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NCI NEEDS $107 MILLION MORE IN FY 1982 THAN ASKED FOR KEY PROGRAMS, R01s AND P01s, NEW INITIATIVES

Members of the Senate and House health appropriations subcommittees, both of which have now heard NCI's presentations on the 1982 fiscal year budget, tried without much success to draw Director Vincent

(Continued to page 2)

In Brief

SURGICAL ONCOLOGY PROGRAM ANNOUNCEMENTS DUE FOR PUBLICATION BY JUNE; AACR/ASCO PROGRAM

TWO PROGRAM announcements for the new surgical oncology grants planned by NCI's Div. of Cancer Treatment will be published before June, with Oct. 1 the receipt date for applications. One program announcement will be issued for R01 (traditional) and P01 (program project) grants, the other for P20, planning grants. R01 applications will be reviewed by NIH Div. of Research Grants study sections, and P01 applications by the NCI Program Projects Review Committee. Planning grant applications also may be reviewed by an NCI committee but that has not yet been determined. DCT is hoping the review can be completed early in 1982 so that the division's Board of Scientific Counselors will have an opportunity to see how applications fared and possibly make funding recommendations before they go to the National Cancer Advisory Board in May, 1982. . . . **REGIONAL COOPERATIVE** groups RFA has been drafted by DCT but is still waiting HHS approval of the cooperative agreement mechanism which NCI intends to use for the new groups as well as, eventually, the existing ones. . . . **AACR/ASCO** program notes: **ALLAN CONNEY**, Hoffmann-La Roche, will deliver the G.H.A. Clowes Memorial Lecture April 27, "Enzyme Induction by Foreign Chemicals and Carcinogenesis by Polycyclic Aromatic Hydrocarbons." The AACR Presidential Address, by **BAYARD CLARKSON** of Memorial Sloan-Kettering Cancer Center, is entitled, "The Elusive Goal," scheduled for April 28. **LAWRENCE EINHORN**, Indiana Univ., will present the Richard and Hinda Rosenthal Foundation Award Lecture on "Testicular Cancer: A Model for a Curable Solid Tumor," on April 29. **EMIL FREI III**, Sidney Farber Cancer Institute, will deliver the 12th Annual David A. Karnofsky Memorial Lecture on "Clinical Cancer Research: An Embattled Species," on April 30. **YUNG-CHI CHENG**, Univ. of North Carolina, will receive the Cornelius P. Rhoads Memorial Award for meritorious achievement by a young cancer investigator. AACR will have a symposium April 29 on chromatin structure and function, chaired by Vincent Allfrey; and an update on in vitro culture of human tumor cells, chaired by Bruce Chabner, April 30. A joint AACR/ASCO session is scheduled April 30 on cell biology and therapeutics.

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CENTERS, GROUPS, CONSTRUCTION, R01s, P01s, TRAINING UNDERFUNDED IN BUDGET

(Continued from page 1)

DeVita into a discussion of Cancer Program needs which will not be met by the President's request of $1.026 billion.

That amount is only $26 million more than Congress appropriated for NCI this year, the smallest percentage increase for any NIH institute. It is about $50 million more than NCI will get this year if Congress approves the President's rescission request.

It also is $166 million less than NCI had requested in the bypass budget submitted to the White House, the budget which spells out in detail how the institute would spend an optimal amount of money.

DeVita's position as an agency head does not permit him to appear to be asking for budget increases at congressional budget hearings. If he had responded with descriptions of how he would use another $50 or $100 million, he could have been accused of "budget busting" and the next day be pushing a broom in the Clinical Center.

Public witnesses at hearings of the House and Senate appropriations subcommittees no doubt will offer their own suggestions on Cancer Program needs and the money they require. Subcommittee members interested in supporting the best possible program could read the bypass budget.

The Cancer Letter has compiled a modest list of funding deficiencies which if allowed to stand will significantly weaken some areas, severely damage some, nearly eliminate others. Here they are, senators and congressmen:

• Cancer centers. The 1981 budget is $69.8 million, and for 1982 it is $74.9 million. Neither of those budgets will permit funding of cancer center core grants at recommended levels, but rather at the current level plus about 10 percent.

Additional amount needed to fund at peer review recommended levels (total for both years): $6.5 million.

