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NEW OPPORTUNITIES STILL ABOUND IN IMMUNOLOGY PROGRAM, TERRY AND OTHER NCI EXECUTIVES SAY

Immunology has been considered the "hottest new field" in cancer research long enough now to have almost lost the right to be considered "new." There are still plenty of new opportunities, however, NCI Immunology Program executives told the President's Cancer Panel last week.

Panel Chairman Benno Schmidt previously had criticized the immunology contract program as being unnecessary. There is such widespread interest in the field throughout the scientific community that it ought not to be necessary to stimulate interest in any particular area through contracts, Schmidt argued, maintaining that investigator-initiated

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In Brief

NEW CONTRACT TO SPEED DRUG DEVELOPMENT PLANNED; GROUPS TO GET $5.6 MILLION EXTRA

NEW EFFORT to speed up NCI's drug development program has resulted in one RFP (see RFPs Available, this issue) to consolidate, expand large scale extraction, isolation of plant products. This is the job that follows identification of a new potential anticancer agent. It has been done under contracts with Parke Davis and Monsanto with a total annual effort of approximately four man years. The new contract will increase that effort by 50% and place it in the hands of one contractor. Parke Davis and Monsanto will continue developing synthetic anticancer agents under their existing contracts, probably with an increase in that workload. Other steps are being considered to reduce the time between identification of a new agent and clinical trials, now as much as four years. . . . **COOPERATIVE GROUPS** whose applications were approved for supplemental funds to finance multimodality expansion will get a total of $5.6 million in new money. That figure was established after Congress overrode the appropriations bill veto. In addition, $800,000 earmarked for the Western Cancer Study Group has ☆ been reprogrammed to surviving groups. . . . **GREGORY O'CONOR**, associate director for international affairs, will leave NCI to become director of the Colorado Comprehensive Cancer Center. . . . **GUIDELINES** developed by the Recombinant DNA Molecule Program Advisory Committee for research involving recombinant DNA molecules will be further discussed at the committee meeting April 1-2. The proposed guidelines for research which the committee says "promises to revolutionize both biological research and its practical application" deals with safety features (containment), experimental guidelines and "experiments that should not be performed" because of the possible dangers that may ensue if containment fails. Copies of the proposed guidelines are available from the committee, William Gartland, executive secretary, NIH Westwood Bldg, Room 922, Bethesda, Md. 20014.

☆ OCC / Dennis Doris checked & confirmed that the Group no longer exists

GRANTS SUPPORT 70% – $40 MILLION – OF EXTRAMURAL IMMUNOLOGY RESEARCH

(Continued from page 1)

immunology studies would best be supported through grants.

William Terry, associate director for the immunology program in the Div. of Cancer Biology & Diagnosis, led a presentation to the Panel in response to Schmidt's remarks. He pointed out that in the 1975 fiscal year, 70% of extramural immunology research was supported by grants, with only 30% for contracts. NCI spent $55.6 million on immunology grants and contracts–$38.6 million in grants through the Div. of Cancer Research Resources & Centers, $13 million in contracts through Biology & Diagnosis, $1.5 million in grants (to the cooperative groups) through the Div. of Cancer Treatment, another $1.5 million in contracts through DCT, and $1 million in contracts through the Div. of Cancer Cause & Prevention.

The total broke down to $40.1 million for grants and $15.5 million for contracts.

"I'm reassured by those numbers," Schmidt said. "I think that's a proper balance between grants and contracts."

Barbara Sanford, program director for immunology in DCRRC, has primary responsibility for overseeing the $38.6 million grants program in that division. She outlined these areas as those in which the best opportunities lie:

• Continued support of basic immunobiology. "The current level of scientific interest in such problems as the role of the major histocompatibility locus in immune reactions is very high and scarcely requires additional stimulation by NCI. On the other hand, adequate support is urgently needed and it is, therefore, important that the DCRRC Immunology Program continues an active effort to secure assignments of basic immunobiology grant applications. Support of workshops and other types of informational exchange on topics in rapidly advancing areas of immunology also seem justified."

