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DCPC Board Approves Concepts For New Minority Enhancement Awards Program, Two RFA Reissues

Cancer center core grant supplements for a new minority enhancement awards program received enthusiastic concept approval from the Board of Scientific Counselors of NCI's

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In Brief

Centers Survey Generates Only 56 Responses; GAO To Report On NCI's Dissemination Efforts

CANCER CENTERS may not be the controversial issue that NCI and the National Cancer Advisory Board had thought it was. Only 56 responses had been received by the Jan. 1 deadline to the letter sent out by John Durant, chairman of the NCAB Centers Committee, to more than 5,000 individuals. The letter asked for comments on a wide range of issues regarding centers (**The Cancer Letter**, Oct. 23 and Nov. 27), including the one that has been bothering center executives for some time--where the program should be housed at NCI. The NCAB and NCI Director Vincent DeVita were looking for some guidance in development of any recommendations for changes in the program which might be incorporated into renewal of the National Cancer Act this year. The deadline for responses has been extended to Feb. 1. . . . **GENERAL ACCOUNTING** office, the congressional investigative agency, is working on another probe of NCI. This time, Congressman Henry Waxman (D.-CA), asked for a report on how well NCI is disseminating results of cancer research progress. The report is due this spring. . . . **NOVA**, weekly science program produced for public television, will present a one hour program Feb. 23 featuring Steven Rosenberg and his interleukin-2 research. The program is titled, "Battles in the War on Cancer: A Wonder Drug on Trial." The program will show how clinical research is carried on at NCI, will follow three patients treated at New England Medical Center by David Parkinson, and will get into the controversy involving Robert Oldham and Biotherapeutics Inc. over charging patients for experimental therapy. The following week, on March 1, the two part series will show "Battles in the War on Cancer: Breast Cancer--Turning the Tide". . . . **ROSWELL PARK'S** advanced education program in maxillofacial prosthetics has received the accrediation classification of "approval" from the Commission on Dental Accreditation of the American Dental Assn. Norman Schaaf is chief of dentistry and maxillofacial prosthetics at RPMI.

DCPC Board Increases New Minority Program To $1 Million A Year

(Continued from page 1)
Div. of Cancer Prevention & Control at the Board's meeting earlier this month. So enthusiastic was the Board's response that it voted to almost triple the amount of money set aside for the program and double the size of the awards.

The Board also approved reissuing two RFAs--one, for cooperatative agreements for data based interventions for cancer control which resulted in seven funded awards to state health departments last year; the other for randomized trials on pancreatic cancer pain reduction, which produced 14 unfundable applications last year.

The Board also approved concepts for a new contract supported dietary survey and collection of food composition data; and non-competitive development of software for statistical analysis of survey data, and cancer control research for American Indian and Alaska natives.

The Cancer Centers Minority Enhancement Awards program was initiated by the Cooperative Minority Biomedical Program in the Div. of Extramural Activities. That program is headed by Lemuel Evans, who presented the concept to the DCPC Board. Only a portion of the funds will come from the DCPC budget.

Research objectives in the program will include smoking behavior in minority youth; studies of communication strategies for presenting information to minorities about cancer and its prevention; investigations of patient perspectives of cancer risks; the design and evaluation of interventions to minimize and prevent distress of minority patients with cancer; the development of pilot studies for minority clinical prevention trials; and psychosocial studies and perception of cancer risks in minorities.

Specific research strategies will include:

1. Targeting and facilitating the involvement of minority populations in cancer control research.

2. Investigating the impact of cancer therapy and control advances on minorities in community medical practice settings.

3. Increasing the involvement of minority primary health care providers and other specialists in treatment and other cancer control research, thereby providing both educational opportunities for health providers and facilitating interchange of information about current advances in cancer control research.

NCI staff had proposed that $375,000 a year be set aside for the five year program, with awards limited to $75,000 each.

"This is an extraordinarily important program," Board member James Holland said. The Board's Centers & Community Oncology Committee, which heard Evans' presentation of the program earlier, "felt it was too little money, and the size and number of awards (four to five) was too small."

Holland's motion to approve the concept, modified to allocate $1 million a year and to double the size of each award, was approved unanimously.