Recommended levels are not just figures plucked out of the air. They are amounts determined by peer review as those required to perform the peer review-approved activities of the centers. In a sense, the budget increases represent a flowering of the centers. With their organizational structures in place, responsibilities defined and missions outlined, they are now recruiting the basic and clinical scientists and the young investigators to carry out those missions. They are developing the shared resources, purchasing equipment, establishing the outreach programs, organizing the professional and public educational activities—fitting the pieces together that will enable them to capitalize on the information flowing from the labs.

One of the success stories from the National Cancer Program has been the development of more than 60 cancer centers around the country into a vital force with a profound impact on the Program. The centers are in varying stages of development, and to limit them every year to small cost of living increases will prevent full utilization of them as a major resource for the Cancer Program.

• Cooperative Groups. Like the centers, the Cooperative Groups this year and in 1982 will not be funded at full peer review recommended levels. The 1981 budget for the groups is $35.5 million, and for 1982, $38 million.

Additional amount needed to fund at full recommended levels: $6 million.

The national Cooperative Groups were given the mandate in 1975 to expand into multimodality therapies following their string of successes in assisting in the development of cancer chemotherapy. Their budgets were increased to pay the extra costs involved (in most cases, not nearly covering all the costs—Cooperative Groups, with many members contributing their time, staff time and other resources, remain one of the best bargains in cancer research). Clinical research with two, three or four disciplines is considerably more costly than with one, and the complexicity of data management and analysis has vastly increased. Starting in 1981, however, the money available is not enough to pay the costs, as approved by peer review, and the groups are being funded only at 70 percent of recommended levels. The same situation will exist in 1982.

• Construction. Despite an obvious, growing and well documented need, this program has dropped from $34.7 million in 1973 to $1 million in 1981 and again in 1982.

Additional amount required for NCI's share of estimated needs: $24 million each year for five years, starting in 1982.

A National Cancer Advisory Board survey determined two years ago that construction needs for the succeeding five years would total more than $300 million. NCI's share, on the 50-50 matching fund basis, would be $150 million (***The Cancer Letter,*** Feb. 20). The NCAB recommended that NCI earmark $25 million a year for five years for construction, still leaving the estimated needs $25 million short. NCI each year has attempted to budget that amount or close to it for construction, but each time the White House has cut it back drastically.

Meanwhile, the construction gap has grown wider, as Sen. Harrison Schmitt, chairman of the Senate Health Appropriations Subcommittee, attempted to bring out at his subcommittee's hearing. Eventually the lack of facilities will inhibit growth of cancer research. Even now, many facilities do not meet federal animal care standards or chemical or biological hazard regulations.

Construction is another bargain for the Cancer Program. Local sources invariably more than meet the

matching fund requirements. The results are cancer research and/or clinical care facilities which provide the Cancer Program a greater return than required on NCI's investment.

• Institutional training grants. Cuts were made by eliminating payment for indirect costs and the allowances of $3,000 for each predoctoral trainee and $5,000 for each postdoctoral trainee.

Additional amount required to restore those funds: $7.3 million for 1981, $9 million for 1982.

Institutions might scrape around and find ways to increase their own contributions for a year or two. The program will be doomed, or at best severely cut back in breadth and quality, without restoration of those funds.

While the need for certain disciplines, such as medical and pediatric oncologists, may not be as acute as it once was, that cannot be said of many others. Epidemiologists and pathologists are in short supply. [illegible]

funded. Priority scores are very subjective, and scientists who have served on NIH study sections admit that the difference between 190 and 220 can be very small. The chances are excellent that a grant with a 215, 220, or 225 score will turn out to be every bit as productive as one with 190.

How much are we losing when top quality grants go unfunded? If it happens too often to a top notch investigator, he will lose interest and go into something else. We will never know the extent of that loss, the questions his work may have answered.

It would seem that funding 40 percent of the top grant applications as determined by the best scientists NIH can recruit to review them is not too much to ask.

• New programs. In this category, include three additional regional cooperative groups (above the three budgeted with 1981-82 money), at $500,000 each; $1.5 million needed to make up the deficit in

"LANDMARK" FINDINGS REPORTED ON IF GENES, OVARIAN AND PANCREAS MARKERS

Investigators at Roswell Park Memorial Institute, with collaborators at other institutions, recently have released results of their work in three separate areas of research which have been described as "very important," "highly exciting," and "landmark papers."