• Identification and characrerization of human tumor associated antigens. "Although a large number of human tumor associated antigens have been reported, it is generally not clear whether the antigenic specificities being detected are related to individual or cross-reacting tumor antigens or to fetal, histocompatibility, or autoimmune antigens. Identification and characterization of new human tumor antigens requires a combination of clinical, immunological and biochemical expertise. Since a multidisciplinary team focusing on this problem appears to be the most promising approach, program projects in this area are being encouraged."

• New approaches to immunotherapy. "Although some success is being achieved with the immunotherapeutic approaches now in use, most investigators involved in clinical immunotherapy agree that new approaches are needed. The development of rational, effective immunotherapy is dependent to a large extent upon increased understanding of the immune system and how it can be manipulated. There is also a need, however, for careful model studies on new approaches, preferably stressing mechanisms of action rather than simply the testing of new agents according to various schedules. Investigators are being encouraged to submit grant applications for projects of this type.

"One type of immunotherapy in which there has been a recent resurgence of interest is the use of antibodies to deliver radiation of drugs to tumors. Since a number of laboratories throughout the world are now involved in this type of effort, a workshop or conference in this area might be useful and is under consideration.

"Among other areas where stimulation of increased activity is needed, either by encouragement of grant applications or by sponsorship of conferences or workshops, are: immunosuppressive factors produced by tumor cells and viruses; mode of action of adjuvants; physiologic and polygenic aspects of immunogenetics; monoclonal antibody toward viral antigenic determinants; and radioimmunoassays for newly established human tumor associated antigens."

• Encouragement of young investigators. "Efforts at attracting able young investigators into immunology have high priority in the Immunology Program. Small regional meetings between young investigators and leaders in the field are being tried on a pilot basis as a means of stimulating interest in tumor immunology."

Sanford commented that "there are already promising leads which suggest that effective methods of immunodiagnosis, immunotherapy, and immunoprophylaxis can and will be developed. All of these practical approaches, however, clearly depend upon an adequate understanding of the immune reaction; thus an investment in basic immunology at this time seems most likely to facilitate development of the other areas. It is for this reason that immunobiology is the area presently receiving the greatest emphasis in the immunology grants program.

Recent advances and emerging areas of interest include, Sanford said:

"One of the most exciting developments in the past few years has been the discovery of the critical role of the major histocompatibility complex in cell to cell interactions. Of particular interest in relation to cancer is the emerging evidence suggesting that tumor specific antigens may represent modified histocompatibility antigens.

"Another important area which is now rapidly developing is an analytical approach to cellular immunology. A relationship between cell surface antigens and functional characteristics has been demonstrated; for example, suppressor T cells have been shown to carry different Ly antigens than helper T cells. An-

other approach which allows a different type of analysis of lymphocyte subpopulations is provided by recently developed methods for separating antigen specific lymphocytes. Taken together, these advances give great promise for an increased understanding of the lymphocyte in the near future.

"The demonstration of spontaneous killing of human target cells by lymphocytes in culture has also received considerable attention. It is particularly important that this phenomenon be investigated and understood, since it is a complicating factor in the interpretation of in vitro tests of cell mediated immunity in man.

"Modulation of the immune response by anti-idiotype sera is another approach currently generating much interest. The observation that a specific immune response can be stimulated or suppressed even in the absence of the relevant antigen has provoked interest not only in understanding the basic mechanism involved, but also in investigating the possible application of this type of manipulation to cancer and transplantation, as well as to infectious disease.

"Evidence is accumulating which suggests that most 'spontaneous' tumors are of low immunogenicity. This has two obvious implications: (1) the usual laboratory study which involves highly immunogenic tumors induced by viruses or chemical carcinogens does not provide an appropriate model for the study of spontaneously occuring human malignancies and (2) in designing approaches to immunotherapy, the usually low immunogenicity of tumor cells is an important factor which must be taken into account.

"The hypothesis that immune surveillance serves to protect individuals against development of tumors has continued to come under severe attack. A substantial body of data has been developed which indicates that immunosuppressed hosts do not generally demonstrate an overall increase in tumor development. There is, in fact, even some recent evidence suggesting that under certain conditions an immune response may stimulate the development of tumors. The role of the immune system in carcinogenesis is still not clear, however, and there is promise of controversy in this area for some time to come."

