THE CANCER LETTER

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OBEY SURPRISES EVERYONE, INCLUDING HIMSELF, AND PLUGS FOR MORE MONEY FOR NCI, NHLBI

"I'm surprised to be in this position, given my biases . . . I think you're underfunding the Heart and Lung and Cancer Institutes."

(Continued to page 2)

In Brief

MOLONEY, MANAKER, 11 OTHER NCI STAFF MEMBERS RETIRE; TERRY TAKES LEAVE FROM IMMUNOLOGY JOBS

JOHN MOLONEY, whose entire career except for the last two years has been spent in viral oncology at NCI, retired last week. Moloney went to work as a technician at NCI in 1947 under Ray Bryan, a pioneer in tumor virus work. He earned his PhD at George Washington Univ. while working at NCI, eventually became head of the Virus Cancer Program. It was a highly visible, controversial "and in my mind, successful program," Moloney said. "It's the only area where research has moved ahead and developed an understanding of human cancer." VCP was dismantled in Arthur Upton's reorganization of NCI, as the extramural support was switched from contracts to grant. Moloney spent the last two years as assistant NCI director, overseeing long range planning for the Frederick Cancer Research Center. Moloney said he has no immediate plans and will listen to job offers. . . . **ROBERT MANAKER**, another major figure in viral oncology, also retired last week as chief of the Laboratory of Molecular Virology. He had been at NCI since 1956. The rush to retirement, spurred by a quirk in federal regulations which permitted employees to retire at slightly higher pay if they went out before March 1, included 11 other NCI staff members: Phil Stansley, grants program manager in the Div. of Cancer Cause & Prevention; Fred Shaw, Research Contracts Branch; Pauline Wall, chief of the Graphics & Audiovisuals Section in the Office of Cancer Communications; Walter Hershey, property management officer; Harry Wood, head of the Office of Extramural Research & Resources in the Developmental Therapeutics Program; Walter Schneider, chief of the Nucleic Acids Section in the Div. of Cancer Biology & Diagnosis; William Banfield, senior investigator in DCBD's Laboratory of Pathology; Clifford Hewitt and Frank Sordyl, chemists in the Div. of Cancer Treatment; Brenda DeMoll, biological data clerk in DCT; and Helen Schommer, clerk typist in the Div. of Research Resources & Centers. . . . **WILLIAM TERRY**, who has been holding down four jobs at NCI for much of the past year, has given up two of them for the present. He has taken a leave of absence from the positions of director of the intramural Immunology Program and chief of the Immunology Branch. The former position will remain vacant; Richard Hodes, who heads the Immunotherapy Section, is the acting chief of the Immunology Branch. Terry remains acting director of the Div. of Cancer Control & Rehabilitation and acting NCI associate director for cancer centers.

DEVITA TELLS NATCHER SUBCOMMITTEE FOUR CORE GRANTS WILL GO UNFUNDED

(Continued from page 1)

That was David Obey speaking, and if he was surprised, it is not hard to imagine how NCI executives and Cancer Program supporters felt when they heard the Wisconsin Democrat make that statement at last week's hearing of the House HEW Appropriations Subcommittee.

Obey has been the subcommittee's most outspoken critic of NCI; in the past he has succeeded in holding down appropriations for NCI and in transferring millions from NCI to other agencies.

Obey made his comments to NIH Director Donald Fredrickson, who testified at the hearing with NCI Acting Director Vincent DeVita.

Referring to the subcommittee's efforts "to deal with political pressures", Obey said those pressures had led to budgets "I felt were overly generous to NCI and some other institutes while budgets for the rest were penurious. This year you have been overly generous to the institutes I have lobbied for in the past."

Obey reached that conclusion based on Fredrickson's position that NIH intended to fund one third of approved grants in the 1981 fiscal year. Obey elicited from Fredrickson that the budget for the National Heart, Lung & Blood Institute would permit funding of only 20 percent of approved project grants and the NCI budget would allow funding of only 31 percent of approved grants.

"What I'm getting at, is I don't understand why you try to stabilize grants institute by institute, rather than across the board at NIH," Obey said. "That is not consistent with funding the best science."