One group located at least eight leukocyte and a single fibroblast interferon genes on chromosome 9 in humans; another found a familial enzyme deficiency related to the incidence of ovarian cancer which could be useful in early diagnosis of the disease; and the third found that ascinar cells from the pancreas apparently contribute to a circulating antigen which can be detected, and thus potentially is a useful marker protein.

The leukocyte and fibroblast interferon genes are located on human chromosome 9.

David Owerbach, Dept of Biochemistry & Physics, Univ. of California (San Francisco); William Rutter, chairman of that department at UCSF; Thomas Shows, chief of genetics at Roswell Park; and Patrick Gray, David Goeddel, and Richard Lawn, of Genentech, San Francisco, are the authors. Their paper will appear in the May issue of *Proceedings of the National Academy of Sciences.* Excerpts from the paper:

The interferons are a family of proteins produced by various animal cells in response to viral infection or other inducing agents such as double stranded RNA, mitogens or certain nonviral microorganisms. Released interferon confers viral resistance on target cells; it also affects cell proliferation and the immune response.

Three antigenically distinct types of human interferon have been classified according to their cells of origin: fibroblast interferon (FIF or IFN-β), leukocyte interferon (LeIF or IFN-α, produced prominently in β lymphocytes), and immune interferon (IFN-γ) which is produced by mitogen or antigen stimulated T-lymphocytes. Recently fibroblast and leukocyte interferon genes have been cloned using recombinant DNA techniques. There may be a single fibroblast interferon gene but at least eight different leukocyte interferon genes have now been identified.

Several cytogenetic techniques have been used to localize interferon genes to specific chromosomes. Most approaches involve the use of aneuploid human cells or cross-species hybrid cells. Chromosomal localization based on interferon production is subject to question since multiple factors may be involved in interferon induction. Cell hybrid studies led several authors to assign fibroblast interferon genes to chromosomes 2 and 5, while others have correlated fibroblast interferon production with chromosome 9. The ability of target cells to respond to the antiviral action of interferon has been localized to human chromosome 21. This chromosome probably codes for an interferon receptor molecule. Other genetic loci may also be involved in modifying the interferon response. We have been able to directly assay the chromosomal location of the human fibroblast and leukocyte interferon structural genes by hybridization of DNA from human-mouse cell hybrids with radioactive probes from purified cDNA clones of those interferons....

The technique of blot hybridization with radioactive probes from purified cDNA clones to filters containing DNA from human-mouse hybrid cells has been utilized to determine the chromosome localizations of a number of human genes including β-globin, insulin, growth hormone, chorionic somatomammotropin, prolactin, adrenocorticotropin and now the interferon genes. One advantage of this technique is that the structural gene is assayed directly whether or not it is expressed in the cell assayed. Previously, fibroblast interferon genes were localized to human chromosomes 2 and 5 by one group and human chromosome 9 by another. Our results demonstrate that both fibroblast and leukocyte interferon structural genes are located on chromosome 9 in humans.

The chromosome assignment of leukocyte interferon genes has not been previously reported. Recently, genomic DNA fragments containing closely linked leukocyte interferon genes have been obtained. Thus the human leukocyte interferon genes appear to be closely linked on chromosome 9. Other gene families having a high degree of sequence homology (greater than 80 percent) have also been shown to be tightly linked; these include the β-like globin genes on chromosome 11, the α-like globin genes on chromosome 16, and the growth hormone and chorionic somatomammotropin genes on chromosome 17. Human fibroblast interferon DNA sequences contain only 50 percent sequence homology with the leukocyte interferon sequences, but are still located on the same chromosome. The degree of closeness of fibroblast and leukocyte interferon genes may be resolved by further cloning of large DNA fragments.

In addition, the localization of these genes on chromosome 9 may be more precisely determined by examining cell hybrids containing different translocated segments of chromosome 9.

Frequency of an allele for low activity of α-L-fucosidase in serum may be increased in epithelial ovarian cancer patients.

Joseph Barlow, Richard DiCioccio, Phyllis Dillard, and Khushi Matta, of the Dept. of Gynecologic Oncology at Roswell Park; and Leslie Blumenson of the Dept. of Biostatistics, Roswell Park, are the authors. Excerpts from their paper, which has been submitted to the *Journal of the National Cancer Institute:*

Individuals with fucosidosis, a rare inborn error of metabolism characterized by progressive mental and motor retardation, have a deficiency of α-L-fucosidase activity apparently only in serum. Family and

population studies suggest that the level of α-L-fucosidase in serum of normal individuals is controlled by two alleles exhibiting autosomal inheritance with an additive gene-dosage effect. Individuals with low activity of α-L-fucosidase in serum (variant phenotype) apparently are homozygous for one allele (low activity allele); while individuals with intermediate and high activity are heterozygous and homozygous, respectively, for the alternative allele (high activity allele).