Sanford singled out some important recent contributions supported by grants. They included:

E.A. Boyse, Sloan Kettering Institute—Evidence has been obtained that functionally distinct T-cell subclasses exhibit different cell surface markers. Generation of these subclasses was shown to be a differentiative process independent of antigen.

Baruj Benacerraf, Harvard Univ.—Lysis of tumor target cells by syngeneic cytotoxic T lymphocytes was shown to be inhibited to a large extent by allo-antisera directed to antigens coded for by certain regions of the H-2 complex. These findings suggest that tumor associated antigens best able to elicit cytotoxic T lymphocyte responses may represent altered or modified H-2 antigens.

Herman Eisen, MIT—High levels of immunoglobulins with the T15 idiotype were found in normal serum of BALB/c mice, suggesting tolerance to this idiotype. It was shown that all BALB/c mice have B cells that can recognize and respond to the idiotypes of virtually all myeloma proteins of BALB/c origin. This could mean that each individual potentially has B cells that can respond to idiotypes of their own immunoglobulins. This finding supports the hypothesis that interaction of idiotypes and anti-idiotypes can result, under physiological conditions, in the regulation of immunoglobulin production.

Richmond Prehn, Institute for Cancer Research—Data supporting the role of "Immunostimulation" during tumor development was obtained. It was found that partially immunocrippled nice that were partially restored by syngeneic spleen cells were more susceptible to oncogenesis than were those either not restored or maximally restored and that there is no increase in spontaneous or induced tumors in congenitally athymic mice.

Osias Stutman, Sloan Kettering—It was demonstrated that the immune deficit of the congenitally athymic nude mouse markedly increased susceptibility to polyoma virus infection. These results contrast with the investigator's earlier observation that the immune deficit of the nude mouse had no detectable effects on oncogenesis by methylcholanthrene or urethan. It was also shown that the nude mouse can develop a late but rather efficient resistance to polyoma oncogenesis which seems to be mediated by B cells and is thymus independent.

Darcy Wilson, Univ. of Pennsylvania—Methods have been developed for separation and functional studies of sub-populations of antigen-specific lymphocytes. Using negative selection, it was possible to recover a sub-population of T cells which lacked specific allogeneic reactivity but were still functionally normal in helper effects for allogeneic B cells. Conversely, using positive selection for cells with enriched reactivity to a particular histocompatibility antigen, it was possible to demonstrate quantitatively normal helper effects of these cells for non-histocompatibility antigens. This work raises interesting questions about the nature of the T cell receptor.

Terry said there was "a good deal of coordination" among the immunology programs of the four divisions. "The people operate well together and I would say the program is well coordinated," Terry said.

Ronald Herberman, chief of the laboratory of immunodiagnosis in Biology & Diagnosis, and Dorothy Windhorst, who heads the immunotherapy program in the division, discussed projects supported by contracts in their respenctive areas. Terry discussed existing immunobiology contracts.

Terry referred to several RFPs issued last year for projects in which proposals are now being evaluated. One, titled "New approaches to immunotherapy," is

an example of a project in which his advisory committee feels it "has the capacity to define areas of need and can direct the way to go," Terry said. The RFP asks for "creative approaches to the use of the immune system for cancer therapy," with both animal and human studies.

Another RFP, for studying "Immunogenicity of spontaneous animal tumors," was for an area in which "not a single grant supports this kind of work," Terry said. "One might intuitively think that a lot of investigator-initiated work was being done, but there isn't." Terry said there were nine or ten responses but that he had not yet seen them. "Maybe no one has any good ideas here, or maybe it will be too expensive, but we felt we should find out."

Terry said there were about 40 responses to the RFP calling for clinical evaluation of immunodiagnostic tests for cancer. NCI wants to evaluate assays with potential for the immunodiagnosis of cancer and asked labs which have developed a serologic assay to submit their data to Terry's group. If the preliminary data supports the assay's ability to discriminate between cancer patients and controls, NCI will supply a coded panel of sera with which to test it. If the assay gives distinguished performance on the serum panel, NCI will send an RFP to the requestor.

A different use of an RFP, Terry said, is the one titled, "Cells involved in the immune response to tumors." It called for investigation of the role of cell interactions and/or an analysis of the function of individual subpopulations in the generation and/or suppression of immune response to tumor cells. Terry said there was much activity already in this area, in both the grant and contract programs, but "it is an exceedingly complex, difficult area. We will not have overkill with another RFP. The committee feels it is an area where we have not peaked and there is a need for more work."

