Library
Office of Cancer
NCI Bldg.

THE CANCER LETTER

Vol. 18 No. 6
Feb. 7, 1992

(c)Copyright 1992 Cancer Letter Inc.
Price $215 Per Year US, Canada.
$240 Per Year Elsewhere

P.O. Box 15189 Washington, D.C. 20003 Telephone 202-543-7665

President's FY93 Budget Holds NCI To $2 Billion, Gives NIH 5% Increase; Coalition 'Disappointed'

The election year budget President Bush released this week would provide $9.4 billion to the National Institutes of Health in fiscal 1993, an increase of $443 million or almost 5 percent over the current year. In a sharp turnaround from Bush's previous budgets, funding for the National Cancer Institute would be held nearly level. The President proposed $2.01 billion for NCI, only a $30 million increase over the

(Continued to page 2)

In Brief

Dingell Vows To Broaden Indirect Cost Inquiry; Gallo, Fauci Make 'Most Prolific Scientists' List

REP. JOHN DINGELL (D-MI) this week vowed to broaden his investigation of the indirect costs charged by universities and nonprofit research institutions receiving federal research money. Dingell, chairman of the House Energy & Commerce subcommittee on oversight and investigations, said new audits provided "stunning findings" of widespread abuse. . . . **NCI'S ROBERT GALLO** is number nine in a list of the world's most prolific scientists in the past decade, having published 428 papers from 1981-90, an average of one every 8.5 days, according to "Science Watch." NIAID Director **Anthony Fauci** is 17th, with 338 papers, and **Donnall Thomas,** Fred Hutchinson Cancer Research Center, is number 18 with 328 papers. Number one is USSR chemist **Yury Struchkov**, with 948 papers. . . . **DEBORAH MAYER,** National Cancer Advisory Board member and oncology lecturer, MGH Institute of Health Professions, Boston, gave birth Jan. 25 to an 8-pound baby girl, named Amelia. . . . **NCAB MEMBERS** and selected NCI executives attended a reception Jan. 27 held by Marilyn and Dan Quayle at the vice president's residence. Earlier in the day, Marilyn Quayle spoke at a press conference announcing eight regional Breast Cancer Summits at cancer centers around the U.S. (**The Cancer Letter,** Jan. 31). . . . **CRYSTALS OF HIV-1** are orbiting the Earth on the space shuttle Discovery in an experiment on the crystallization of complex proteins at zero gravity. The crystals were prepared by **Stephen Hughes** of the NCI Frederick Cancer Research & Development Center; crystallographic studies were done by **Edward Arnold** of Rutgers Univ. . . . **PHILLIP PIZZO,** chief of NCI's Pediatric Branch, received a $10,000 scientific excellence award from the American-Italian Foundation for Cancer Research. . . . **HHS HONORED** five in NCI's Div. of Cancer Treatment for work on the problem of taxol supply: Michael Grever, Saul Schepartz, Matthew Suffness, Gordon Cragg, and Kenneth Snader.

President Seeks $9.4 Billion For NIH, $2.01 Bil. For NCI

(Continued from page 1)

FY92 Congressional appropriation of $1.98 billion.

That would provide NCI with only a 1.5 percent increase from the FY92 appropriation. Bush's previous two budgets, FY91 and FY92, sought 4 percent and 5.6 percent increases, respectively.

Reaction from the cancer community last week was dissatisfaction that the President did nothing to build upon the Congressional support shown NCI in fiscal 1992.

"The National Coalition for Cancer Research is disappointed that the momentum gained last year for the National Cancer Institute is diminished in the President's budget request for fiscal year 1993," said Robert Day, president-elect of the Coalition. "The NCCR will be meeting on Feb. 19 to examine in detail the impact of the budget proposal."

Compared to NCI's FY92 operating level of $1.951, reflecting a $15 million transfer to other institutes and other reductions, the President's budget looks a little better, with a nearly $60 million or 3 percent increase.