"That reflects the purchasing power of the individual institutes," Fredrickson answered.

Obey pointed to examples in which two grant applications on the same subject were referred to different institutes, with the one with the lower priority being funded while the other was not.

"It is certainly true that I support funding only the best science," Fredrickson said. "But the structure of the institutes and distribution of funds makes it impossible to fund equally at priority levels."

Obey was critical of the decision Fredrickson made earlier this year to use raw study section priority scores in determining funding of grants rather than normalized scores.

Fredrickson explained that the use of normalized scores was adopted as a policy in 1971. After a study of the process last year, Fredrickson in a controversial decision switched to the use of raw scores in funding grants. "We adopted one system, without a unanimity of opinion."

"Not all institute directors agree with that?" Obey asked.

"About 50-50," Fredrickson said.

"I understand it was 7-4 against," Obey said.

"More like 5-5," Fredrickson said.

"I guess we're getting different stories," Obey replied. "It seems to me that you took what this committee thought was a rational approach to funding and screwed it up royally. . . . You have tried to solve some political problems with the institute directors."

Obey expressed interest in the NCI Biological Response Modifiers program and—unlike some others in Congress who have been critical of NCI for not spending more on interferon—appeared to support the approach NCI is taking.

"I understand that your judgment and that of the [Mihich] Subcommittee is that the Biological Response Modifiers Program would not be helped by a predetermined and well defined scheme rather than let scientists have a free hand," Obey commented.

"It's analogous to the Drug Development Program," DeVita answered, suggesting that NCI will "provide a skeleton" around which investigator initiated research would develop.

"Would forcing the program into a certain direction by requiring more money for interferon [as some congressmen and senators have urged] limit research on other biological modifiers?" Obey asked.

DeVita agreed, although insisting that interferon "at this point seems very promising."

"The point I'm trying to make is that if you focus everything on one substance instead of a broader search, you could find yourself going down the wrong road," Obey said. "I have no idea whether interferon will turn out to be as useful as it appears, but we do not want to force it in that direction and overlook others."

DeVita noted that NCI plans to support clinical trials with interferon on 450 patients "before we make a big investment in manufacturing it." He told Obey the budget for interferon in the 1981 fiscal year was adequate to support those trials and other preliminary development work.

Subcommittee Chairman William Natcher (D.-Ky.) asked DeVita, "If you had to name one major accomplishment in the last five years, what would you say?"

"I can't do just one," DeVita answered. "Perhaps I could name one in each area."

Natcher asked for details on accomplishments to be submitted for the hearing record. "When we go to the floor with this bill, people will want to know what we have accomplished." He pressed DeVita for a brief statement on advances in the last 10 years.

DeVita mentioned the development of chemotherapy as an effective treatment modality, new diagnostic techniques, discoveries on cell transformation, and development of theories on promoting agents.

Fredrickson commented that in the annual NIH lecture presented last week by Thomas Waldmann, chief of the Metabolism Branch in the Div. of Cancer

Biology & Diagnosis, Waldmann discussed how "we have unravelled the whole puzzle of how the immune system works. This will have great relevance to other diseases." That work was accomplished using funds in the NCI budget, Fredrickson said. "NCI supports a great deal of research which will enrich the entire field of biomedical science."

Natcher and Robert Michel (R.-Ill.), the subcommittee's topranking minority member, tried with little success to get DeVita and Fredrickson to say NCI could use more money than requested in the President's budget. HEW headquarters has cracked down hard on what is called "budget busting" by agency representatives. DeVita thus has had to avoid answers which could be interpreted as appeals for budget increases.

"Are there ample funds in the budget for cancer research?" Natcher asked. DeVita said there are.

"As much as you requested?"

"As much as we need," DeVita answered.

"Did the White House reduce your budget request?" Michel asked. Fredrickson said that the President's budget is less than NCI had originally requested.

Only when Michel specifically asked the amount of NCI's request did DeVita answer: $1.170 billion. The White House cut that by $170 million.

"With the inflation factor, there are those who would say that you got a sharp cut. What is your argument to counter that?" Michel asked.