Board member Lloyd Everson, chairman of the Centers & Community Oncology Committee, noted that the Board was committing money other than DCPC's.

"That's why Dr. Holland made that recommendation," another Board member cracked.

"This is important enough for Dr. (Peter) Greenwald (DCPC director) to open his musty purse and help out," Holland said.

"We'll try to find the money somewhere in NCI," Greenwald said.

In response to Board member Frank Meyskins' questions on what minorities would be involved, Evans said it would include all ethnic minorities, the three major ones of which are Blacks, Hispanics and Native Aemricans.

Lucius Sinks, chief of the Cancer Centers Branch, said the program would be open to all centers with core grants, not just comprehensive centers.

Board member Mary-Claire King pointed out that a survey of patients in the Community Clinical Oncology Program found only seven percent were minorities, "although 30 percent of cancer deaths are in minority populations."

The RFA for data based interventions for cancer control was proposed for reissue because a number of applications in the first round received scores close to the funding level, and 35 state health departments still do not have any NCI funding for cancer prevention and control.

Board member Donald Iverson said he opposed the reissuance. "I think it is premature until we determine if the model works. It may, but to commit this kind of money ($7.4 million over seven years) before the model is tested is not wise." He suggested waiting a year.

Leslie Boss, program director, pointed out that it would be a year to 18 months before awards could be made through the reissue. Also, "it will take five years to determine if it works or not."

The Board voted unanimously to approve the concept.

The first RFA for pancreatic cancer pain reduction resulted in 14 applications, seven of which were approved with unfundable priority scores. William Straile, program director, said that reviewers and staff, after discussing the applications, concluded and recommended the following:

1. The work outlined in the RFA is capable of being done. The RFA is realistic in its requirements and in its objective to form an interinstitutional research network. Adequate patient populations are available.

2. The work proposed is a worthwhile application of clinical research to a dreadful form of cancer.

3. The RFA is well presented and should not be changed significantly if republished.

4. The review committee concluded that several of the applicants are fully qualified and could have written successful applications but instead chose to disregard one or more requirements of the RFA.

5. The reviewers unanimously recommended that the RFA be republished.

6. None of the applicants fully addressed the basic requirements of the RFA: First, to provide primary expertise in pain research; second, to provide expertise in pancreatic cancer research; and third, to show evidence for the availability of an adequate pancreatic cancer patient population at the applicant institution.

7. Research was to be done collaboratively among the successful applicant institutions. A research program was to be proposed for this research network. Several of the applicants inadequately addressed this requirement.

Everson's committee had recommended approval on a 3-2 vote. Board member Edward Bresnick suggested that the new RFA should spell out more clearly the requirements that had been missed by the first applications, and Straile agreed. The full Board then approved the concept.

Major objective of the contract for dietary surveys and food composition data will be to acquire existing individual food intake data on free living individuals on self selected diets in various international populations. The primary goals are to obtain existing dietary survey and food intake data for selected countries and to establish a computerized data base using a recently developed classification system for documentation of the dietary data obtained. This dietary survey and food intake data base will provide nutritionists and epidemiologists with a valuable research tool for better understanding the relationship between diet and cancer, the staff report said.

Some Board members were skeptical.

"I see good news and useless news here," John Ultmann said. "The good news is that this does not look at food disappearance (in which consumption is measured by adding the total quantity of food produced to the quantity imported, from which is subtracted the food exported, fed to livestock, and put to nonfood use). It looks at actual food that is prepared and consumed. The useless news is that it is naive to presume that what they eat on the day of a survey is what they ate all their lives. Also, the critical time for carcinogenesis may have been in their youth, when they were eating differently."

"This is the blind leading the blind," Holland said. "I suggest you scrub this and start with a cohort of 20,000 children. Follow them, which I would expect to be part of a prevention program for 50 years."

"That would make the Women's Health Trial look like small potatoes," Greenwald said. "One does not obviate the other. There are huge international differences in cancer incidence. It is worthwhile to think through a multinational study of different diets and different cancer rates."

Iverson added that "regardless of the limits of dietary data, we have learned a lot. It gave us a lot of clues, even if it is not definitive."

