI staff members and the National Cancer Advisory Board feel are sufficient scientific references to support an effort to obtain legislative authority for regulation of tar and nicotine content of cigarettes.

Ford had asked NCAB Chairman Jonathan Rhoads to furnish him with the scientific evidence backing up the Board's earlier request that a federal agency be given regulatory power over cigarettes. Such power is now specifically denied to FDA and the Consumer Product Safety Commission, the most likely agencies to undertake such regulation.

The Board approved a statement citing numerous studies which link cigarette smoking to lung cancer and to other cancers and respiratory and cardiovascular diseases.

The statement was accompanied by a reference appendix listing specific studies. The appendix noted that "the scientific literature in smoking and health cannot be reported here in detail, because of its vastness. This document offers guidance to selected publications giving critical analysis of the scientific literature, prominent among which are the annual reports to Congress by the United States Surgeon General on the health consequences of smoking, as compiled by the National Clearinghouse for Smoking and Health.

"The additional listing of specific scientific references does not imply that other studies are less important or valid, but simply offers selected examples.

"Some of the latest information on consumer statistics and trends in disease incidence is still unpublished, but it can be described and defended by expert witnesses should hearings become necessary."

It is unlikely that even with the President's all-out support Congress would pass a bill permitting the enforcement of tar and nicotine limits. The tobacco industry is adamant in its opposition, and tobacco-state congressmen and senators have effectively blocked most efforts in the past opposed by the industry.

The Board recognized this and suggested another move the President could make: a personal appeal to the industry to step up the process it has been carrying out voluntarily over the last 20 years in reducing tar and nicotine content.

"The next step is up to the President, to decide whether or not to ask Congress for the necessary legislation," Rhoads commented.

"He's been sitting over there (in Congress) for 28 years listening to some very vocal congressmen say we haven't got the evidence," Panel Chairman Benno Schmidt said. "He's asked us for that evidence."

The statement approved by the Board (but not the appendix) follows:

WHEREAS:

1. A very low incidence of primary lung cancer is observed in non-smokers, but the overwhelming majority of the over 80,000 current annual deaths in the U.S. alone is observed among habitual cigarette smokers. The dose-response relationship between the number of cigarettes smoked and incidence of cancer of the lung has been established beyond doubt by numerous epidemiological studies in man.

(Notable examples are: A study by Hammond and Horn where, compared to non-smokers, the risk of dying of lung cancer is eight times more for habitual smokers of less than 10 cigarettes a day, 10.5 times for 10 to 20 cigarettes, and 23.4 times for smokers of over 20 cigarettes daily. Similarly, Doll and Hill found that in England the same risk is 18.4 times higher for habitual smokers of 1 to 14 cigarettes daily, 19.86 times for 15 to 24 cigarettes, and 23.43 times higher for smokers of over 25 cigarettes daily. The differences among these and other studies are to be found in the different populations studied, different cigarettes consumed and different survey times, but a similar dose-response trend is confirmed by the scientific evidence available.)

2. Carcinoma of the larynx and oral cavity, and certain respiratory and cardiovascular diseases also have shown a dose-response relationship with smoking of cigarettes, and evidence for less pronounced cigarette smoking dependence has also been found for cancer of the esophagus, of the bladder, of the pancreas, and other forms of disease.

3. Epidemiological studies in ex-smokers indicate that a diminution of risk of lung cancer takes place after cessation of the habit, and continues to diminish with time.

(A notable example of evidence is the study by Doll and Hill where, compared to non-smokers, the risk of dying of lung cancer for continuing smokers is 18.29 times, decreasing to 9.57 times for those that have quite smoking for over 5 years, 7 times for those between 7 and 9 years, 2.57 times between 10 and 20 years and 2.75 times for over 20 years after cessation of smoking.)

4. Toxic components are found in both the condensate and the gas phase of cigarette smoke. But the primary sources of toxicity so far indentified are tar and nicotine and probably carbon monoxide, nitrogen oxides and hydrogen cyanide.

5. The experience of the last 20 years indicates that the consumer can be accustomed to the use of milder cigarettes without causing appreciable marketing changes. The sales-weighted approximate average cigarette yield of commercial cigarettes marketed in the United States during 1973 was 19.2 milligrams of tar and 1.3 milligrams of nicotine (FTC standards), reflecting current consumer demand and acceptability. However several popular brands are still being marketed with tar contents of 28 to 30.5 milligrams and nicotine content as high as 2.2 milligrams according to FTC reports.