DeVita stayed with the same answer he had given previously to the Senate HEW Appropriations Subcommittee and to the House Health Subcommittee (see below). The $1 billion in the President's budget will fund "our high priority" programs, he repeatedly said.

"What would be some of the low priority programs which will not be funded?" Michel asked.

"There will be reductions in funds for research training and cancer control," DeVita answered. "There are other examples."

"You propose level funding for cancer centers ($66.4 million)," Michel commented and asked for an assessment of the impact on the centers program.

"It means there will not be as many core grants which will be funded," DeVita said. "There will be others for which funds will go up."

"What will be the criteria for getting more money, or none?" Michel asked.

DeVita said the guide to that will be priority scores. Later, responding to a question by Edward Roybal (D.-Calif.), DeVita said the centers budget would permit no new core grants and that four competing renewals probably would not be funded.

Michel noted the 45% increase in NCI funds for the National Toxicology Program (to $65 million) and asked the reason for it. DeVita said that amount is necessary to get the program up to the level of 100 new chemicals a year going on test.

Joseph Early (D.-Mass.) was critical of the amount requested for NCI. It is wrong, he said, to ask for the same amount NCI is getting this year. "Dr. DeVita has talked about all the progress being made. Maybe this is the year we should be talking about a $2 billion budget instead of $1 billion. . . . You should tell us how much you can effectively spend, and let us determine how much we can afford to give you."

Early asked DeVita if the Drug Development Program is getting enough money. "We're going to get there. Our responsibility is to see that we get there as fast as possible," Early said.

"The Drug Development Program is healthy," DeVita insisted.

"Is there enough money to do all we should be doing?" Early asked. DeVita said that there is.

"Do you agree, Dr. Fredrickson?" Early asked.

"It is difficult to establish any limit on biomedical science," Fredrickson said. "Given the amount of money available, it is adequate."

"That's the political answer," Early said. "The problem is that is the money sufficient to give us the highest quality research. I went along with you in the past. We are seeing breakthroughs in the drug areas. I don't see enough money in the budget to take advantage of that."

"You can purchase a lot of science with a billion dollars," Fredrickson said. He added that in terms of constant dollars, NCI's budget has "stabilized" at its level of 1976.

Early returned to interferon, suggesting that more money could be used.

"Those 450 patients will tell us a lot," DeVita said. "There is no question, that if it works brilliantly, we will have to readjust our priorities."

"Twenty years ago, interferon seemed exciting," Early said. "I think our mark up [of the appropriations bill] should be governed by what you tell us you need."

"I think we're putting enough into interferon," Fredrickson said.

"If you say we've got enough money in interferon to do what we have to do, I'll accept that," Early said. "Is there any high quality research not funded?"

"There is always some not funded," DeVita said.

"Is this year in cancer more exciting than in the past? Do we need to spend more?"

"This is an exciting year in cancer research, but we're not at a level of having a cure for cancer," Fredrickson said.

"I hope the year you tell us, this is the year to do it, we really pour the dollars into it," Early said.

Silvio Conte (R.-Mass.) asked DeVita to "speculate on how many years it will take to unlock the question of how cancer is caused."

"We have the tools to do that," DeVita said. "How long, 10 years, 20 years, would be a pure guess. But we have the technology, and frequently when we think something will take five years, it only takes two."

"If you had $20 million above the budget request, what would you fund?" Conte asked.

DeVita said he would increase the research training budget.

Natcher, returning to the prospect that four center core grants would not be funded in 1981, asked how much money would be required to fund them. DeVita responded that core grants average about $1 million each.

"If the committee adds $4 million to the request, would it go to fund those centers?" Natcher asked. DeVita declined to assure him it would.

WAXMAN SUBCOMMITTEE HEARS SUPPORT FOR CANCER ACT RENEWAL, ONE AGAINST

Doug Walgren (D.-Pa.), one of the younger members of the House Health Subcommittee, tried repeatedly to draw DeVita into admitting that the budget request for NCI was inadequate at the subcommittee's hearing last week on renewal of the Cancer Act (*The Cancer Letter*, Feb. 29).

