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PRESIDENT'S BUDGET: $64 MILLION CUT FOR NCI, NO START ON YEAR 2000 GOALS, DROP 240 GRANTS IN 1985

Not only did the White House not request anything close to NCI's bypass budget figure for the 1986 fiscal year budget—an amount necessary to start getting the elements in place required to meet the Year 2000 goals—but the President actually asked Congress for $64 million less than NCI is receiving this year. The budget, which went to Congress Monday, is $324 million less than the bypass budget.

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In Brief

WEINSTEIN NAMED PERMANENT DIRECTOR OF COLUMBIA COMPREHENSIVE CENTER; GOTTSMAN HEADS INSTITUTE

BERNARD WEINSTEIN, who has been acting director of the Columbia Univ. Comprehensive Cancer Center since Sol Spiegelman died two years ago, has been appointed to the position on a permanent basis. Weinstein, widely known for his research in carcinogenesis, has been at Columbia since 1961. The university also announced that Maxwell Gottsman has left his position as head of the biochemical genetics section of NCI's Div. of Cancer Biology & Diagnosis to become director of the Institute of Cancer Research, which Spiegelman also held.... **JACK OWENS,** executive vice president of the American Hospital Assn., will be the luncheon speaker at the Assn. of Community Cancer Centers meeting March 16. His topic: "Can Voluntary Hospitals Survive in the '80s?".... **LOMBARDI CANCER** Research Center at Georgetown Univ. has started a support group for its patients under the direction of Charles Tartaglia, coordinator of the Counseling and Consultation Clinic.... **SOUTHERN RESEARCH** Institute announced these promotions: Steadman Harrison, nine years with the Institute, has been named head of the Chemotherapy Div. Donald Dykes, involved in chemotherapy research there since 1961, is the new head of the Tumor Biology and Treatment Section. Daniel Coleman has been named head of the Biotechnology Div. Roderick Beittel is head of the Combustion Research Section.... **HENRY MONTES** is the new executive secretary of the Board of Scientific Counselors of NCI's Div. of Cancer Prevention & Control. He has been on the staff of the Dept. of Health & Human Services Disease Prevention & Health Promotion office. He replaces Mary Sears, who retired from NCI last year. Montes also will work on cancer control programs involving Hispanic populations.... **JOHN MADIGAN,** formerly coordinator of government relations for the American Cancer Society, has been appointed Washington representative for ACS, Alan Davis, vice president for government relations, announced. Former Sen. Birch Bayh, now a Washington lawyer, remains as political and legislative counsel to the Society.

WHITE HOUSE AGAIN IGNORES BYPASS BUDGET; "FORWARD FUNDING" AFFIRMED

(Continued from page 1)

The bypass budget is that which is developed by NCI and the National Cancer Advisory Board independent of NIH and the Dept. of Health & Human Services. It is submitted directly to the President. As has nearly always been the case since the bypass budget was authorized by the National Cancer Act of 1971, the President and the Office of Management & Budget totally ignored it.

The White House budget message also confirmed OMB's intent to force NIH to fund only 5,000 new and competing renewal grants in the 1985 fiscal year despite the fact that Congress has already appropriated enough money to pay 6,526 grants. OMB is getting around the anti-impoundment laws by decreeing that NIH obligate for three years funds for about 650 of the 5,000 grants, thus technically using up all the money appropriated by Congress for RO1 and PO1 grants. This "forward funding" ploy, while blatantly contrary to the intent of Congress, appears to be legal. Members of Congress and the biomedical research community are outraged, even more so than leaders of both parties who have expressed anger and dismay over the President's budget in general.

Here's how forward funding will impact NCI in the current, 1985 fiscal year:

*Congress had appropriated money to support and NCI was prepared to fund 1,030 new and competing renewal RO1 and PO1 grants. That number will be slashed to 790.

*This will have the result of cutting $40 million from NCI's budget.

*The priority score payline, viewed as far too low even at the originally projected 170, will be cut to about 160.

The 1986 budget request again holds NIH to 5,000 new and competing renewal grants. If Congress complies, or does not write into law a provision to prevent forward funding, the impact on NIH and NCI would be even greater, driving the payline down further as the cost of grants continues to escalate even with moderate inflation.