Previously, elevations of protein-bound fucose in sera of gynecologic cancer patients were reported. This prompted an investigation of α-L-fucosidase levels in sera of gynecologic cancer patients. We now report a statistically significant deficiency of α-L-fucosidase activity in sera of epithelial ovarian cancer patients which implies an increase in the frequencies of the variant phenotype and the low-activity allele for α-L-fucosidase in serum....

Sera of ovarian cancer patients exhibited a statistically significant deficiency of α-L-fucosidase activity. This deficiency could not be attributed to an inhibitor of α-L-fucosidase in sera of ovarian cancer patients, as judged by mixing experiments with sera of healthy females. Furthermore, the absence of an association between deficiency of α-L-fucosidase activity and either stage of disease or tumor burden provides additional evidence against an inhibitor, since the amount of such an inhibitor would probably increase with severity of disease.

The decreased activity of α-L-fucosidase in sera of ovarian cancer patients does not reflect a generalized deficiency of glycosidases, since β-D-mannosidase and N-acetyl-β-D-glucosaminidase activities were not deficient. In addition, the lower activity of α-L-fucosidase in sera of ovarian cancer patients is not universal among neoplasias, since the activity in cervical and breast cancer patients was not significantly different from healthy females.

Family and population studies have suggested that levels of α-L-fucosidase in serum are genetically determined by two alleles exhibiting autosomal inheritance with an additive gene dosage effect. Pedigree analysis of ovarian cancer patients for levels of α-L-fucosidase in serum were consistent with these reports. This, together with the observations discussed above, suggest that deficiency of α-L-fucosidase activity in serum of ovarian cancer patients is not a result of disease but is genetically determined.

Analysis of population data showed that a variant phenotype for low α-L-fucosidase activity in serum is three-fold more prevalent in ovarian cancer patients than in healthy females and that the allele controlling this low activity is two-fold more prevalent.

An explanation of these observations would be that α-L-fucosidase deficiency in serum of females is a hereditary condition associated with increased risk for developing epithelial ovarian cancer. If so, then assays of α-L-fucosidase activity can be used to identify females in the general population with a higher risk for developing ovarian cancer. This could be of great aid in early diagnosis. Ovarian cancer has a high cure rate if treated in its early stages. Unfortunately, most patients currently are diagnosed at advanced stages of disease where the cure rate is poor, thereby making ovarian cancer the most lethal gynecologic tumor. Thus, an aid for early diagnosis may improve the outlook for this insidious disease. Moreover, the observation of an association between deficiency of α-L-fucosidase in serum and ovarian cancer raises the intriguing question of whether or not this deficiency is related to the etiology of ovarian cancer.

Purification and characterization of a human pancreas-specific antigen.

Rueyming Loor, Takashi Shimano, Mary Lou Manzo, Lance Van Dusen, Lawrence Papsidero, and T. Ming Chu, Dept. of Diagnostic Immunology Research & Biochemistry, Roswell Park; and Jan Nicolai and Guido Tytgat, Dept. of Internal Medicine, Div. of Gastroenterology, Univ. of Amsterdam, are the authors. Excerpts from their paper, which will appear in *Biochemica et Biophysica Acta,* 668 (1981):

The specific antigenic determinant(s) of a tissue may be characteristic of a tissue type, and, therefore, reflect the occurrence of a particular tissue. Presence of tissue-specific antigen in human pancreas was first reported in 1956 by Witebsky and associates. However, no further characterization of this antigen was reported. The specific proteins of pancreas can be endocrine cell (α and β cells in islets of Langerhans) or exocrine cell acinar and ductal cells) origin. In addition to the important physiologic functions, the cell type specific antigens of pancreas, such as insulin, glucagon, somatostatin and pancreatic polypeptides, are valuable in reconstructing a three dimensional model of the islets of Langerhans. The islets of Langerhans were first demonstrated by using cell type specific antigens and their antibodies. Attempts also have been made to identify antibodies against tissue-specific antigens which occur in the sera of patients with various types of pancreatic disease.