DCRRC Director Thomas King agreed that coordination between his division and Terry's program "is remarkably good."

Schmidt acknowledged he was convinced the contract program was sound, emphasizing that the quality depended on the quality of peer review.

Terry insisted that there was no reason why peer review could not be just as good with contracts as it is with grants.

The problem with contracts, unlike grants, Schmidt said, "is when they (the review groups) yield to the temptation to do more refining, or when you get a peer review group that's a little less ornery than the study sections. But you've got a splendid program going, and that's the bottom line."

The final bottom line, Panel Member Lee Clark suggested, was the impact on the cancer patient. He said investigators at his institution (Univ. of Texas System Cancer Center–M.D. Anderson Hospital) believe that at least half of their patients who die with cancer actually die from infections and not the cancer. Most of the infections occur because of the immunosuppressive effect of the therapy, primarily chemotherapy, although sometimes radiotherapy and even surgery result in immunosuppression, Clark said.

A program was started in 1974 at M.D. Anderson, without any grant or contract support, to test the immunocompetence of cancer patients. Those found to be immunoincompetent were placed in a protected environment until until their level of immunity increases.

"We're using some rather crude tests," Clark said. "We need better tests, and we're working on that now."

MDA BREAST CANCER STUDIES PROMISING; NEJM PUBLISHES BONADONNA FINDINGS

Immunotherapy also has an important role in breast cancer clinical studies at M.D. Anderson, Clark said. He feels those studies may produce results at least as good as and perhaps better than the CMF study of Gianni Bonadonna (published last week in the *New England Journal of Medicine* and reported last October in ***The Cancer Letter***).

The M.D. Anderson study is under the direction of Jordan Gutterman, associate professor of medicine in developmental therapeutics. Four regimens are being followed, the longest of which has been used for 22 months, so the data must be considered preliminary. All patients entered in the program had four or more positive axillary nodes in which recurrence within 18 months following surgery without chemotherapy is 50%.

The immunostimulant BCG is used in two of the regimens. With BCG alone, five of 22 patients recurred after 22 months, with no deaths. Adriamycin plus BCG used on 31 patients had two recurrences and one death after 18 months.

Another study used CMF (cyclophosphamide, methotrexate and fluoracil) plus vincristine and adramycin. There was one recurrence out of 19 patients, with no deaths, after 13 months.

In the fourth study, adriamycin replaced methotrexate in the CMF combination. After nine months, there have been two recurrences out of 23 patients.

Publication of Bonadonna's findings in a medical journal should provide a strong impetus toward acceptance of the CMF adjuvant therapy by the medical profession without waiting for long-term data (see ***The Cancer Letter,*** Feb. 13). Bonadonna's article was accompanied by an editorial written by James Holland, chairman of the Mt. Sinai Dept. of Neoplastic Diseases and director of the Mt. Sinai Cancer Center, urging just that.

"The CMF treatment . . . has produced results nothing short of spectacular," Holland wrote.". . . Much research remains to be done (Can the extent of radical surgery be decreased? Should the treatment be used in the absence of axillary metastasis? Should the

drugs be changed? Should immunotherapy be added?) but this should not impede the adoption of the treatment by qualified physicians for patients who cannot participate in this research. The study is a primer on how powerful a tool the controlled clinical trial is as a research method. The conclusions can be accepted with confidence.

"The study from the National Cancer Institute of Italy shows the value of both medicine and surgery in cancer therapy," Holland continued. "How many hundreds of thousands of lives can be improved, or indeed saved, by application of the present information in the coming decade? The risks of carcinogenesis, fatal drug intoxication, and other morbidity are certainly of much less hazard than the certain death that inexorably follows clinically evident metastatic cancer."

WHITE HOUSE AGREES TO PAY RAISE FOR NCI CHIEF; CONGRESS OK NEEDED

The White House has agreed to go along with a plan to increase the salaries of the director of NIH, the National Cancer Institute, and the National Heart & Lung Institute which would have the immediate effect of keeping Frank Rauscher as director of NCI and the National Cancer Program.