Almost all funding categories at NCI either would be forced to take cuts in 1986 from 1985 levels or be held to the same amounts. But by far the largest cut would be in the RO1-PO1 pool, inflicting major damage on basic research, the area which NCI Director Vincent DeVita and other members of the NIH leadership have always insisted would be protected at all cost. With more than $40 million cut from the competing grants pool and more than $15 million from the noncompeting grants pool (the result of funding the second year of 1985 competing grants with 1985 money), the horrendous total of nearly $56 million would be cut from ROIs and POIs in 1986 from the 1985 level.

Funding for cancer center core grants would be cut almost $2 million from the 1985 level of $83.9 million; intramural research would be cut by almost $3 million, probably the result of the pay cuts President Reagan is asking all federal employees to take; research management and support would decrease by $2.3 million for the same reason; and cancer control would drop by almost $1.3 million.

Construction, while held to the same level as this year, fares rather well, considering that its budget more than doubled from 1984 to 1985. The differences in the construction budget shown in the two tables on page 3 may be accounted for by the fact that the $6.9 million figure includes construction either on the NIH campus or at the Frederick Cancer Research Facility; the $6.5 million figure is only for construction grants.

When broken down by budget activity, all except construction take substantial cuts—more than $16 million in cause and prevention research, $5 million in detection and diagnosis, more than $20 million in treatment research, and nearly $20 million in cancer biology.

The budget message sent to Congress revised NCI's 1985 total upward from the total that came out of the 1985 appropriations bill. First, $4.3 million was cut, in a rescision sent along with the budget representing cuts in travel, printing and public affairs spending. Congress had decreed those cuts in the 1984 Deficit Reduction Act. Then, because the formulae for determining each institute's share for NIH central services was changed, NCI picked up about $12 million, making the total for 1985 $1.190 billion.

Armand Hammer, chairman of the President's Cancer Panel, expressed his concern about the White House budget actions.

"I don't need to emphasize the seriousness of the impact on biomedical research this would have," Hammer told the National Cancer Advisory Board Monday, referring to the reduction in numbers of grants. "I assure you I won't be reluctant to make our views known to the Administration." Hammer said he had already talked with George Keyworth, director of the White House Office of Science & Technology Policy, about the situation.

Will Hammer have access to his friend Ronald Reagan to argue the case for the Cancer Program, as one of his predecessors, Benno Schmidt, did with Richard Nixon? Will it have any effect if he does? The fate of the Year 2000 effort might depend on it.

NCAB member Enrico Mihich commented,

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PRESIDENT'S 1986 NATIONAL CANCER INSTITUTE BUDGET
(By Mechanism)
(Dollars in Thousands)

	1985 Column of the 1986 Budget (Comparable)	1986 President's Budget	Changes Amt
Research Projects:			
Noncompeting	$356,417	$341,062	-$15,355
Competing	175,835	135,298	- 40,537
Subtotal, Research Projects	532,252	476,360	- 55,892
(SBIR)	(9,110)	(9,000)	(-110)
Cancer Centers	83,871	81,981	- 1,890
Research Career	6,907	6,907	--
Organ Systems	1,000	1,000	--
Clinical Education	5,000	5,000	--
Cooperative Clin Res	49,279	49,279	--
Minority Biomed Supprt	3,400	3,400	--
Other Research Related	3,475	3,475	--
Total Research Grants	685,184	627,402	- 57,782
Training (NRSA)	30,838	30,838	--
R & D Contracts	141,824	141,824	--
Intramural Research	202,574	199,664	- 2,910
(Management Fund)	(59,004)	(59,799)	- (-795)
Research Management & Support	60,555	58,229	- 2,326
(Management Fund)	(8,622)	(8,739)	- (117)
Cancer Control	62,834	61,555	- 1,279
Construction	6,500	6,500	--
TOTAL NCI	**1,190,309**	**1,126,012**	**- 64,297**

PRESIDENT'S 1986 NATIONAL CANCER INSTITUTE BUDGET
(By Budget Activity)
(Dollars in Thousands)