Recently, several antigens, pancreatic oncofetal antigen, oncofetal pancreatic protein, tumor-associated antigen, oncofetal pancreatic antigen, pancreatic cancer-associated antigen, and ascites fluid glycoprotein, have been reported to be associated with pancreatic cancer. None of these antigens, however, has been shown to be pancreas organ-specific. Histotype-specific antigens may prove useful as tumor markers such as prostatic acid phosphatase for prostate cancer and thyrocalcitonin for medullary carcinoma of the thyroid.

In our laboratory an antiserum has been raised which reacts specifically with human pancreas as determined by immunologic reactivity. Using this tissue

specific heteroantiserum, a pancreas-specific antigen has been identified and purified from the saline extract of human pancreas. In this report, purification and characterization of this pancreas-specific antigen are described. The content of pancreas-specific antigen in pancreatic juice from normal individuals and from patients with cholelithiasis, pancreatitis as well as from patients with pancreas cancer is also presented....

Purification of a pancreas-specific antigen from human pancreas has been described in this study. This antigen has a molecular weight of 44000, a sedimentation coefficient of 3.4 S and a single isoelectric point of 4.9. Data also have been presented to show that pancreas-specific antigen is located in acinar cells of the pancreas and is a secretory protein in nature. Secretin is well known to stimulate watery pancreatic juice high in salt content and low in enzymes; while cholecystokinin-pancreaozymin enhances pancreatic secretion especially in its production of enzymes.

The secretion of pancreas-specific antigen from acinar cells of pancreas seems to be greatly enhanced by the administration of cholecystokinin-pancreozymin. Pancreas-specific antigen, therefore, may be synthesized in the acinar cells and then secreted into pancreatic juice. However, the purified pancreas-specific antigen was found to be devoid of any known enzyme activity examined.

A pancreas-specific isoantigen was identified in pancreatic acinar cells of human, rabbit and rhesus monkey by Rose et al. and Metzgar about two decades ago. However, no further isolation or characterization of this antigen has been reported thereafter. Nerenberg et al. recently reported a human pancreas specific protein isolated from saline extract of pancreas. This antigen is a glycoprotein and possesses a molecular weight of about 225000 as estimated by gel filtration. Immunofluorescence studies show that the antigen is diffusely present in cytoplasm of pancreatic acinar cells. The molecular size of this antigen clearly distinguishes it from the presently reported antigen.

Human pancreatic juice generally is composed of electrolytes and proteins, including amylase, lipase, trypsinogen, chymotrypsinogen, procarboxypeptidase A and B, ribonuclease, deozyribonuclease, proelastase and trypsin inhibitor.

The proteolytic enzymes in freshly secreted juice possess no hydrolytic activities which require activation. Trypsinogen can be activated by mucosa enterokinase and chymotrypsinogen, procarboxypeptidase A and B are subsequently activated by active trypsin. By computer analysis of the isoelectric focusing protein patterns, pancreatic carcinoma has been shown to produce quantitative and qualitative changes in the pancreatic secretions which may be used to differentiate them from secretions of normal pancreas. The presently isolated pancreas specific antigen content in pancreatic juice of pancreatitis and pancreas cancer patients is quantitatively higher than in normals.

Pancreas-specific antigen in pancreatic juice may be useful in diagnosis of pancreatic disease. In addition, pancreas-specific antigen may serve as a marker for investigating hormonal regulation of cholecystokinin-pancreozymin on the pancreatic secretion. The biological significance of the newly identified pancreas-specific antigen in physiology and/or pathology of pancreas merits further study.

THE GREAT CHARLIE MOERTEL SHOOTOUT DRAWS LAUGHS, CRITICISM IN TUCSON

Charles Moertel called it "the second half of the Jay and Charlie show." Emil (Tom) Frei called it "the great Charlie Moertel shootout." Others who heard Moertel's needling talk, "How to Succeed in Adjuvant Trials Without Really Trying" called it hilarious and "right on the nose." And what still others called it is not printable.

Moertel followed Emil (Jay) Freireich on the program in the opening session of the Third International Conference on Adjuvant Therapy of Cancer in Tucson. The two have opposed each other in the past over the issue of randomization vs. historical controls. This time, it was Frei who took Moertel on.