Still, other institutes would receive greater increases over their FY92 appropriations:

--National Heart, Lung & Blood Institute, $1.245 billion, increase of $46 million, or 3.8%.

--National Institute of Dental Research, $166.7 million, increase of $6.2 million, 3.8%.

--National Institute of Diabetes & Digestive & Kidney Diseases, $699.8 million, increase of $35.8 million, 5.3%.

--National Institute of Neurological Disorders & Stroke, $615.1 million, increase of $32 million, 5.4%.

--National Institute of Allergy & Infectious Diseases would have a budget over $1 billion for the first time, an increase of $39 million, or 4%.

--National Institute of General Medical Sciences, $862 million, increase of $43 million or 5.2%.

--National Institute of Child Health & Human Development, $545 million, increase of $20.8 million, or 3.9%.

--National Eye Institute, $285 million, increase of $14 million, 5.1%.

--National Institute of Environmental Health Sciences, $261.5 million, increase of $7.6 million, 2.9%.

--National Institute on Aging, $407.2 million, increase of $20.2 million, 5.2%.

--National Institute of Arthritis & Musculoskeletal & Skin Diseases, $214.9 million, increase of $10.4 million, 5%.

--National Institute on Deafness & Other Communication Disorders, $157.3 million, increase of $7.5 million, 5%.

The office of NIH Director Bernadine Healy receives $203.4 million under the President's budget, an increase of $60.1 million, or 4 percent, over the FY92 level. This contains an 80 percent increase in funding for the Women's Health Initiative, which was funded at $25 million in FY92.

In addition, the director would continue to have authority to transfer up to 1 percent of the total amount in any NIH account to any other "emergency, high-priority activities the director may so designate. Provided further that no such appropriation shall be increased or decreased by more than 1 percent by any such transfers and that Congress is promptly notified of the transfer."

Funding for construction and equipment for intramural NIH use would take a $31.3 million cut.

More 'Delayed Availability'

The budget request continues the new practice of delaying a portion of the NIH budget until the last day of the fiscal year. This method was used for the 1992 budget to get around restrictions on the amounts that could be obligated for the fiscal year.

Under the President's 1993 budget, a total of $322 million will be delayed NIH-wide, spread among the institutes.

NCI would not be able to obligate $216.8 million until Sept. 30, 1993. The 1992 budget required NCI to delay $233.4 million until Sept. 30, 1992.

NIAID would be required to delay $51.4 million, compared to a delay of $45.6 million in FY92.

Cancer Institute Estimates

NCI's budget office this week released its estimates of funding by mechanism under the President's budget. The Cancer Institute plans to deal with a nearly flat budget by keeping certain mechanisms flat: cooperative groups, cancer centers (including the new SPORE program), cancer education, research careers, Minority Biomedical Support Grants, contracts, and the "other grants" line, which includes science evaluation, conference support, the new Shannon grants, and small instrumentation grants (see table).

Research project grants (R01s, P01s) would get an

THE CANCER LETTER

Editor: **Kirsten Boyd Goldberg**
Founder & Contributing Editor:
Jerry D. Boyd

Editorial/Subscriptions Office
PO Box 15189, Washington, DC 20003
Tel: (202) 543-7665 Fax: (202) 543-6879

Subscription rate $215 per year North America, $240 elsewhere. ISSN 0096-3917. Published 48 times a year by The Cancer Letter Inc., also publisher of The Clinical Cancer Letter. All rights reserved. None of the content of this publication may be reproduced, stored in a retrieval system, or transmitted in any form (electronic, mechanical, photocopying, facsimile, or otherwise) without prior written permission of the publisher. Violators risk criminal penalties & $100,000 damages.

increase of $63.3 million, from $889.9 million in FY92 to $953.2 million in FY93.

The prevention and control line, which received a $21 million increase in FY92, would fall by $15 million under the President's budget.

Construction funding would drop back to zero, from $12 million in FY92, $7 million of which was for Congressionally mandated proton beam research.