The three would get a raise to $65,000. Rauscher now receives $37,800 and has said that financial hardship has led him to consider accepting a high paying job offer from industry.

No legislative authority now exists to permit the raises; the plan is to add it as a rider to a bill now pending in Congress.

NCI ADVISORY GROUP, OTHER CANCER MEETINGS SCHEDULED IN MARCH, APRIL

Diagnostic Research Advisory Group—March 2, NIH Bldg 31 Room 7, open 8:30—10 a.m.

Breast Cancer Task Force—March 3, Bethesda Holiday Inn, 8:30 a.m.—5 p.m., all open.

National Cancer Advisory Board Subcommittee on Environmental Carcinogenesis—March 3-4, NIH Bldg 31 Room 7, March 3; National Library of Medicine Billings Auditorium, March 4; 9:30 a.m. both days, all open.

Breast Cancer Diagnosis Committee—March 4, NIH Bldg 31 Room 7, open 9—10 a.m.

Breast Cancer Treatment Committee—March 4, Landow Bldg Room C418, open 8:30—10 a.m.

Committee on Cancer Immunotherapy—March 4, NIH Bldg 10 Room 4B14, open 1—1:30 p.m.

Breast Cancer Experimental Biology Committee—March 4, NIH Bldg 31 Room 9, open 8:30—9:30 a.m.

Breast Cancer Epidemiology Committee—March 4-5, NIH Bldg 31 Room 8, open March 4, 9—9:30 a.m.

FDA Oncologic Drugs Advisory Committee—March 4-5, Parklawn Bldg (5600 Fishers Ln., Rockville, Md.), Conference Room G, open March 4, 9 a.m.—3:30 p.m., March 5, 9 a.m.—noon.

Div. of Cancer Treatment Board of Scientific Counselors—March 8-9, NIH Bldg 31 Room 10, 9 a.m. both days, all open.

National Large Bowel Cancer Project Working Cadre—March 8-9, Shamrock Hilton, Houston, open March 8, 9—10 a.m.

Tobacco Working Group—March 10, NIH Bldg 31 Room 8, 9 a.m., open.

Cancer of the Bone, Soft Tissue and Melanoma—March 11, Roswell Park Continuing Education in Oncology, registration required.

National Bladder Cancer Project Working Cadre—March 11-12, Bethesda Holiday Inn, open March 11 8:30—9 a.m.

Committee on Cancer Immunology—March 14-16, Landow Bldg Room C418, open March 14, 7—7:30 p.m.

Future Direction of the Research Program in Radiological Diagnosis of Cancer, Workshop—March 16, NIH Bldg 31 Room 3A10, 9 a.m., open.

Cancer Control Supportive Services Review Committee—March 16, NIH Bldg 31 Room 9, 9 a.m., open.

Diagnostic Radiology Committee—March 17, NIH Bldg 31 Room 6, open 8:30 a.m.—noon.

Committee on Cancer Immunodiagnosis—March 17-19, Landow Bldg Room C418, open March 17, 7—7:30 p.m.

National Advisory Board Subcommittee on Centers & Construction—March 21, NIH Bldg 31 Room 8, open 7:30—9 p.m.

Subcommittee on Diagnosis & Treatment—March 21, NIH Bldg 31 Room 6, open 4—4:30 p.m.

Subcommittee on Carcinogenesis & Prevention—March 21, NIH Bldg 31 Room 8, open 4—4:40 p.m.

National Cancer Advisory Board—March 22-24, NIH Bldg 31 Room 6, open March 22, 9 a.m.—noon; open March 23 1:30—5 p.m.; open March 24, 9 a.m.—adjournment.

Virus Cancer Program Scientific Review Committee A—March 22-23, NIH Bldg 37 Room 1B04, open March 22, 9—9:30 a.m.

Clinical Trials Committee—March 24, NIH Bldg 31 Room 8, open 8:30—9 a.m.

Committee on Cancer Immunotherapy—March 25, NIH Bldg 10 Room 4B14, open 1—1:30 p.m.

Virus Cancer Program Advisory Committee—March 25-26, NIH Bldg 37 Room 1B04, 10 a.m. both days, all open.