"Do you feel efforts supported by this budget should be maintained or reduced?" Walgren asked.

"We are carefully funding high priority areas," DeVita said. He mentioned the National Toxicology Program as one for which funding would be increased.

"Would you estimate the degree to which inflation has diminished the buying power of research dollars?" Walgren asked.

"That varies," DeVita said. "Areas which use a lot of petroleum products have very high inflation. The Drug Development Program is one, and inflation there is 15-18 percent. The average is probably about nine percent."

"Is it satisfactory to you to simply pursue high priority programs?" Walgred asked.

"Within that budget, no high priority program has been left unfunded," DeVita insisted.

"Are you comfortable with the fact that the Administration is doing less for you in 1981 than in 1980?"

"I'm comfortable, for the reasons stated," DeVita said.

Walgren noted that last year the Administration budget proposed funding only high priority research. Some of those items would have to be cut or dropped, given the level budget and inflation, he said. "Now something has happened to make them less a priority. Is that a correct assumption?"

DeVita commented to the effect that some changes had been made, and some savings had been effected.

"There will be similar savings this year, with programs funded with less effort when measured by constant dollars?"

"That is correct," DeVita said.

"What I'm hearing is that some areas are not as high priority as they have been in the past," Walgren said. "I would like to see some statement explaining that." DeVita agreed to supply a statement for the record.

Walgren commented that a 10 percent inflation means a cut in the NCI budget of $100 million and asked for a statement on how and where the cuts would be made. DeVita again agreed to supply the statement for the record.

"Would it be proper to ask for NCI's bypass budget?" Walgren asked.

"We can provide that," DeVita said.

The budget bypass authority permits NCI to submit its budget request, with specific details on how the money would be spent, directly to the White House Office of Management & Budget, without permitting NIH or HEW to alter it.

HEW submits its own budget for NCI to the White House, and invariably it is the HEW figure—always much lower than NCI requested and usually the same as the previous year—which winds up in the President's budget.

The budget bypass was an issue at the hearings on renewal of the Cancer Act and has been brought up frequently by other committees. Andrew Maguire (D.-N.J.) and others who have expressed criticism of the Cancer Program have questioned the value of the budget bypass.

The efforts by Walgren, Early, Natcher and Conte to get a fix on NCI's real needs for 1981—frustrated by the heavy hand of HEW—clearly demonstrate the value of the budget bypass. No other institute of NIH can bring forth at congressional request a document submitted to the White House spelling out how it would spend a budget 17 percent higher than the request permitted by HEW brass.

Other institutes probably could, if ordered by Congress, come up with plans for spending more money than requested by the White House. But NCI's plan is an official document, put together by NCI executives and budget staff after hundreds of hours of planning and discussion and thorough, detailed reviews of each program. It is also reviewed by the National Cancer Advisory Board before it goes to the White House, bringing in a strong element of public and nongovernment scientific input to the process.

It is a public document, permitting every constituent of the Cancer Program to know where he stands in the original budget request, and permitting the public and Congress to know what programs and projects will not be funded as the result of Administration cutbacks.

When Early said, "Tell us how much you need," DeVita was under orders not to do that. Early will find his answer in the bypass budget. Information on which programs will go unfunded is also there; whether they are "high priority" or not is a question of semantics. "High priority" as DeVita used the term included only those programs which could be funded under the budget request. Anything that could not be funded is not "high priority."

Maguire told DeVita that he was "pleased to see in your testimony an increased awareness of prevention. . . . If you had to break down NCI research and funds into three parts—basic research, treatment and prevention—what percentage would you assign to each?"

"I don't know if that would be a good way to go about it," DeVita said. "One of my great joys for the last one and a half months (since he became acting director) was to review the programs in environmental carcinogenesis headed by Dr. (Joseph) Fraumeni. I don't doubt that 80 percent of cancers are related to environmental carcinogenesis. But it is not so easy to apply that 80 percent to the budget."

Maguire asked how much of NCI's budget does go into prevention, and DeVita said "about 32 percent."

"Dr. Fredrickson said it was about five percent," Maguire said.