	1984 Actuals (Comparable)	1985 Column of the 1986 Budget (Comparable)	1986 President's Budget
Research:			
Cause & Prevention	$276,985	$301,792	$285,391
Detection & Diagnosis	64,878	72,343	67,292
Treatment	345,938	372,099	351,683
Cancer Biology	219,770	241,140	222,079
Subtotal	907,571	987,374	926,445
Resource Development:			
Cancer Centers Support	80,294	84,805	82,892
Research Manpower Development	36,395	45,326	45,366
Construction	2,726	6,944	6,926
Subtotal	119,415	137,075	135,184
Cancer Control	65,911	65,860	64,383
TOTAL NCI	**$1,092,897**	**$1,190,309**	**$1,126,012**

"Of paramount importance in the effort to reach the Year 2000 goals is acceptance of the bypass budget. I wonder if Congress realizes it would be very useful if the bypass budget were to be implemented as the NCI budget instead of the OMB budget, as was originally intended in the National Cancer Act."

DeVita, constrained as a member of the Administration from criticizing the budget, instead emphasized what he felt was the importance of getting the National Cancer Act renewed. "At a time like this when science is moving along at a mind boggling rate, it is time to get the National Cancer Act reauthorized as it stands," DeVita said. "It provides the director with the authority to move with speed to take advantage of opportunities as they arise. That is the single most important message we can send out—reauthorize the Cancer Act, as is."

DeVita was stressing "as is" because the bill which made it through Congress last year only to be vetoed by President Reagan did not include some of the special authorities provided in the National Cancer Act of 1971. The provision NCI considers vital is that which permits it to review its own grants and contracts, except for RO1s, and to appoint members of the review committees without going through NIH. In absence of that provision, the NIH director could delegate that authority back to the NCI director, but DeVita does not want to have to count on that.

Mihich directed these questions to DeVita: "Has the need for reauthorization been stressed in relation to the Year 2000 goals? What has NCI done, what could we do, to stress the importance of the bypass budget to the Year 2000 goals?"

"Those are tricky questions," DeVita said. "When we work through NIH channels, we don't get a chance to explain our arguments for the bypass budget. We do within NIH, but I can't go beyond that. I'm not able to use the bypass budget in normal channels as effectively as I might... Our position within NIH has been blurred somewhat. We need reauthorization of the National Cancer Act as is, to restate the message by Congress and the American people that they support the investment in the Cancer Program."

The Federation of American Societies for Experimental Biology strongly objected to the reduction in research grants resulting from forward funding.

In a letter to the health appropriations subcommittees of both houses of Congress, FASEB President Joe Grisham, chairman of the Dept. of Pathology at the Univ. of North Carolina Medical School, urged that "the Administration's ill conceived plan be promptly reversed and that 6,526 new and competing research grants be provided by NIH in FY 1985... This is a highly technical matter that Congress and the U.S. General Accounting Office will have to review."

Grisham said the Administration plan "is contrary to congressional intent which was to provide funding for between 6,200 and 6,800 RO1s in FY 1985. It unfairly reduces RO1s by some 23 per cent and, in fact, cuts new and competing grants almost 500 below the FY '84 support level. It renews roller coaster funding of NIH and surely will be discouraging to established scientists and promising young researchers, leading to further but unwanted attrition in our vital field."

As an indication of the urgency for quick action to reverse the Administration's plan, Grisham pointed out that some scientists are already reporting they have received phone calls warning of the loss of NIH grants even though they have achieved what would normally be considered very favorable priority scores. "We also understand that some of the NIH institutes are holding back a portion of their grant money in anticipation of using it for multiyear awards later in the fiscal year," Grisham said.

FASEB views the Administration plan as "arbitrary and damaging to NIH," Grisham said. The scheme is a "major setback to the effort to understand, treat and ultimately cure disease—and through such means as biotechnology to enhance the competitive industrial strength of the United States."

Congressman Edward Roybal (D.-Calif.), third ranking Democrat on the House Labor-HHS Appropriations Subcommittee behind Chairman William Natcher, fired off a letter to President Reagan expressing his concern about the "unprecedented action which would have the effect of undermining the conference agreement reached on support for biomedical research in the Labor-HHS Appropriations Bill."

The conference agreement (between the House and Senate on the 1985 money bill which was signed by the President) was bipartisan, Roybal pointed out. It "reflected a strong commitment to sustain this nation's biomedical investment by making available additional funds for 1,500 new and competing research grants and over 40 new research centers."