Cancer Control Intervention Programs Review Committee—March 26, Landow Bldg Room C418, open 8:30—9:30 a.m.

Drug Development Committee—March 26, NIH Bldg 37 Room 6B23, open 9—9:15 a.m.

Committee on Cancer Immunotherapy—March 31-April 2, Landow Bldg Room C418, open March 31, 7—7:30 p.m.

Recombinant DNA Molecule Program Advisory Committee—April 1-2, NIH Bldg 31 Room 8, open April 1 9 a.m.—5 p.m., open April 2 11 a.m. —adjournment.

Third Symposium of CMEA Countires on Toxicological Testing of New Drugs—April 6-8, Prague.

Oncology Nursing—Major Treatment Modalities—April 8, Roswell Park Continuing Education In Oncology, registration required.

First International Symposium on Facial Prosthetics—April 19-23, Arnhem, Netherlands.

First International Congress on Patient Counseling—April 21-23, Amsterdam.

Drug Development Contract Review Committee—April 26, NIH Bldg 31 Room 7, 10 a.m.

Third International Symposium on Detection & Prevention of Cancer—April 26—May 1, New York City.

International Symposium on Medical Genetics—April 27-29, Debrecen, Hungary.

Div. of Cancer Biology & Diagnosis Board of Scientific Counselors—April 30-May 1, NIH Bldg 37 Room 4E08, open April 30 9 a.m.-5 p.m.

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 & 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 NO1-CP-65777-56

Title: *Markers for evaluation of preneoplastic lesions in the respiratory tract*

Deadline: *March 31*

In man, cancer of the lung may have a latent period of 20 years or more, during which preneoplastic lesions can be found in the respiratory tract. Although the presence of such lesions may be detected by the technique of sputum cytology, there is a paucity of formal criteria for evaluation of the status of preneoplastic lesions in the respiratory tract. The objective of this RFP is to develop new criteria and new methodology which will enable investigators to make a better analysis of such preneoplastic lesions. In this regard the experience of many investigators in the field of liver carcinogenesis may be usefully referred to. Since several good animal models of human bronchogenic carcinoma now exist, it may be desirable to investigate this problem in one of the appropriate animal models. Proposals that involve analysis of preneoplastic respiratory tract cells of tissues from either human or animal material will be given equal consideration.

The basic objective of this project is the establishment of new criteria, either morphological, immunological, or biochemical, which will enable a more exact determination of the extent and severity of respiratory tract preneoplasia. Whether the methods employed are morphological, immunological, or biochemical, the emphasis should be on techniques that can be objectively scored and do not rely solely on subjective impressions of the investigator. The major objective of this project is thus the development of diagnostic markers which would have wide-spread application in many laboratories for study of pathogenesis of lung cancer.

The government estimates that performance of the above described services will entail approximately 1 - 2 professional man years of effort per year.

Contract Specialist: Melvin Hamilton
Cause & Prevention
301-496-6361

RFP NCI-CM-67070

Title: *Large scale extraction and isolation of plant products*

Deadline: *March 26*

The contractor shall exert its best efforts to provide and operate a natural products derived material preparation laboratory to (1) develop existing or new processes, procedures and techniques for the extraction and isolation of materials from plant sources, and (2) prepare plant product derived materials in quantities sufficient for evaluation in cancer research.

The government will supply all plant products to be processed. Requests for compounds by the project officer will cover a variety of naturally occurring plant substances in quantities ranging, in general, from 1 gram to the multi-kilogram level.

Additionally, the contractor shall isolate, purify, and characterize antineoplastic substances from government furnished sources; perform stability, solubility, and analytical studies and purifications and characterizations of materials isolated; and conduct stability or safety studies in handling and storing of substances assigned to the preparation laboratory.

Major emphasis will be on the preparation of desired plant derived materials in pilot plant scale (kilogram) and will involve grinding, extraction, isolation, preparation and scale-up from a process either developed under this contract or supplied from the originating chemical contract. Process development for scale-up will be required, and production will require access to pilot plant equipment including at least a five hundred gallon glass lined reactor as a minimum.

Examples of compounds which will have to be extracted from plants are: nitidine, maytansine (5 grams from 20,000 pounds, tripdiolide, and indicine-N-oxide.