"I think that is too low. I haven't talked with him about that." He insisted that $313 million of NCI's budget is in prevention, with 24 percent in treatment.

"If I add correctly, that leaves 44 percent for basic research," Maguire said. "Is that the right balance? Are you happy with it?"

"That is about right," DeVita said.

"If Dr. Fredrickson's figure is accurate . . . I assume you would feel that is not enough?"

"I think the difference is attributable to definitions," DeVita answered. "I feel comfortable with the percentage as is, after looking over all programs."

"Previous witnesses have suggested that prevention might be taken out of NIH," Maguire said. "They accept the premise that NCI is a research institute, and should have no part in approaching prevention."

"That revolves around whether research including humans is fundamental," DeVita said. "I think prevention belongs there. Parts of prevention might be better somewhere else."

Gregory O'Conor, director of the Div. of Cancer Cause & Prevention, added, "We like to feel that prevention done in our division is not only trying to identify determinants of cancer, but also in lab and epidemiology studies, how those determinants work, and how we can intervene before exposure or before it becomes clinical cancer."

"It is your feeling that prevention and cause are inseparable, and that we need to know more about prevention?" Maguire asked.

"The study of mechanisms is closely related to strategies one would design through research to intervene," O'Conor said. "Where the agent or process is clearly identified, the strategy of preventing exposure is at hand. We should take every opportunity to eliminate those."

"When a chemical is carcinogenic in animals, would it be in the same category with respect to prevention strategies?" Maguire asked.

"That is still a matter of research, of risk assessment and extrapolation to humans," O'Conor said. "More research, and a lot more effort is needed."

"More effort? Where?" Maguire asked.

"Studies on extrapolation of animal findings to humans."

"But where it is clearly carcinogenic in animals, isn't that important?" Maguire asked. O'Conor agreed that it was.

Irwin Bross, director of biostatistics at Roswell Park Memorial Institute, was the only witness testifying against renewal of the National Cancer Act. The Cancer Program ought to be abolished, he said. "It was a poor program to begin with and has become steadily worse until it is now beyond remedy. The only hope is to terminate it and make a fresh start."

Bross said those in charge of the Cancer Program "are dead set against any research strategy but their own and have blocked any innovative research strategies and any effective action to prevent cancer." Other Bross gems:

—His analysis of mammography shows that using it as a screening tool "is going to cause several times as many breast cancers as it can possibly cure."

—Obtaining money—"Even NCI money, under false pretenses is properly called fraud." Virus research, he said, is "a gigantic fraud." Those doing virus research, now that they have stopped working on a cancer vaccine, are continuing to get money for "recombinant DNA research."

—Current work in carcinogenesis and other basic research "is also a fraud."

—"Any of the so called experts who have testified in favor of reauthorization by piously calling for more studies to discover the cause of cancer are either quacks, frauds, or just plain stupid."

"You've cut through all ambiguities," commented Subcommittee Chairman Henry Waxman (D.-Calif.). "I'm taken aback."

Tim Lee Carter (R.-Ky.), senior GOP member of the subcommittee, told Bross, "You're doing a lot of talking and not getting anywhere. . . . I've been here many years, and I've never heard anything so ridiculous."

POSSIBLE EFFORT TO BALANCE FY 1981 BUDGET DARKENS FUND INCREASE PROSPECT

As if NCI did not already have enough problems trying to fit the Cancer Program for the 1981 fiscal year into the same amount of money the program is spending this year, an even more dismal prospect looms on the horizon.

The Carter Administration last week let it be known that it was considering an all out effort to balance the 1981 budget as an inflation fighting technique. All agencies except Defense were alerted to start preparations for cuts that would reduce the overall budget by about $15 billion.

How much that would impact HEW and then NCI was not clear by presstime. NCI executives worked over the weekend, mulling over projects and pro-

grams which might be reduced, delayed, or killed.

Because some of the money obligated under 1980 appropriations authority would be spent in the 1981 fiscal year which begins next Oct. 1, a reduction in further 1980 obligations might be considered. It is the outlays in 1981 which would be the Administration's target, since outlays more than obligations have a significant impact on the economy.