Board member James Gaylor pointed out that the proposed study was not a recall survey but a seven day survey of what is eaten at that time.

Eleven members voted to approve, with Ultmann and Robert McKenna opposed and Holland and Kenneth Warner abstaining.

The Board deferred action on a concept for a contract supported program to improve the routine office practice of selected preventive services by primary care providers. The cost, $20 million over five years, caused members to ask that a working group study the proposal and report back at the next meeting.

Details of the concept statements follow:

Cancer centers minority enhancement awards. An estimated 10 five year grants would be funded, not to exceed $150,000 each, with a total annual budget not to exceed $1 million.

NCI is committed to reducing the cancer mortality disparity between minorities, especially Blacks, and the general population. One approach to achieving this objective is through a cooperative effort with the NCI Comprehensive Minority Biomedical Program, with the Cancer Centers Program expanded to broaden minority involvement in programs research the latest and most effective measures in cancer control and clinical treatment research.

Critical to this goal is the delivery of state of the art cancer treatment and control modalities to underserved Black and minority populations. Cancer survival statistics verify that American Blacks have substantially lower cancer survival rates than American Whites with the same disease. By targeting segments of the population with the highest mortality, it is hoped that this initiative will have significant impact on minority population cancer survival. This effort will contribute to NCI supported centers of excellence to better enable NCI's research to reach and support those minority populations which are particularly susceptible to cancer.

This initiative would seek to involve cancer centers which access large or predominantly minority populations in an effort to promote minority group participation in cancer control research. Supplemental support would broaden the operational base of each center so as to facilitate the expansion of cancer control efforts in early detection, prevention, screening, pretreatament evaluation, treatment, continuing care, and rehabilitation; and the increased involvement of minority population primary care providers early in the course of clinical treatment. The program effort would also promote involvement in treatment clinical reserch at the institutional level with a focus on protocol development related to minorities. The effort would seek to support programs carrying out diet and nutrition cancer control research activities and would hopefully coordinate the contributions of investigators from various relevant disciplines, e.g., psychology and nutrition.

Another purpose of this initiative is to expand and promote the inclusion of minorities in NCI supported training programs (e.g., cancer epidemiology) at centers in order to fully exploit the existing research potential in the context represented by the minority segments of the indigenous populations.

The supplement would support increased minority involvement in a variety of acitivities at the centers including the enrollment of increased numbers of minority patients on cancer treatment and cancer control protocols. Currently funded centers and/or their affiliates interested in increasing minority participation in cancer control reserch studies may submit a supplemental application for this purpose. It is expected that successful pursuit of activities supported by this supplement during the initial project period would result in their inclusion in subsequent submissions for competitive renewal of the parent grant.

Funds may be requested for data management, supplies, salaries of professional and/or support personnel, computer time, administrative expenses, etc., in accordance with policies for cancer center support grants.

Initial review will be conducted by the Div. of Extramural Activities of NCI, with final review by the National Cancer Advisory Board. All cancer control research protocols must be approved by the Cancer Control Research Protocol Review Committee.

Data based interventions for cancer control. An estimated 10 cooperative agreements will be awarded for seven years, at an estimated total cost of $7.4 million.

Goals of this program are to fully utilize existing data for the planning and execution of cancer control programs on the state level which are consistent with the NCI Year 2000 goals and to develop demonstration projects in the use of such data for planning and execution of cancer control intervention programs.

The state health department is the organization most responsible for the health of the population of that state. The majority of health departments have been involved in cancer control activities in only peripheral ways such as the funding of cancer incidence registries, Pap programs through maternal health activities, or limited participation in tobacco use prevention and cessation activities. SHDs are responsible for the development of the health plan for the state and for the inclusion of a cancer control section in that plan. All SHDs have direct access to the state's legislature for the funding of health programs. For all of these reasons, the SHD is a critical organization to involve in cancer prevention and control activities as NCI strives to reach the Year 2000 goals.