In some cases as much as 20,000 lbs. of plant material will have to be processed to provide enough of the active compounds for preclinical toxicology and phase I clinical trials. In other cases, small batches of plant material will be processed to provide enough of the candidate compounds for advanced evaluation in model tumor systems. In an effort to assist NCI natural products chemical fractionators, 100 to 500 lb. extractions will be made of various plants and the extracts will be shipped for work-up to these fractionators.

It is anticipated that the total project will require six technical man-years of effort per year.

Contract Specialist: Stephen Gane
Cancer Treatment
301-427-7470

RFP NCI-CM-67046

Title: *Production of bulk chemicals and drugs*
Deadline: *Approximately April 12*

The objective of this project is the preparation by synthesis of quantities of bulk chemicals and drugs, (1 gram to multikilogram) for use as potential anticancer agents. The major emphasis will be on the preparation of the desired material in multikilogram scale and will involve resynthesis and scale-up from the chemical literature. Methods will be available for small scale runs in many but not all instances. Process development for scale-up will be required.

The facilities must have the capacity for performing all types of chemical synthesis, including access to pilot plant equipment (minimum of a 500 gallon glass lined reactor required). All products must be completely assayed as to identity and purity. A well instrumented analysis laboratory and adequate library facilities must be available.

The principal investigator must be trained in organic chemistry, preferably at the PhD level or equivalent, from an accredited school with extensive experience in chemical synthesis and process development. The principal investigator must be named and all technical personnel must be assigned to the project a minimum of 50% of the time, preferably 100% of the time. It is anticipated that such a project will require a minimum of 10 technical man-years of effort per year. The effort may be undertaken in levels of either 5 or 10 technical man-year contract(s). The proposal may be at either or both levels of effort and should clearly indicate the level(s) being proposed.

Contract Specialist: W.T. Harris
Cancer Treatment
301-427-7470

RFP NCI-CM-63776

Title: *Preparation of radiolabeled materials*
Deadline: *April 1*

The contractor shall provide and operate a preparation laboratory for the synthesis of commerically unavailable radioactive labeled materials in varying amounts as selected by the project officer. Major emphasis will be on the preparation of the desired radiolabeled compounds via synthetic procedures and will involve a wide variety of compounds, such as heterocyclic compounds, alkaloids, folic acids, alkylating agents, nucleosides, nitrosoureas, etc. Compounds required may include one or more of the following radioactive elements: carbon, tritium, deuterium, phosphorous, sulfur, nitrogen, etc., and a broad AEC or equivalent license will be required. Methods of synthesis will be available for "cold runs" in many but not all instances. Development of new and/or existing synthetic procedures will be required.

Many of the materials may be toxic and potentially carcinogenic, in addition to being radioactive. Adequate containment and safety facilities must be available.

All materials must be assayed for chemical and radiometric identity and purity.

Materials assigned and their priorities of production are determined day by day as results of current investigations of the Div. of Cancer Treatment are reviewed and consolidated; consequently, a listing of materials to be made for this procurement is not available. Assignments will be made to the extent of direct effort provided under the contract. Broad versatility will be required of the technical personnel assigned since interest may develop in any chemical area.

It is anticipated that the total project will require a minimum of eight technical man-years of effort per year. The government will consider multiple awards of four technical man-years each or one award of eight technical man-years.

Contract Specialist: W.T. Harris
Cancer Treatment
301-427-7470

RFP NO1-CP-65776-56

Title: *Development of animal model for oat cell carcinoma of the lung*
Deadline: *March 31*

Cancer of the lung is now the leading cause of all cancer deaths in the United States. Oat cell carcinoma accounts for between 15 and 20% of all lung cancer deaths and has a particularly poor prognosis. Some groups of industrial workers, such as uranium miners and men exposed to bis-chloromethyl ether have had a particularly high incidence of this form of lung cancer. Although acceptable animal models for other forms of lung cancer, such as squamous cell carcinoma, currently exist, there is not a definitive animal system for inducing oat cell cancer. The object of this RFP is to develop such a system, so that the pathogenesis of this form of cancer may be further studied.