Roybal also objected to reductions in 600 full time positions at NIH, as ordered by OMB.

"A full assessment of the situation must be made prior to any decision which could adversely affect the level or number of awards in support of basic and clinical research, multidisciplinary research centers, biotechnology resources, and recruitment of new investigators including minorities and women."

The letter was also signed by Democrats Joseph Early, Louis Stokes and Steny Hoyer.

PREVENTION CLINICAL TRIALS HEADS GREENWALD'S PRIORITY LIST IN 1986

Warning that the federal government's effort to reduce its deficit will place NCI "in a very tight situation this year and next," Div. of Cancer Prevention & Control Director Peter Greenwald listed his priorities for cancer control at last week's meeting of the division's Board of Scientific Counselors.

Greenwald said the restricted budget (which may not be so restricted if Congress adds to the President's budget request for NCI) "may have implications for the most vital programs of this division—our cancer centers, cancer training, cancer control and other activities... We are not sure to what extent research opportunities may go unfunded. However, I would like to relate to you how I perceive the priorities within cancer control and look forward to your suggestions about them. This could affect our resource allocations within the next year or two."

Here are what Greenwald said are "our highest priority areas within cancer control:

1. "Clinical trials in cancer prevention including the preclinical and related research needed to get us into the trials.

2. "Every aspect of the smoking prevention and cessation effort is important, including particularly the concept dealing with heavy smokers. If we have the opportunity for added emphasis, it will go to those directed at youth (including smokeless tobacco) and at minorities.

3. "Evaluation of the Clinical Community Oncology Program.

4. "Cancer control capacity building in state and local public health agencies, including the concepts on avoidable mortality and technical resource units. NCI intends to make this a major long term commitment as we believe that the tie to state and local health agencies is one of the most promising ways to build the infrastructure necessary to have a solid cancer prevention effort across the United States.

5. "The Cancer Control Science Associates Program intended to help build a cohort of competent young scientists in cancer prevention and control. We will take the first five trainees this July, assuming there is any flexibility at all in our personnel ceilings. Any observer of the dramatic advances at the basic science level recognizes the crucial importance of having a large and steady group of young investigators to these advances, and the need for young investigators to keep the United States at the forefront of biomedical research in the future. We have the same need for training programs in cancer control—a need for sufficient young scientists in order to assure that cancer control can achieve its full potential as we move into the future. Thus, the Cancer Control Science Associates Program and our small grants program in cancer control which also helps extramural trainees have a very high priority."

Greenwald acknowledged that he had not mentioned "a number of important areas. Some of these may require more in the way of leadership than funding or are still developmental at this point. We might have to consider thinking these programs through in more depth and postpone any major funding for another year or two. In the leadership area, I would include some of the health promotion activities related to smoking, diet and breast cancer detection, some of which can be accomplished through networking with our centers and community oncologists, voluntary agencies, state and local health agencies, industry and other agencies of the federal government.

"There are a few areas that we may have to defer for awhile if our budget is kept level. From 1984 to 1985, the cancer control budget rose by only one per cent, while that of NIH as a whole rose by 15 per cent. NCI's budget increased 9.5 per cent. NCI gave its highest priority to extramural investigator initiated research. Investigators don't always realize this priority (given to RO1-PO1 research) since cancer control is very visible. It also provides the balance and potential for public impact that may help us obtain the budgetary support for basic research. In any event, if we are kept level, two efforts we might not fund are new efforts seeking to measure the impact of preventive education on work place behavior change or new studies of the traditional cancer screening techniques, except for some work on the adoption and diffusion of these techniques."

Moving to another subject, Greenwald discussed the report by the National Academy of Sciences Institute of Medicine on the organizational structure of NIH. That report has not been well received by NCI.

Greenwald said some of the IOM proposals "would tend to increase centralization and increase the involvement of advisory counsels in both broad program and policy issues and in the oversight of intramural research. My chief reaction to this report was that it seemed to ignore the fact that several of the key recommendations already are in place at NCI. Furthermore, the current arrangement of having very strong individual institutes, such as NCI, is working well, and no rationale was given for the suggestions for increased centralization. In fact, in some areas such as the cancer centers and cancer control programs, we still must work at building a good understanding beyond NCI."