Moertel's lecture went something like this:

To be successful in an adjuvant chemotherapy trial, certain principles must be observed. First, selection of a name of the drug regimen is all important, as demonstrated by MOPP and COP. With a regimen of 5-FU, levamisole, oncovin, and platinum, the catchy acronym FLOP almost guarantees success. Selection of patients and criteria for response is important, permitting various manipulations which assure impressive results.

"You can throw out certain patients, because of spelling errors and other minor variations. But, oh, dear, one was a responder. Well, that was an honest investigator error. Let's leave him in." The unevaluable patients include those who die, unevaluable because they were too ill to get the full doses.

FLOP thus is found to have a therapeutic response of 55 percent and is pronounced a success, Moertel's story went. The investigator moves up to department chairman, gets invited to the American Cancer Society's Science Writers Seminar where he can loll on the beach (Ed. note: There was very little lolling at the seminar this year, due to murky, drippy Florida weather), and eventually becomes director of a comprehensive cancer center.

Heavy handed though it was, Moertel's story had even his critics laughing uproariously. Some of them were not laughing later, however.

"I thought it was funny," commented one noted clinical investigator. "Certainly some of those things happen, but not often enough to invalidate every-

thing we do. Did you see some of those guys out there who are in private practice? They loved it. It's difficult enough to get them to work with us. I'll be hearing about this from them for a long time."

Frei had the task of summarizing the conference on the final day. After doing so for the scientific sessions, he said, "Now we come to the great Charlie Moertel shootout. It was funny, clever, right 10 percent of the time, and disturbed me greatly. Not that we shouldn't step back, look at ourselves, and laugh at ourselves. It is important to have a sense of humor. But the business we are about is very, very serious.

"Unfortunately, Charlie," Frei continued, "you are a renowned oncologist, director of a major cancer center. What you have said is very negative, and will be picked up in the community in which we work. Many are skeptical, and there is a lot of cynicism. I am absolutely certain your paper will be quoted to me extensively. I wish you hadn't said it."

Lawrence Einhorn, who presented results of his superb testicular cancer studies during the conference, had this lighthearted response to the controversy.

His group at Indiana Univ. once considered using a regimen consisting of cyclophosphamide, levamisole, adriamycin, and platinum. They abandoned the plan when someone pointed out that people might be deterred by the acronym.

"Platinum, vinblastine and bleomycin (the combination used so successfully in his studies) doesn't spell anything, so it is referred to as the Einhorn regimen," Einhorn said. "So there is some value in not having a cutesie name."

Freireich discussed informed consent vs. prerandomization in his presentation. Limitations of randomized trials, he said, include that "they frequently give the wrong answer, they create enormous problems for physicians and patients, and most important, we've never devised a way to study the results. . . .

"How can we test the hypothesis that a randomized trial gives better answers? The answer is to do a randomized trial. . . . We should remember that the purpose of a clinical trial is not to detect differences between treatments but to find more effective treatment."

Important questions to be answered include, Freireich said, "When does a treatment move to the adjuvant setting? How is that determination made?" In view of the fact that a percentage will not need it, and that all treatment has some morbidity, and possibly some mortality, those questions are vital, he said.

The question of which techniques are proper and appropriate for doing clinical research has not been settled, Freireich said. "That is an area for research. Historical data, properly analyzed, can be used effectively."

Frei called Einhorn's findings "an absolute home run." In 100 consecutive cases of stage 1 and 2 testicular cancer treated at Indiana Univ., 98 are alive and disease free. Most important, the study demonstrated that the drug regimen is just as successful in rescuing relapsed patients as it is used as adjuvant therapy.

Physicians have two choices in treating stage 1 and 2 testicular cancer, Einhorn said. "One is to use adjuvant chemotherapy (after primary treatment) and you probably will reduce recurrences to zero." The second is to not use adjuvant chemotherapy, follow patients closely and treat on relapse, "probably with the same results."

Other developments described at the conference evoked similar enthusiastic reactions. They included:

- Data from various reports on breast cancer trials providing overwhelming evidence that adjuvant chemotherapy is improving relapse free survival.
- Solid evidence, probably the most convincing yet, from several studies that postmenopausal breast cancer patients can benefit from adjuvant chemotherapy.
- Preliminary reports from the National Surgical Adjuvant Breast Project that tamoxifen added to adjuvant chemotherapy is increasing relapse free survival in postmenopausal estrogen receptor positive breast cancer patients.
- Convincing evidence from the Milan group that six cycles of CMF is as effective as 12 cycles in prolonging relapse free survival of breast cancer patients.
- The work of Univ. of Arizona investigators in compiling results of breast cancer trials by four groups, including one in Italy and another in England (others are the Arizona group and the Southwest Oncology Group), using them to develop a computer data base, demonstrating that results were comparable for the same regimens at all four locations, and developing a combined controls group against which other contemporary studies can be measured.