Cutbacks in 1980 awards would probably require submission of a recision request to Congress.

In the President's budget for 1981, NIH had sought to stabilize the total number of grants it supports at 5,000. One of the suggestions for meeting HEW assigned reductions, when and if that comes about, was to slash the grants number to 3,000. Such a drastic cut appeared incomprehensible to NIH executives, the longer they thought about it, and that figure was dropped from the discussions.

An NIH policy on reductions probably will involve an overall percentage reduction in the funding of approved grants (established at about 33 percent in the budget), with some flexibility left to the institutes on pay lines. Some existing contracts probably would be a prime target; they are easier to reduce, stretch out, or phase out than are grants. Only the highest priority new contracts would be awarded.

There was no final decision by presstime announced by President Carter that he would go after the balanced budget. Even if he does not, the climate at the moment is not one which would encourage the notion that Congress will substantially increase appropriations for the Cancer Program.

GAO CANCER CONTROL REPORT DELAYED BY NCI OBJECTIONS, TO BE REWRITTEN

The long awaited report of the General Accounting Office's investigation of the Cancer Control Program, which NCI executives and program participants awaited with considerable trepidity, has been delayed by NCI's apoplectic reaction to a draft of the report.

GAO, the congressional investigating agency, as a matter of practice submits a draft of its report to the agency being investigated for its comments. Those comments are then incorporated into the finished version of the report, which usually varies little from the draft.

The Cancer Control report, however, elicited such a strong reaction from NCI that GAO agreed "to go back to the drawing board," one NCI executive said.

Was the objection based on factual matters in the report? On GAO's analysis and conclusions? On GAO's recommendations?

"I can answer that with one word," said Matt Solomon, who heads GAO's office at NIH. "Yes."

GAO will not reopen the investigation, but the report will be rewritten as a result of NCI's objections. It could be ready for release within the month.

NCI "had an awful lot of comments they wanted us to address," Solomon said. "Our main concern is to give NCI a fair shake."

NCI executives did challenge some statements presented as facts and provided GAO with additional information to support their case. GAO agreed to drop some portions of the report which NCI felt strongly were incorrect or unfair and about which, presumably, NCI was able to back its position with facts.

The investigation did not include the troubled Community Based Cancer Control Program. The six contractors already were undergoing merit review, and GAO decided it did not have the time nor staff to probe that program. NCI's decision to phase out three of the six CBCCP contracts was based on recommendations of the merit reviewers and was not related to the GAO investigation.

The investigation was initiated at the request of Congressman David Obey (D.-Wisc.).

ASSESSMENT OF RADIATION EFFECTS RESEARCH SET FOR MEETING AT NIH

The future direction of federal research on radiation effects will be discussed at a public meeting March 10-11 at NIH. The meeting, "A Proposed Federal Radiation Research Agenda," is sponsored by the Committee on Federal Research into the Biological Effects of Ionizing Radiation, which is chaired by Donald Fredrickson, NIH director.

Participating in the meeting will be radiobiologists and other experts in the field, health officials, legal and ethical advisers, and representatives of consumer and public interest groups.

Current standards and guides in radiation protection are based on estimates of cancer and genetic risks. Thus the degree of control advocated is directly related to the validity of the risk estimates. The goal of the federal committee is to develop a comprehensive, government wide radiation effects research program which ultimately will reduce the uncertainty in radiation risk estimates.

On the first day of the meeting participants will present and discuss papers on the current status of radiation biological research and issues of public concern. Among the issues are the legal, ethical and economic constraints to developing an extensive knowledge base on the effects of radiation, the environmental and hereditary conditions that may mediate those effects and the applicability of animal and cellular radiation studies to humans.

On the second day, experts will present elements of research considered essential in a comprehensive federal effort. These elements include epidemiology, genetics, therapeutic applications and technology development. Public comment is invited during and after the conference.

Texts of the papers to be presented, as well as written public comments submitted in time for inclusion, have been printed and bound. These work-

ing papers are available from the NIH Office of Communications, Bethesda, Md. 20205, 301-496-2535.