LUNG CANCER PREVENTION DIET STUDY CONCEPT TABLED BY DCPC ADVISORS

A concept proposal for a lung cancer risk intervention and followup study aimed at finding out if dietary changes could reduce the incidence among smokers, and if smokers could be induced to change their diets, was tabled by the Board of Scientific Counselors of NCI's Div. of Cancer Prevention & Control.

DCPC Director Peter Greenwald told the Board at its meeting last week that the NCI Executive Committee had had some reservations about the $3 million, five year proposal and had asked for the Board's opinion. That opinion was: take it back to the drawing board.

As written by DCPC staff, the project would support two to four contracts. Its goals would be to evaluate the relationship between dietary risk factors and subsequent lung cancer mortality among former heavy smokers who have reduced or stopped smoking; identify specific foods which may be protective; and evaluate the ability to change dietary behavior in a high risk population through the provision of authoritative and up to date information and specific recommendations through the mail.

For example, an effort would be made to increase the proportion of the intervention group which consumes dark green and deep yellow vegetables four times per work or more from a baseline of 30 per cent to a target of 50 per cent.

The staff proposal noted that although several retrospective studies and a few prospective studies suggest a lung cancer protective effect of dietary carotenoids, only one large scale prospective study has been carried out in the U.S., that by Shekelle et al. That study followed 2,000 men, observed a total of 33 lung cancers, and detected a strong dose response for a carotene index, particularly among longer term smokers.

The proposed study would:

—"Follow 10,000 high risk men, observe over 100 lung cancer deaths per year.

—"Increase our understanding of which foods in the American diet may be protective so as to provide a firmer basis for recommendations. In the Shekelle study the original diet records were lost, so no information on foods was available, nor was a precise carotene index possible.

—"Test relatively inexpensive approaches to changing dietary habits.

—"Potentially reduce cancer incidence by refining our recommendations and evaluating our techniques for changing dietary behavior."

The study would be targeted toward populations of already identified high risk individuals for whom smoking status and recent clinical, radiographic or cytologic data exist. An example of such a population is the cooperative early lung cancer detection trials which enrolled about 30,000 heavy smokers aged 45 or older in a clinical trial in the early 1970s to determine whether sputum cytology in addition to radiography could enhance early detection (it did) and improve survival (apparently not). Potential participants would be contacted by mail, with appropriate introduction and informed consent. Participation might be expected to be reasonably high, since these individuals already demonstrated their willingness to take part in a long term and much more demanding trial.

Serum would be collected from all participants at baseline and retained in long term storage for future analyses. In addition, participants would complete a questionnaire which collects information on known risk factors and dietary information. The questionnaire would be readministered after two and four years. A National Death Index search would be performed in the last year of the study.

Approximately 1,000 low carotene respondents would receive quarterly mailings during the second year, using three mailed intervention approaches. Dietary changes would be assessed by questionnaire after the intervention, and by serum carotene analysis. The difference in dietary change between the intervention groups and a control group would be examined.

Board member Kaye Kilburn reported that the Prevention Committee had agreed the proposal "is a necessary and very thoughtful approach." He acknowledged concerns about it, including whether it might dilute smoking cessation efforts, "but I don't think it will. The committee supports this."

"I have the opposite opinion," Board member Lewis Kuller said. "This is a big mistake. The issue before us is, does a chemopreventive agent, in this case betacarotene, prevent cancer. The issue is, does NCI want to commit money to a study to find out if betacarotene prevents lung cancer in people who smoke, or former smokers. A study to find out if mailed material increases consumption of green and yellow vegetables is piddling around, a waste of resources, and not getting down to the main issue."

"Lew has posed this as an either/or question," said William DeWys, director of DCPC's Prevention Program. "So often in biology, the answer is both. We are doing definitive studies of betacarotine in occupational cohorts and smokers. If they are positive, we need to know how we can best intervene."

"If you want to find out if a mailed questionnaire works, that's a different study," Board member Robert Day commented. "You wouldn't need that size

of a population."

"This is a waste of $3 million," Kuller insisted.

"I don't agree with that," Board member David Hegsted said. "With that high risk group available, I think we should do the study. I am worried about using questionnaires to monitor diet."