RFPs AVAILABLE

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

SOURCES SOUGHT

Project No. NCI-CP-FS-11008-77

Title: *Cancer following tonsil irradiation, physical examinations and blood studies*

Deadline for Statement of Capabilities: *April 22*

The Environmental Epidemiology Branch of NCI

has been conducting an epidemiologic investigation of individuals who received therapeutic irradiation as children or adolescents for lymphoid hyperplasia (primarily enlarged tonsils) at the Children's Hospital Medical Center in Boston. Approximately 1,650 exposed and 1,650 non-exposed individuals (who received surgery only) treated between 1938-1969 are being followed and sent questionnaires regarding health status.

The purpose of the overall study is to evaluate the late effects associated with head and neck irradiation in childhood and to quantify these effects in terms of radiation dose, age at exposure, latent period, and sex.

This contract is for services to conduct a physical examination with blood studies on approximately 1,500 study subjects (750 radiation exposed individuals and 750 non-exposed individuals). This study will include physical examinations of both exposed and non-exposed study subjects.

The contractor will provide the examination rooms, nurses, physicians, laboratories, freezers for blood samples, and all other necessary items for the conduct of the physical examinations and blood studies. Only those persons living in the Boston area will be asked to come in for the examination. This should amount to approximately 1,500 individuals.

A physical examination will be performed to detect thyroid nodules and head and neck cancers. Blood serum will be drawn and serum calcium determined to evaluate possible radiation effects on the parathyroid. A more intense examination will be performed on a subsample, including a technetium scan. A limited study of serum thyroglobulin in random samples of both groups of patients will be considered.

Both exposed and non-exposed individuals will be examined in a "blind" fashion by the physicians. The patients will be interviewed by someone outside the examination room, and, to the extent possible, the examiner will not know exposure status.

The contractor must have access to the individuals being studied, the medical and radiotherapy records for the period 1938-1969 and collaborative ties with the Children's Hospital Medical Center in Boston. Written proof of this access and collaboration must be submitted and the contractor must be established experts in the clinical detection of radiation-related head and neck disease. The contractor should submit resumes and organizational capability statements demonstrating their ability to perform this work especially in the detection of radiation related head and neck disease, the ability to conduct serum calcium and technitium scans plus extensive laboratory capabilities.

Ten copies of the resume of experience and capabilities must be submitted.

Contract Specialist: Patrick Williams
RCB Blair Bldg Rm 123
301-427-8888

RFP 263-81-P(60)-0137

Title: *Maintenance of a breeding colony of miniature swine (set aside for small business concerns only)*

Deadline: *April 27*

NCI is seeking a facility capable of 1) maintaining a breeding colony of approximately 120 miniature swine, 2) maintaining records, and 3) providing for the transportatation of two to four live pigs to NCI once or twice a week.

The contractor shall furnish services, qualified personnel, and material, equipment and facilities, not otherwise provided by the government under the terms of this contract, as needed to comply with the following specifications:

The facility must be located in an area zoned for the production of livestock. Space and enclosed breeding facilities must be adequate for a breeding colony of this size and must conform to the standards for animal care described in *Swine,* published by the National Academy of Sciences, 1981, No. 15BNO-309-01923-0) copies provided on request).

The contractor shall supply animal care and maintenance for a colony of miniature swine consisting of 20-30 female breeders, 3-4 male breeders, and their offspring (approximately 150 piglets per year). The contractor shall provide transportation of two to four pigs approximately six months of age per week to the NCI. The contractor must be able to meet the delivery schedule specified by the project officer. The vehicle used for transportation must conform to the standards outlined in the NIH manual issuance *Procurement and Transportation of Swine* Part 3046-1.6. This document is available through the contract office.

In view of the requirements of the proposed contract, it is essential that the offeror's facilities be in approximately a 50-mile radius of the NIH campus, Bethesda, Md.

Contracting Officer: Hugh Mahanes Jr.
RCB Blair Bldg Rm 332
301-427-8877

The Cancer Letter _Editor Jerry D. Boyd

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