THEREFORE:

The NCAB recommends legislative and/or regulatory action by the Federal Government as follows:

1. A government agency should be empowered to set maximum cigarette levels of tar and nicotine that will become progressively lower than the 1973 averages of 19.2 milligrams and 1.3 milligrams respectively. Such decreases should be undertaken slowly enough to insure that no important increase in number of cigarettes consumed does occur. These actions should insure that a range of cigarettes including some with very low tar and nicotine contents continue to be available.

2. Because smoking has a severe impact on cardiovascular and respiratory diseases, the government agency empowered to regulate maximum emission of undesirable smoke components should get appropriate technical advice from the National Heart & Lung Institute.

3. Pending the accomplishment of the foregoing recommendations through changes in the existing law, the President of the United States might consider making a public personal appeal to the tobacco and cigarette industry for voluntary, and rapid effort towards preferential marketing of low tar and low nicotine cigarettes, and towards reduction of other smoke components that may be recognized as hazardous.

4. The public must be informed that there is currently no known formula for a safe cigarette, and that the restrictions here suggested are likely to produce, but cannot guarantee a reduction of hazards from smoking. For health protection, the safest course is not to smoke at all. It is particularly important that education in the schools be continued and improved to prevent future generations from acquiring smoking-related diseases.

Contract Awards

JRB ASSOCIATES WIN $3.6 MILLION NCI PLANNING SUPPORT CONTRACT

JRB Associates, a McLean, Va. management firm, has won the $3.6 million systems planning support contract for NCI for the second year in a row.

The job of providing logistics and administrative support for NCI's various planning efforts originally went to Auerbach Associates. JRB won out over Auerbach and others when the contract was recompeted last year.

NCI is still analyzing data generated by the planning conferences held earlier this year, when the National Cancer Plan was updated. JRB is helping to "massage" that data; will set up and help manage other NCI conferences this year; and is making projections on resources, construction and training needs.

Other contract awards include:

Title: Breast cancer detection demonstration project
Contractor: College of Medicine & Dentistry of New Jersey, $183,333.

Title: Technical services in support of the Cancer Communications
Contractor: The Mitre Corp., $483,819

Title: Radioisotope labeling of bleomycin for tumor scanning
Contractor: Washington Hospital Center, Washington D.C., $37,000

Title: Chemotherapy studies in patients with breast cancer
Contractor: Mayo Foundation, $243,067

Title: Combination testing of drugs and data preparation
Contractor: Leo Goodwin Institute for Cancer Research, Fort Lauderdale, $20,041

Title: Continuation of induction, biological markers, and therapy of tumors
Contractor: Hazleton Laboratories, $426,246

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. Some listings will show the phone number of the Contract Specialist, who will respond to questions about the RFP. Contract Sections for the Cause & Prevention and Biology and Diagnosis Divisions are located at: NCI, Landow Bldg. NIH, Bethesda, Md. 20014; for the Treatment and Control Divisions at NCI, Blair Bldg., 8300 Colesville Rd., Silver Spring, Md. 20910. All requests for copies of RFPs should cite the RFP number. The deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP NCI-CB-53893-31

Title: *Detection of circulating antigen–antibody complexes in cancer*
Deadline: *Jan. 7, 1974*

It has been reported that serum of cancer patients and of animals with cancer contain antibody-antigen complexes where the antigen presumably is tumor associated and/or specific. The presence of such circulating complexes has been deduced from the ability of the sera to block the destruction of tumor cells by lymphocytes presumably sensitized to the tumor, and by the deposition of complexes in the kidneys of some tumor bearing individuals. At present, there is no unequivocal evidence proving the existence of such circulating antibody-antigen complexes.

NCI is interested in finding laboratories that are capable of developing methods and techniques for the detection of circulating antibody-antigen complexes in serum of patients and/or animals with cancer. The first objective of this contract is to establish beyond doubt the existence of circulating antibody-antigen complexes in the serum. Demonstration of blocking activity in serum is not deemed as sufficient proof for the presence of such complexes.

The second objective is the development of tools that permit the rapid, unequivocal detection of such complexes on a quantitative basis. The third objective is the comparison of levels of complexes in cancer patients versus benign disease and normal controls, and the study of the significance of the complexes in serum for the pathogenesis, prognosis, and diagnosis of the disease. For example, is blocking by such complexes an in vivo phenomenon? Are the complexes deposited in the patient's kidneys? Can the presence of such complexes reveal something about tumor associated antigens or the immune response of the patient to his own cancer?