In the last round, a number of the applications received scores close to the funding level. Also several of the applications funded were from states whose applications for the technical development RFA (a previous DCPC RFA) were not approved, indicating the educational benefits of having once applied. The program encourages maximum utilization of existing data to foster more rational planning of cancer control efforts through the SHD setting, more effective resource allocation, more focused programming, better integration of data into operational aspects of programs, improved program evaluation, and increased awareness among public health professionals of the specific cancer related health problems of the population of the state. The first RFA resulted in 19 applications of which 17 were approved and seven funded in FY 1987. At present, 35 state health departments remain without NCI funding for cancer prevention and control activities through either the technical development or data based intervention grants. Program staff is confident that a large number of these states are able to respond successfully particularly with the increased orientation to the application process and the RFA itself that will be provided to this round of potential applicants. Only states not previously funded will be eligible to apply under this RFA.

This concept assumes the following:

A. Staff of state health departments have varying degrees of understanding of the cancer problem of their state's population, and some will require more work than others to reach the point at which interventions can be undertaken.

B. Involvement of a coalition of individuals/organizations from throughout the state is essential for the most effective planning and intervention process to occur.

C. Involvement of state legislators in the process is important for the success of cancer related legislation and for the continuation of funding of programs and activities in conjunction with or after the time of the grant.

Four phases, flexible in their timing, are anticipated to be funded over a seven year period:

*Data review and evaluation--Data for the population of the state should be evaluated both on cancers and risk factors for cancers related to the Year 2000 goal. This phase may last for up to nine months. In some states some of this information may already have been collected and utilized. Where such is the case, applicants may request to move immediate-

ly into the appropriate later phase.

*Planning--The data that has been reviewed and evaluated is to be interpreted and incorporated into a specific cancer plan for the state that can be endorsed by a variety of agencies and institutions throughout the state. Plans will also be developed for the specific interventions that are to be part of the grant process. This phase would last approximately nine months overlapping somewhat with the first phase in its activity. Again, some of this work may have been previously accomplished, and, where shown to be so, applicants may choose to begin in a later phase.

Obviously, the first two phases are critical for the planning of the intervention phase. At the end of the planning phase there will be a formal review process utilizing both NCI and non-NCI reviewers to evaluate progress in the first two phases and the proposed intervention and evaluation plan.

*Pilot testing and initiation of intervention activities--Interventions determined in the planning phases to be defined by the data and important within the priorities of the state will be pilot tested and initiated within this phase. Such interventions might include demonstration projects within certain geographic areas such as counties (e.g. breast cancer screening through mammography programs) or major efforts to organize and facilitate intervention statewide (e.g. that required for an all encompassing diet or tobacco program).

A key aspect of this phase is the education of state legislators as to the cancer problem that exists within the state including its risk factors, what can be done about the problem, and what resources are necessary to respond to the problem. This phase should be no longer than three years, and the combined first three phases no more than four years.

*Evaluation--The three year period of evaluation will allow for assessment of program outcome over time as well as feed into continued program planning. The evaluation is intended for all aspects of the state's cancer control program and will not be limited to the proposed intervention. Incidence, mortality, risk factor and program data will continue to be evaluated, and legislative activity will be noted.

Based on experience to date with grants with state health departments and on comments from a meeting of health department representatives brought together to help plan this next effort, the RFA resulting from this concept will have some minor revisions from the previous RFA. Such differences include (1) use of the cooperative agreement mechanism to allow greater interaction and technical assistance by NCI staff; (2) lengthening all phases to provide a more reasonable time frame for the effort; (3) progression through the phases as the grantee demonstrates readiness, as the cooperative agreement mechanism allows for sufficient interaction with NCI staff and verification of the progress of the program; (4) emphasis on using information from prior grantees to focus the data evaluation; (5) evaluation of cancer prevention and control programs in the state at baseline and in the evaluation phase; (6) opportunity for applicants who have already completed earlier phases of the program to apply for the appropriate later phase.

The total amount estimated for each award would be $765,000 data collection over the seven years and $645,000 for the intervention, over six years.

Prospective randomized studies correlating current treatment procedures with pain reduction in pancreatic cancer. Five three year awards are anticipated, at a total cost of $400,000 per year.