The meeting will be at the NIH Clinical Center, Bldg 10, Masur Auditorium, from 8:30 a.m. until adjournment each day.

For further information concerning the meeting contact: Charles Lowe, special assistant to the director, NIH, Bldg 1 Room 103, Bethesda, Md. 20205; 301-496-3283.

IMMUNOTHERAPY CONFERENCE

The Tumor Immunology Program of NCI is sponsoring an international conference on "Immunotherapy of Cancer: Present Status of Trials in Man" April 28-30 in Masur auditorium at NIH. The program includes immunotherapy of stage 1 and 2 malignant melanoma and disseminated malignant melanoma; colorectal, gynecologic and head and neck cancer; acute myelogenous leukemia; acute lymphocytic leukemia, lymphoma and myeloma; bladder cancer and neuroblastoma; and lung cancer.

NCI CONTRACT AWARDS

Title: Breast Cancer Detection Demonstration Project—long term followup
Contractors: Emory Univ., $241,286; Univ. of Louisville, $457,563.

Title: Breast Cancer Detection Demonstration Project, six month extension and phaseout
Contractor: Albert Einstein Medical Center, Philadelphia, $85,990.

Title: Immunologic study of RNA (type C) viruses, continuation
Contractor: Scripps Clinic & Research Foundation, $166,845.

REQUEST FOR APPLICATIONS

RFA NIH-NCI-BCPCB-80-1

Title: *Studies of immunocompetent cells infiltrating human breast cancer*
Deadline: *June 1*

The Div. of Cancer Biology & Diagnosis of NCI invites grant applications from interested investigators for studies of the immunologic activity of cells invading breast cancer tissue.

This type of grant solicitation (RFA) is utilized when it is desired to encourage investigator-initiated basic and clinical research projects in areas of special importance to the National Cancer Program. The research stimulated by this RFA is supported through the customary NIH grant-in-aid and follows the policies for regular research grants. However, the RFA solicitation represents a single competition, with a specified deadline for receipt of applications. All applications in response to the RFA will be reviewed by the same initial review group of NIH.

The present RFA announcement is for a single competition with a specified deadline of June 1, 1980 for receipt of applications. Applications should be prepared and submitted in accordance with the aims and requirements described in the following sections:

BACKGROUND INFORMATION

DCBD through the Breast Cancer Program Coordinating Branch sponsors both fundamental and clinical research grants and contracts in a continuing search for biologic markers of breast cancer. In the past few years, it has been shown that the reaction of lymphoid cells and histiocytes to human mammary carcinoma, as determined by immunologic examination of draining lymph nodes and inflammatory cells which infiltrate the tumor, may be important prognostic indicators. This request for applications is intended to encourage submission of investigator-initiated research grant proposals designed to identify immune mechanisms which are relevant to prognosis of the breast cancer patients.

Recently, methods for determining the enzyme content and surface markers on tumor infiltrating cells have been used to characterize these cells. Some investigators find T-lymphocytes predominant in most tumors with a lymphocytic infiltration. Studies of acid phosphatase, nonspecific esterase and receptors for the Fc portion of the immunoglobulin molecule indicate that many cells of the monocyte/macrophage series may be present. Natural killer cells have also been isolated from tumors. Earlier studies had identified plasma cells and demonstrated local immuno-globulin production.

Methods for separation and functional characterization of the cells invading tumors have been worked out in experimental animal systems. Some work with isolation and morphological characterization of these cells has been accomplished in human tumors, including mammary carcinoma. This project should be designed to develop methods for isolation and functional characterization of inflammatory cells (especially macrophages and lymphoid cells) invading human breast tumors. Correlation of such analyses to pathological and clinical findings should lead to better understanding of the prognostic significance of intratumor inflammatory cells.

The morphologic and functional characteristics of of cells found in primary and metastatic lesions must be known and the relationship of the numbers and functional capacities of these cells to histologic type of the tumor and prognosis of the patient determined. Proposals should address themselves to the identification and description of the patient population which will be studied; methods of cell isolation and characterization; methods to be used in relating the results to diagnosis and/or prognosis, including criteria for pathological classification; methods of collecting and maintaining clinical data and methods of statistical analysis appropriate for the expected sample size.