"I don't believe that it is not known that mailed information can impact behavior," Board member Robert Cooper said.

"We're asking specifically if it can alter diets," DCPC Director Peter Greenwald said. "If it does work, it can save a lot of money."

"I think the answer is known," Cooper said. "The only thing that is not known is if it will increase the consumption of vegetables."

"There are two studies in the proposal," Board member Laurence Kolonel said. "One is to see if certain types of foods prevent lung cancer. That study should have been done before the other lung cancer clinical trials. Another is whether mail intervention will work. "I don't know how you would break out the costs."

Gladys Block, who would be project officer for the study, said that the mail portion of the proposal would cost about $500,000 in the first year.

Day offered the motion to table the concept, with the suggestion that staff "come back in May with a revised proposal." The motion was approved, with only Jerome DeCosse opposed.

The Board approved the concept of modifying the interagency agreement with the U.S. Dept. of Agriculture for diet and nutrition studies by adding $1.2 million to the $2.2 million already committed to the project from FY 1984 through 1986, and extending it for another five years at an extimated cost to NCI of $1 million a year.

"This is one of the best things the division is doing," Kuller said. "It builds on resources that exist. It is good science. It is an excellent program, doing all kinds of research on how chemopreventive agents work."

Cooper objected to the five year renewal before the current effort is evaluated. Greenwald said the project would undergo a site visit this summer, chaired by a member of the DCPC Board.

The vote to approve the concept was unanimous.

NCI TO SUPPORT SUMMER STUDENTS WITH GIFT FUND, SEEKS SOME HELP

NCI intends to use some of its accumulated gift funds to support 39 students in its summer training program this year and hopes that funds may be raised from other sources—especially industry—to increase that number.

Director Vincent DeVita told the National Cancer Advisory Board this week that the reduction in the number of positions allocated to NCI as ordered by the White House would have killed the summer training program except for the gift money. Those are funds contributed to NCI, which is permitted by law to accept them, with the director allowed to spend them pretty much as he sees fit. Using it to support the summer trainees avoids having those positions counted against the NCI total.

DeVita told the Board that industry is hiring away NCI staff members trained in biotechnology "faster than we can train them." The number of 39 summer trainees is fewer than NCI has supported in the past, and he indicated that since they are in such great demand by industry, industry might be interested in helping continue the program.

ORGAN SYSTEMS PROGRAM R01 GRANTS HOLDING THEIR OWN IN DRG REVIEW

When the old Organ Site Program was dismantled and reshaped into the present Organ Systems Program, the most important change (and perhaps most traumatic) was moving the review of grants from the OSP working groups back to NIH. Most of them now are being reviewed by the NIH Div. of Research Grants study sections.

Supporters of the old program had feared that many of the grants would not fare well at DRG, feeling that a bias against some of the targeted research would be reflected in poor scores.

Those fears apparently were unfounded. During the 1984 fiscal year, the first full year of review back at NIH, which ended last Sept. 30, Organ Systems Program RO1 grants held their own in competition with other RO1s.

Overall, 149 of 174 RO1 Organ Systems Program grant applications were approved, and 45 were funded. That is 30 per cent of approved grants being funded, which is close to the NIH average for RO1s.

Of the five programs, bladder did the best on a percentage basis, getting five of 12 approved grants funded, for 42 per cent. Prostate funded nine of 24 (38 per cent), large bowel five of 24 (21 per cent), pancreas two of 12 (17 per cent), and breast 24 of 77 (31 per cent).

In this survey, reported this week to the National Cancer Advisory Board by Andrew Chiarodo, chief of the Organ Systems Section in the Div. of Cancer Prevention & Control, grants included were not limited to those submitted by grantees of the former program. The present portfolio includes all RO1s oriented to specific sites.

The 1984 awards totaled $22.5 million, with $2.3 million for bladder, $3 million for prostate, $2.9 million for large bowel, $685,000 for pancreas, and $12.8 million for breast. The balance is the

$939,000 for the Organ Systems Coordinating Center at Roswell Park Memorial Institute.

Those figures do not include the clinical trials groups formerly supported by the Organ Site Program. Those have been transferred to the Div. of Cancer Treatment, in the Cooperative Group Program.