Pain is the presenting symptom and the most prominent complaint in the majority of pancreatic cancer patients. The specific objective of most pancreatic cancer treatment trials is to evaluate survival or disease free interval. The quality of life and relief from pain are seldom evaluated. Surgical, radiation and chemotherapeutic treatments have been used alone and together in the treatment of pancreatic cancer. Many medical oncologists believe that chemotherapeutic intervention results in reduction of pain in pancreatic cancer, but these claims have not been adequately documented. Varying degrees of pain relief have been reported to follow radiation therapy, but that also lacks confirmation and validation. Other approaches directed specifically to relieve pain in these patients include neurolytic, neuropharmacologic, neurosurgical and psychosocial interventions. However, systematic correlations between pancreatic cancer treatment and pain relief have not been carried out. Consequently, there is considerable controversy about the most effective procedures for pain control in these patients.

This initiative proposes a prospective study of correlations between the various treatment procedures employed with the resultant degree and duration of relief of pain and psychological distress with improvement in quality of life. Some treatments which might be examined include pancreatectomy/pancreaticoduodenectomy, pancreatic duct decompression, and relief of jaundice by endoscopic and percuteneous transhepatic techniques, as well as chemotherapy and radiation. Among the procedures implemented specifically for the relief of pain which may be included in this study are alcohol or phenol neurolysis of the coeliac plexus, neuropharmacologic drugs including new technologies for their administration, neurosurgical and psychologic interventions including hypnosis. Also of potential value is a study of psychopharmacologic agents, including antidepressants. Because pain and psychosocial factors play such an important part in pancreatic cancer management, they need to be assessed together and serially. Specifically, pain and psychological distress will be studied serially before and during all therapeutic approaches. All of the variables will be monitored simultaneously.

The study must be multidisciplinary and multi-institutional.

Dietary surveys and food composition data. One three year contract anticipated, at a cost of $350,000 per year.

The majority of evidence linking diet and cancer is based on international correlation studies comparing cancer incidence or mortality with food disappearance data based on figures derived from food balance sheets. These studies, although very useful in providing leads to further research, are faulty. The per capita intake figure is inaccurate as the measure of food actually eaten because it does not account for food produced by individuals who farm and garden; for waste in stores, by vendors, and other food service facilities, and homes or for differences in consumption within a country by different age and sex groups.

Compilation of a dietary data base containing actual dietary intake data from various regions of the world and representing a wide range of dietary patterns will make it possible to compare and contrast the findings from different epidemiological approaches and may yield insights to the diet/cancer relationship which would not otherwise be achievable.

Information on food components not included in the Food & Agriculture Organization (FAO) of the United Nations food balance sheets will be collected, e.g. additives, insecticides, contaminants. Food preparation techniques, e.g. smoking, pickling, curing, can also be taken into account.

Because of the ongoing international effort to improve quality, quantity and availability of food composition data worldwide, more complete information is becoming available.

A major objective of the project is to compare the FAO food disappearance data and other descriptions of food intake considered more complete and their associations with specific forms of cancer. The countries are selected according to adequacy of the cancer data bases and, ideally, do represent high and low rates of specific cancers. Thus, the countries will be selected on the basis of the existence and availability of good quality cancer incidence and mortality data, as well as existence and availability of good quality dietary intake data. An example is the current research interest in gastric cancer prevention. Surveys in Costa Rica, Chile, Egypt and Japan would satisfy the requirements of good gastric cancer statistics and good quality food intake data.

Other potential users of this dietary data base include research epidemiologists and nutritionists, particularly in the area of cancer prevention, and various governmental agencies responsible for policy decisions and public health.

Using specified classification for dietary surveys and food intake data, existing data will be collected for the selected countries having cancer incidence data available. Evaluation of dietary intake data for inclusion in the data base will be carried out, e.g. methodology, statistical procedures and data interpretation. Food component data used to calculate dietary surveys will be evaluated and updated. The contractor shall submit data to NCI for review of adequacy, i.e. validity and reliability. After the first 18 months of the contract, the Prevention Committee of the BSC will review the status and progress of the contract with possible re-evaluation of the contract if progress is not satisfactory.