The basic objective of this project is the establishment of a reproducible system, in a small rodent, for induction of lung cancer that bears the strongest possible resemblance, both in terms of cellular morphology and pathological behavior, to human oat cell cancer. It is expected that the investigator will establish a defined route of administration of a chemical carcinogen or combination of carcinogens, to yield the appropriate tumor response. The resulting tumors should be fully characterized, both in terms of their morphological characteristics and in terms of any appropriate biochemical markers. The pathogenesis of the disease in the experimental animal should be characterized as fully as possible.

Primary interest is in an animal species which already provides an adequate model for study of human bronchogenic carcinoma, but consideration may be given to other species if there is a particular rationale. A screening approach to the development of an oat cell model is not intended in this effort and such proposals will be considered non-responsive.

The government estimates that performance of the above described services will entail approximately 1 - 2 professional man years of effort per year.

Contract Specialist: Melvin Hamilton
Cause & Prevention
301-496-6361

CONTRACT AWARDS

Title: Incorporation of 10 additional projects, involving alterations, renovations, A&E services, maintenance and upgrading of the Frederick Cancer Research Center facilities.
Contractor: Litton Bionetics, $239,299.

Title: Role of circulating tumor antigens in immunotherapy
Contractor: Scripps Clinic & Research Foundation, $103,424.

Title: Clinical oncology program
Contractors: Methodist Hospital of Indiana, $71,447; Bon Secours Hospital, Methuen, Mass., $71,688; Southwest Texas Methodist Hospital, San Antonio, $73,465; Valley View Hospital, Ada, Okla., $50,561; and St. Mary's Community Hospital, Walla Walla, Wash., $69,531.

Title: Design task for surveys of patient attitudes and knowledge about cancer control and rehabilitation
Contractor: Research Triangle Institute, $40,400.

Title: Continue the Detroit SSMA population based cancer registry
Contractor: Michigan Cancer Foundation, $1,690,-526.

Title: Studies on the possible viral etiology of human malignancies
Contractor: Baylor College of Medicine, $74,150.

Title: Epidemiologic studies of drug induced cancer
Contractor: Johns Hopkins Univ., $144,000.

Title: Etiologic studies of cancer in New Jersey
Contractor: New Jersey Dept. of Health, $83,078.

Title: Breast cancer detection demonstration project
Contractor: Georgetown Univ., Washington, D.C., $265,109.

Title: Chemotherapy studies of central nervous system solid tumors
Contractor: Arthur D. Little Inc., $378,527.

Title: Studies and investigations on new techniques for the study of cell kinetics of breast cancer
Contractor: Allegheny General Hospital, Pittsburgh, Pa., $163,400.

Title: Induction, transplantation & preservation of plasma cell tumors in mice
Contractor: Litton Bionetics, $310,474.

Title: Preparation of carcinogens compounds
Contractor: Midwest Research Institute.

Title: Preparation of various N-nitroso compounds
Contractor: Univ. of New Hampshire, $91,840.

Title: Development of cell strains from ductal and endocrine portions of the pancreas
Contractor: American Type Culture Collection, Rockville, Md., $71,244.

Title: Studies on polycyclic hydrocarbon metabolism in the respiratory tract
Contractor: Univ. of Stockholm, $175,547.

Title: Studies on pulmonary carcinogenesis
Contractor: New York Univ. Medical Center, $959,-563.

Title: Evaluation of assays of circulating tumor associated antigens: clinical usefulness of the AFP test and HCG in the differential diagnosis of testicular cancer
Contractor: Emory Univ., $25,442.

SOLE SOURCE NEGOTIATIONS

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

The propagation and seroepidemiology of EB viruses
The Children's Hospital of Philadelphia.

Production of athymic nude mice
Harlan Industries, Cumberland, Ind.

Production and detection of antibodies to chemical carcinogens and other small molecules
Brandeis Univ., Waltham, Mass.

Studies of modulating factors in respiratory carcinogenesis
IIT Research Institute.

HL-A typing and matching for platelet and luekocyte transfusions
UCLA.

Research on the antitumor resistance of extract (MER) of tubercle baccilli (BCG)
Hebrew Univ.

Perform mixed leukocyte cultures
Hazleton Laboratories.

Biological resources management information system support services
EG&G/Mason Research Institute.

The Cancer Letter—*Editor* JERRY D. BOYD

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