Contractor must have demonstrated immunochemical expertise in the field of antibody-antigen detection, should have general experience in clinical immunology especially with cancer patients, and should have easy access to cancer patients. It is also desirable to have experience in immunopathology, serology, in vivo and in vitro immune reactions of the cellular and humoral type. A syngeneic animal tumor system as a model for working out methodology is acceptable, but the technique must be applicable to the detection of complexes in patients with cancer, where the antigens are not known.

RFP NCI-CB-53894-31

Title: *Role of antibody-dependent cell-mediated cytotoxicity in tumor immunity*
Deadline: *Jan. 7, 1975*

Cytotoxicity of syngeneic tumor cells by antibody-dependent cell-mediated mechanisms has recently been demonstrated in a few systems. It remains to be determined how important this mechanism is for host resistance against tumor growth, and whether detection of antibodies mediating this effect would be useful for detection of tumors or for monitoring of tumor growth.

NCI is seeking laboratories to study antibody dependent cell-mediated cytoxicity in syngeneic or autochthonous tumor systems. The tumor systems to be selected should be directly relevant to a human tumor system, and should be primary or recently derived rather than in transplant for long periods of time. The ability to subsequently proceed from animal models into a human tumor system is desirable, but not a requirement for this project.

The studies should be concerned with some or all of the following objectives:

1. Characterization of the effector cells (origin, membrane properties, functional capacities as determined by cytotoxicity tests) which mediate the cytotoxic effects, within the particular tumor system.
2. Nature of humoral antibodies required, and

correlation of antibody levels to tumor status of the hosts.

3. Demonstration of specificity of observed reactions.

4. Correlation of antibody activity detected by cell-mediated cytotoxicity with an independent measure of antibodies.

5. Study of possible in vivo protective effects of these antibodies, to determine relevance of antibodies to host resistance against tumor growth.

An isotopic assay for measurement of cytotoxicity must be employed, either alone or in conjunction with visual microcytotoxicity assays.

RFP NCI-CB-53895-31

Title: *Measurement of antigens in tissue sections of human tumors*

Deadline: *Jan. 7, 1975*

There have been some indications that the presence or absence of antigens, or quantitative variations in antigens, may be associated with the biological behavior of tumors and may correlate with prognosis. Assessment of antigenic profiles in tissue sections of tumor biopsies may aid in the diagnostic and prognostic evaluation.

NCI is seeking laboratories to:

1. Establish methods for detection and measurement of tumor associated and normal antigens (e.g. organ associated and blood group antigens) in fixed or cryostat sections of tumors. The assay method should be practical for large scale application.

2. Use already available antisera with defined specificities for these studies, and use assay which will permit detection of quantitative variation in antigenic content.

3. Compare antigenic content of sections of normal and tumor tissue.

4. Analyze the relationship between the antigenic content of tumor at the time of diagnosis, with the subsequent biological behavior of the tumors and the clinical course of the patients.

RFP NCI-CB-53896-31

Title: *Antibodies to human organ or tissue associated antigens*

Deadline: *Jan. 7, 1975*

NCI is seeking labs for detection of antibodies to human organ or tissue associated antigens. These antibodies are needed for study of the antigenic profile of normal and neoplastic cells, both from biopsies and in tissue culture. These are needed to type and monitor cultured cell lines according to tissue or origin (e.g. distinguish breast from cervical cells). Such antibodies could also be used to measure quantitative decrease or loss of normal antigens from tumor cells. In addition, antibodies to tissue associated antigens should be able to distinguish cells of different origins in mixed cell populations, and possibly aid in the separation of cell types (e.g. epithelial cells from fibroblasts).

1. Develop antibodies to epithelial cells from different organs, and also to fibroblasts or other stromal cells.

2. Determine specificity of the antibodies and characterize them, particularly for their ability to clearly discriminate between one cell type and another. The assay technique should be capable of reflectingdifferences among single cells (e.g. immunofluorescence), rather than only on large populations of cells. It would also be desirable for the assay to be able to measure quantitative differences in antigenic expression.

3. Both normal tissues and tumors and tissue cultured cells should be studied for the expression of these tissue associated antigens.

RFP NCI-CB-53897-31

Title: *Development of practical techniques for the separation and isolation of human tumor cells and/or fetal cells*

Deadline: *Jan. 7, 1975*

NCI is seeking laboratories for the development of techniques to provide standardized human tumor and control cells, for use in immunological assays (e.g. microcytotoxicity assays and lymphocyte stimulation). There are promising indications of the potential use of cell-mediated assays for monitoring anti-tumor reactivity in tumor patients, and it is important to produce a reproducible source of antigenic target cells for these and other immunological assays.