Specific tasks will be:

1. Planning and evaluation--Initiate contacts and explore sources in each country/region; establish criteria for quality of data; prepare a schedule for collection of the data in each country.

2. Implementation for collection of dietary survey information

For surveys collected and evaluated, the following information will be entered into the dietary intake computer data base--period covered (dates); duration of the observations; sample (size, descriptors, representativeness); dietary collection methodology (records, interviews, etc.); unit of observation--country, region, other geographic unit, family, individual (sex, age, occupation, physiologic state, pathologic state); data collected (quality vs. quantity); data interpretation (food table, nutrients, etc.).

3. Evaluation and updating of food component data--Evaluate and critically review food component data bases used to analyze the dietary surveys; reanalyze the key surveys with improved data bases generated by the international collaboration with the contractor; produce a hard copy of the surveys (food component calculations will be available on line or as printouts); foster and expand the established international network of food component data systems in order to have access to and to efficiently improve the data base quality and quantity.

The concept was presented by Ritva Butrum, who will be project officer.

The noncompetitive contract for development of software for statistical analysis of survey data will cost NCI $100,000 a year for two years, but the entire project is costing $400,000 for the two years. The National Center for Health Statistics is providing the rest of the money, in a contract with Research Triangle Institute.

The other noncompetitive contract (actually an interagency agreement) is with the Bureau of Indian Affairs, to cost $3 million over three years.

NIH Plans To Fund Grants On New "Percentile" System; Affects "Fringes"

NIH is in the process of moving away from funding grants by priority scores and toward a "percentile" system that will be the primary indicator of which grants will be paid.

With the new system, study sections will be asked to rank each grant they review in order, number 1 (for the best) through ascending numbers down to the worst. Then, if NIH determines that it will fund 35 percent of approved grants, they will be the top 35 percent from each study section.

The institutes and program managers will have, as they do now, flexibility to skip over grants and fund exceptions, as they do now.

"Priority score compression" is why those scores are being abandoned as the primary funding indicator. It has been obvious for several years that NIH study sections have been giving increasingly higher scores to the better grants that they review. The reviewers have seen that that was the only way grants they considered as top quality could be funded, with increasing competiton. NIH staff members call that "grade creep." A study section that tried to play it straight would soon seen its grants stalled past the payline, funded only at the discretion of the program managers.

Maryann Roper, NCI acting deputy director, related her alleged reaction upon learning that "some study sections stacked the deck--I was shocked." She went on to tell the Div. of Cancer Prevention & Control Board of Scientific Counselors, with more than a little tongue in cheek, "I can't imaging that objective scientistis would do something like that."

Roper said NCI executives do not feel that the new system will "cause many changes in funding, except at the fringes. We will continue to maintain a pool for funding exceptions, as we have in the past."

Roper added, "Whether study sections will again stack the deck once they learn how the percentile system works, I would rather not comment with Mr. Boyd (of **The Cancer Letter**) in the room."

NIH Director James Wyngaarden has signed off on the new system but it will not be implemented until tested with a few study sections. Also, there are other elements still to be worked out.

Priority scores will still be assigned, but a debate among Div. of Research Grants staff (and other NIH staff members) on whether to go to half unit increment scoring has not been settled.

With the present system, study sections score in one tenth increments--1.2, 1.3, etc., or as the scores are translated, 120, 130. The payline this year is expected to be around 165 to 170.

"Some of us feel scoring that fine is beyond the ability of the reviewers," one DRG staff member told **The Cancer Letter**. Others argue that reviewers ought not be restricted by telling them they can only score in half units.

"As it is now, it is too easy for them fudge a point or two, especially when they know where the payline is," the DRG executive said. "With half units, that would be more difficult to do. Scores would be spread out more."

A third element to the new system would be standardizing verbal descriptors among the study sections. Terms such as "outstanding," or "excellent," or "fair," would be tied to numbers.

"It's an attempt to relate English language to the numbers," the DRG staff member said. "It would be a tool for reviewers. If they think an application is outstanding, then that would help them determine what score it should have, or where to place it in the percentile ranking. The concept is a good one, but I think it will fail. The words are not well chosen."