However, support is not limited to the above subjects. Investigators are encouraged to devise innovative approaches to the understanding of the immuno-

logical activity of cells invading breast cancer tissue.

The support for this program will be the traditional NIH grant-in-aid. Applicants are expected to plan and execute their own research protocol. It is anticipated that this project need not exceed three years. At least two projects will be funded totalling an approximate direct cost of $200,000 for the first year, $214,00 for the second year and $230,000 for the third year. Project start dates early in 1981 are anticipated. Although this program is provided for in the financial plans for fiscal year 1981, award of grants pursuant to this request for application is contingent upon availability of funds for this purpose.

In addition to the usual elements of scientific merit the factors considered in evaluating each application will be:

1. Availability of clinical collaboration for obtaining appropriate materials and numbers of patients.
2. Experience with techniques of cell separation.
3. Experience with characterization of cells.
4. Demonstration of sound arrangements for collaboration of pathologist to correlate functional tests with pathological classification.
5. Plan for data management and statistical analysis.
6. Availability of appropriate personnel and facilities.

Applications must be submitted on form PHS 398, the application form for the traditional research grant. The words "Proposal in Response to RFA: Studies of Immunocompetent Cells Infiltrating Human Breast Cancer" must be typed in bold letters across the top of the page page of the application.

Inquiries may be directed to Bernice Radovich, Breast Cancer Program Coordinating Branch, Div. of Cancer Biology & Diagnosis, Room 4B-04 Landow Bldg., Bethesda, Md. 20205, phone 301-496-6774.

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. Some listings will show the phone number of the Contract Specialist, who will respond to questions. Listings identify the respective sections of the Research Contracts Branch which are issuing the RFPs. Address requests to the contract officer or specialist named, NCI Research Contracts Branch, the appropriate section, as follows:
Biology & Diagnosis Section and Biological Carcinogenesis & Field Studies Section—Landow Building, Bethesda, Md. 20205, Control & Rehabilitation Section, Chemical & Physical Carcinogenesis Section, Treatment Section, Office of the Director Section—Blair Building, Silver Spring, Md. 20910. Deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP N01-CP-05610-56

Title: *Bioassay of retinoid activity by tracheal organ culture system*
Deadline: *May 9*

Bioassay of new retinoid compounds whose synthesis is being supported under the Chemoprevention Program. The particular assay system of interest in this RFP is the hamster tracheal organ culture assay system developed at NCI. A three year cost-reimbursement contract is anticipated for effective pursuit of this project.

RFP N01-CP-05605-56

Title: *Dose response studies on phenolic antioxidants*
Deadline: *April 28*

Study the efficacy of butylated hydroxyanisole (BHA) and butylated hydroxytoleune (BHT) in inhibiting carcinogenesis in the following four organ systems: mammary carcinogenesis, intestinal tract tumorigenesis, pulmonary neoplasia, and liver carcinogenesis. Proposals for one or more organ sites will be accepted. A four year cost-reimbursement contract is anticipated for effective pursuit of this project.

Contract Specialist for above 2 RFPs: Ann Poole
Carcinogenesis
301-427-8764

RFP NCI-CM-07328-29

Title: *Provision of animal facilities and performance of routine experiments and tests*
Deadline: *May 15*

NCI is soliciting proposals from organizations with the capability of providing animal facilities and performing routine animal experiments and tests. The successful offeror will be required to provide a well equipped facility for maintenance of standard laboratory animals which will include up to 1,000 mice, 30 rabbits, 20 guinea pigs, 50 rats, 15 goats, 4 gibbon apes, and 10 dogs.

Additionally the offeror will provide essential veterinary care for the animals and provide technical assistance for performance of routine inoculations of drugs and proteins. In order to provide for the rapid transfer of animal and specimens the successful offeror must be located within a 35-mile radius of the NIH reservation.

It is anticipated that the resultant contract will be incrementally funded for a period of five years.

Contracting Officer: Clyde Williams
Cancer Treatment
301-427-8737

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