Chiarodo reported that four of the groups have identified workshop topics and have scheduled them. The Bladder Program will conduct a workshop April 14 in Ft. Lauderdale on "Pharmacology/Pharmacokinetics of Intravesical Chemotherapy of Bladder Cancer." The Breast Cancer Program will hold one March 6 at NIH (Wilson Hall) on "Biological Markers and New Concepts For Treatment." The Large Bowel Cancer Program has planned a workshop May 21 in Houston on "Chromosomes in Large Bowel Cancer." The Pancreas Cancer Program will have a workshop June 22 in Keystone, Colo., on "Molecular Biology in Cancer." The Prostate Cancer Program will hold a workshop in Bethesda, with the topic to be selected.

RFA 85-CA-10
Title: The role of human papillomaviruses in the etiology of cervical cancer
Application receipt date: June 1

Cervical cancer continues to be a major health problem in the U.S. Invasive cervical carcinoma and carcinoma in situ represent three per cent and 11 per cent respectively of all cancers diagnosed in women. In the past, it had been suggested that this neoplasm and its putative precursor, cervical dysplasia, may be associated with viral infections of the cervix. Recently, a number of laboratory investigations have more strongly associated human papillomaviruses (HPVs) with cervical dysplasia and carcinoma. The presence of HPV DNA has been demonstrated in both cervical carcinomas and dysplasias. In one study, 70-90 per cent of cervical tumors contained DNA from either HPV types 16 or 18. In addition, mild dysplasia appeared to be associated with the presence of DNA from HPV types 6 or 11. A number of established cervical tumor cell lines, e.g., HeLa, have also been examined and found to possess DNA segments of HPV type 18. HPV antigens and cytological markers have also been detected in a large percentage of dysplasias examined.

To firmly establish a viral etiology for cervical carcinoma and/or dysplasia, a study of the putative progression of primary genital papillomavirus infection to dysplasia and carcinoma is needed. Little is known about the temporal relationships or physiological mechanisms involved in such a progression. In order to carry out a study of the progression, more information is needed about the basic mechanisms of virus transmission, infection, replication and oncogenic transformation.

The objective of this RFA is to stimulate basic research on the putative progression of HPV infections to dysplasia and carcinoma in human subjects and to relate this progression to the molecular biology of human papillomaviruses. Examples of such studies (which are not all encompassing) are (1) elucidation of the mechanisms of viral infection, replication and oncogenic transformation; (2) development of better in vitro model systems for HPV transformation and growth using either wild type or genetically engineered HPVs; (3) determination of the rates of regression or progression of cervical lesions in HPV infected subjects; (4) functional and structural characterization of HPV encoded proteins with particular regard to their role in oncogenesis and tissue specificity; (5) determination of the HPV types associated with specific categories of cervical lesions; (6) the nature of the host's response to HPV; and (7) the copresence and possible involvement of other viral agents, such as HSV and CMV, with HPV in the oncogenic process.

Awards will be made as research project grants. Responsibility for the planning, direction and execution of the proposed research will be solely that of the applicant. The total project period for applications submitted in response to this RFA should not exceed five years. Approximately $850,000 will be set aside to specifically fund applications which are submitted in response to this RFA. It is anticipated that six to seven applications will be funded. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of NCI, the award of grants pursuant to this RFA is also contingent upon the availability of funds for this purpose. Nonprofit and for profit institutions within the U.S. may apply. All applications will be classified as new grants. Future competitive renewal applications funded under this RFA will compete with all other unsolicited applications received by NCI. PHS grant policies governing regular research project grants, including cost sharing, apply to applications received in response to this RFA.

A copy of the complete RFA describing the research goals and scope, the review criteria and the method of applying can be obtained by contacting Dr. Alan Schreier, Biological Carcinogenesis Branch, Div. of Cancer Etiology, NCI, Landow Bldg Rm 9A-22, Bethesda, Md. 20205, phone 301-496-1953. Inquiries concerning this announcement are encouraged and should be directed to Schreier. NCI would appreciate the opportunity to clarify any issues or questions.

The concept for this RFA was approved by the DCE Board of Scientific Counselors at its fall meeting and reported in the Nov. 9, 1984 issue of The Cancer Letter.

The Cancer Letter _Editor Jerry D. Boyd
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