The percentile ranks will be spread out over three rounds, to "smooth out" the quality of applications. Some study sections will review grants of lesser quality in one round than they get in the next. Spreading it out over three rounds is intended to dampen that effect, and get more comparability among study sections.

RFPs Available

Requests for proposals described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Blair building room number shown, National Cancer Institute, NIH, Bethesda MD 20892. 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-CO-7114-40

Title: Computer support for cancer information dissemination
Deadline: Approximately March 20

This project involves the purchase, installation and acceptance test of new midrange computer hardware, operating system software and data base management system software. The project will require data base conversion, application software development, maintenance and support for data bases and software and will provide updating, reporting and data distribution functions for the Physician Data Query (PDQ) and Cancerlit data bases, as well as the Cancergram, Oncology Overview and Recent Review publications.

This is a 100 percent small business set aside.

Contract Specialist: Teresa Baughman
RCB Blair Bldg Rm 314
301/427-8877

RFP NCI-CN-85071-43

Title: Cancer prevention and control surveillance master agreement
Deadline: Approximately March 15

The Div. of Cancer Prevention & Control is soliciting proposals to provide information required for cancer control surveillance. The primary approach for obtaining this information is through the conduct of surveys and similar evaluation processes. The term "survey" is used to connote a full range of studies, including probability sample surveys and abstracting data from existing primary and secondary sources for analysis.

It is anticipated that multiple master agreements will be awarded pursuant to the master agreement announcement, each having a five year period of performance. Since master agreements are unfunded, the obligation of funds shall be accomplished solely through the award of master agreement orders (MAOs), issued under the terms of this master agreement.

The MAOs will be issued on either a cost or fixed price basis.

The master agreement holder, upon award of a MAO, shall coordinate the requested surveys, including data collection, processing and reporting for surveillance activities to be designed and developed by NCI alone or in collaboration with other organizations.

Contract Specialist: Diana Wheeler
RCB Blair Bldg Rm 2A07
301/427-8745

Program Announcement

Title: Evaluation and utilization of transgenic animal models in studies of pancreatic cancer
Application Receipt Dates: Feb. 1, June 1, Oct. 1

NCI's Organ Systems Program seeks applications proposing studies to evaluate, develop and utilize transgenic animal model systems for analyzing pancreatic cancer. The goal is to stimulate research in (1) the utilization of available transgenic mouse models of acinar cell pancreatic cancer for studies of mechanisms of carcinogenesis, cell of origin and tumor markers; (2) the establishment and use of transgenic murine model for studies of ductal cell pancreatic cancer; and (3) the establishment and use of transgenic systems in species other that the mouse, chiefly those which have a propensity for ductal cell pancreatic adenocarcinomas such as the Syrian hamster.

Additional studies of pancreatic adenocarcinoma are

needed in order to develop markers for use in early detection, identify mechanisms of carcinogenesis, identify developmental time points in the malignant transformation process, and identify agents which may lead to prevention or control.

There are a number of reasons to believe that research in pancreatic cancer would be enhanced if additional useful animal tumor models were developed. Few investigators are using the tumor models which are currently available for studies of pancreatic carcinogenesis. One objection to most existing models is that they involve development of acinar cell adenocarcinomas rather than ductal tumors. Pathologists who study the human disease define it as ductal rather than acinar in appearance and possibly in origin. One model involving the injection of nitrosamines into Syrian hamsters does provide ductal cell tumors. Nevertheless there is a long time to appearance of true adenocarcinomas, and there are differences among animals in time of appearance and nature of these lesions.

The recent development of transgenic mouse models for pancreatic cancer provides experimental systems which are accessible and manipulable. An accelerated production of transgenic models, using the mouse and additional species, would stimulate the field by providing tools for analyzing how oncogenes or transforming genes function in pancreatic tumorigenesis. Transgenic systems might allow delineation of stages when differentiating pancreatic cells become susceptible to initiation or promotion in carcinogenesis. Also, such systems might make possible the identification of environmental factors influencing these processes.