Techniques have recently been described for the separation of tumor cells from other cells (e.g. gradient centrifugation). Further investigation is needed to develop practical and reproducible procedures for tumor cell isolation from biopsy specimens. In addition, comparable techniques are needed to isolate one type of normal cell from another, in specimens of normal adult tissues or fetal tissues. Since work along these lines is needed for both tumor and fetal specimens, the project could be limited to either one, or both.

1. Perform studies to improve isolation of intact, viable human tumor cells, with high yield and purity, from fresh tumor specimens. The types of cancer to be studied will be one or more of the following types: carcinomas of the lung, colon, and breast, and malignant melanoma. Similar procedures should be used to isolate normal epithelial cells from stromal cells, from normal tissues of similar tissue origin as the cancer.

2. Alternatively, or in addition, perform similar procedures to isolate normal epithelial cells from tissues of first trimester fetuses.

3. Develop better techniques for preservation of these isolated cells in a viable state.

4. After freezing, the isolated cells should retain the capacity for growth in short term cell culture (1 to 4 weeks).

5. The isolated cells will be tested, before and after preservation and after short term growth in culture, for viability, purity of cell type and characteristics (morphological, biological, biochemical and immunological).

RFP NCI-CB-53901-31

Title: *Development and evaluation of macrophage electrophoretic mobility assay for malignant disease*

Deadline: *Jan. 9, 1975*

Field and Caspary reported that the interaction of lymphocytes from cancer patients with a basic protein derived from brain or from tumors gave positive macrophage electrophoretic mobility (MEM) assays (Lancet 2:1337, 1970; Br. Med. J. 2:613, 1971). This assay appeared to clearly distinguish between patients with cancer and normal controls. Pritchard et al (Br. J. Cancer 27:1, 1973) have essentially confirmed these results. If further substantiated, this assay would have considerable value in the immunodiagnosis of cancer. NCI is seeking laboratories to further evaluate this test, determine its possible clinical applications, and to either standardize the current assay or develop an improved method for detection of reactivity.

1. Set up macrophage electrophoretic mobility assay as previously described.
2. Perform MEM assays with lymphocytes from patients with a variety of neoplastic diseases, patients with benign diseases of the same organs, and normal controls.
3. Perform statistical evaluation of results, and relate results in cancer patients to type of disease and disease status.
4. After initial studies demonstrating correlation between test results and cancer, the laboratory must be willing to perform further tests with coded blood specimens provided by a separate local institution, to be designated by NCI.
5. Make modifications in current assay to make it more standardized or develop an improved method for detection of reactivity. The developmental work could be performed in an appropriate animal model system or with clinical materials.
6. Previous experience with the MEM assay is not required, but general experience with assays of human cell-mediated immunity is expected.

Contract Specialist for the tumor immunology RFPs above: Robert S. Townsend
Biology & Diagnosis
301-496-5565

RFP NCI-CN-55198-09

Title: *Clinical oncology program*

Deadline: *Probably mid-January*

NCI is soliciting proposals for a program to establish multidisciplinary teams of clinical oncologists practicing in community hospitals. A consortium of no more than three hospitals may collaborate in the preparation of a proposal, provided that one institution functions as the primary contractor.

There must be a minimum of 300 new cancer admissions to the hospital(s) annually, exclusive of early skin cancer. Only community hospitals without major affiliations with a medical school or comprehensive cancer center are eligible to respond to this RFP. The program is designed to create mechanisms (in the community) for field-testing new methods and techniques for the treatment, rehabilitation and continuing care of patients with cancer.

The contractor will be responsible for the planning phase (which will be limited to a 12 month period) to recruit and identify the manpower and physical resources to carry out the objective of the program. Offerors will be evaluated on technical approach and understanding of the objectives, experience and expertise of the personnel proposed, competence for organizational management and the offerors' resources and facilities. The RFP will be issued in mid-December.

Contracting Officer: Hugh E. Mahanes Jr.
Control & Rehabilitation
301-427-7984

SOLE SOURCE NEGOTIATIONS

Proposals are listed here for information purposes only. RFPs are not available.

Title: Coordination of mammography education programs
Contractor: American College of Radiology

Title: Breast cancer detection demonstration project
Contractors: Samuel Merritt Hospital, Oakland, Calif., and Iowa Lutheran Hospital, Des Moines

Title: Immunological and biochemical studies of mammalian viral oncology
Contractor: Meloy Laboratories

Title: Spontaneous and virus induced neoplastic transformation
Contractor: Meloy Laboratories

Title: Research on oncogenic and potentially oncogenic viruses, virus production and vaccine development
Contractor: Merck & Co., Inc.

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