An issue which is related to the above considerations is that of identifying the cells of origin for pancreatic tumors. Are acinar and ductal cells of the pancreas both derived from common precursor stem cells? Concomitantly, are differences between acinar and ductal cells quantitative or qualitative? There is the possibility that ductal cell adenocarcinomas are derived from acinar cells which have de-differentiated as part of the transformation process. Some in vitro sutdies are consistent with this possibility. For example, AR42J pancreas tumor cells do not appear differentiated, but exposure to dexamethasone induces expression of nearly all the exocrine pancreatic secretory proteins. Similarly, organ cultures of pancreatic rudiments obtained at a stage when pheotypic expression is not yet apparent can be induced to express differentiation end products prematurely.

At the present time, origination of at least two transgenic mouse systems, both resulting in acinar cell pancreatic adenocarcimonas, has been reported. In the development of a transgenic system, expression of a foreign gene can be targeted to cells of the pancreas. A foreign gene is attached to the promoter enhancer region of a pancreas specific gene, such as that for pancratic elastase. Insertion of such a DNA construct into the germ line by injection into a mouse egg results in subsequent expression of the gene in the pancreas cells.

Simian tumor virus 40 causes malignant transformation in a number of systems, and if used as the transforming portion of a construct, results in acinar cell pancreatic adenocarcinomas which develop in mice at about three to six months of age. Such newborn mice show hyperplasia of the pancreas, and there appears to be a two to three fold increase in the number of cells per acinus, with the overall morphology remaining fairly normal. At about one month, the majority of these cells are tetraploid, when hundreds of nodules develop within the pancreas. The nodules proliferate rapidly and by three to four months, give rise to a multinodular, 3-9 gm pancreas. At this time, individual nodules have different characteristic aneuploid DNA contents. Currently, four liens of transgenic mice carrying SV40 are available.

Introduction of pancreatic elastase-SV40 gene constructs into the germ line of mice have provided strains in which 100 percent of the progeny develop pancreatic cancer. Several strains are homozygous with regard to the genetic construct. They need to be evaluated for tumor histopathology and for features of tumor development. They might be useful in studies of mechanisms that bring about carcinogenesis and might be appropriate for use in studies of tumor markers for pancreatic cancer.

It might be possible to attach an oncogene to the promoter-enhancer region of a gene specific for pancreatic ductal cells, thereby targeting transformation event(s) specifically to ductal cells. Such a model would be highly useful in pancreatic cancer research. The feasibility of this approach is demonstrated by the current transgenic mouse models which target transformation to acinar cells. Similar to the SV40 transgenic system described above, introduction of oncogenic (mutated) ras-pancreatic elastase constructs will transform acinar cells. The fetuses develop acinar cell adenocarcinomas, and the mice die a few days after birth. By day 16 of embyrogenesis, just a few days after the pancreas has begun to develop, the pancreas is already huge, perhaps three to 10 times normal size. The acinar structure is clearly abnormal, and by day 20, about the time of birth, the enlarged pancreas is very cystic, and normal acinar structure does not exist. This embryonic tumor model is potentially useful, but since the mice die before breeding age, a colony cannot be established.

In Syrian hamsters, chemical carcinogens induce primarily ductal cell tumors of the pancreas, where in other species the same carcinogens induce acinar cell tumors. This indicates that the development and resulting histopathology of such tumors is influenced by species specific factors. The phenotypic appearance of transgenic adenocarcinomas might be similarly influenced by how introduced constructs interact with host species. If so, then studies of transgenic models might provide answers to questions about pancreatic tumor cell lineage and control of tumor cell differentiation.

Immediate obstacles to the development of additional transgenic pancreatic cancer models are largely operational, such as the availability and manipulability of sufficient numbers of rodent or hamster eggs. Researchers in cellular and molecular biology and in carcinogenesis, who have this capability and have expertise available for developing transgenic animal systems, would be appropriate applicants for this announcement. Also, multidisciplinary teams which have expertise in transgenic systems, molecular biology, reproductive biology and carcinogenesis would be appropriate applicants.

Grant applications should be submitted in the usual NIH process. A copy of the face and summary page should be sent to, and further information may be obtained from, Dr. William Straile, Organ Systems Section, Div. of Cancer Prevention & Control, NCI, Blair Bldg Rm 717, Bethesda, MD 20892, phone 301/427-8818.

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