The only other major area of increase is in intramural research, which will gain what prevention and control has lost, plus some. Funding for intramural research would increase $18 million, from $354.7 million to $372.7 million.

Funding for research management and support, which includes funding for the Office of Cancer Communications, international programs, and many other projects, would increase by $4.6 million.

Again in FY93, as in FY92, National Research Service Awards (NRSAs) would be held flat. This is due to the fact that Congress has not reauthorized the program.

Following are NCI's budget projections, in thousands, using as the base the FY92 estimated budget:

	FY92	FY93	Change
RPGs	889,921	953,241	63,320
Ca.Centers	125,400	125,400	0
SPOREs	17,500	17,500	0
Research Careers	13,281	13,281	0
Cancer Education	6,615	6,615	0
Cooperative Groups	77,902	77,902	0
Minority Biomedical Support Grnts	3,064	3,064	0
NRSAs	37,252	37,252	0
R&D Contracts	203,113	203,113	0
Intramural Res.	354,713	372,716	18,003
Res. Mngment & Support	95,775	95,775	4,694
Prvntn & Control	106,227	91,108	-15,119
Construction	12,000	0	-12,000
Total, NCI	$1,951,541	2,010,439	58,898

AIDS Funding

Total funds to combat AIDS included in the NIH budget and budgets of other agencies, would rise by $101 million to $2.1 billion. This includes a 4 percent increase to more than $1.2 billion for biomedical and behavioral research on HIV. The budget proposes a total increase of $565 million, or 13 percent, for HIV research, treatment, prevention and income support, according to the budget document.

Funding for the Centers for Disease Control would be $1.6 billion, a $96 million increase over FY92, of which $504.6 million is credited to the HIV line item, up from $477 million this year.

Food & Drug Administration would receive $557 million, a decrease from this year's appropriation of $725.9 million. The President said the decrease would be made up with user fees "to cover the costs of regulation of products, including review of applications and inspections and other Federal activities required by law."

Congress, for the last three years in a row and in previous years, has refused to go along with the Administration's user fees proposal.

NCI Halts Routine P01 Site Visits Due To 40% Travel Expense Cut

NCI will discontinue automatic site visits for review of program project grant (P01) applications due to an unusual 40 percent reduction in its program and scientific travel budget for fiscal 1992. The institute also may have to curtail participation of its scientists in professional meetings of medical societies.

NCI was hit with a $1.3 million reduction in travel expenses as its share of an $8 million reduction throughout the Public Health Service. NIH officials decided not to reduce patient travel expenses, thus the scientific programs of the institutes took relatively large cuts.

The travel expense cut grew out of a controversy last spring over the number of PHS scientists scheduled to attend the International Conference on AIDS in Florence, Italy, last June. HHS estimated that more than 400 planned to attend, at a cost of about $1.5 million.

Rep. David Obey (D-WI) and Rep. William Dannemeyer (R-CA) demanded that HHS reduce the number of staff attending the meeting by about half, and then led an effort in the House to reduce all PHS travel expenses.

Obey "was upset at the numbers [of scientists traveling to the AIDS conference]," a spokesman for the congressman told **The Cancer Letter.**

Since the appropriations bill was tight, the Senate decided to go along with the reduction.

"NIH could have gotten huge across the board cuts, which would have been worse than the targeted approach we took," the spokesman said. "We needed the money when it was brought up."

The result was the following language in the House report on the Labor, HHS, Education appropriations bill, page 118, under Acquired Immune Deficiency Syndrome:

"International Travel--The committee was greatly disturbed

by reports in the press, later confirmed by the Department, that almost 400 employees of the Public Health Service were scheduled to attend the International AIDS Conference in Florence, Italy [last June]. While the committee understands that a reasonable number of scientists have a legitimate need to attend such meetings at taxpayer expense, current plans clearly permit a larger number to go than seems reasonable to the average citizen in this country. During a period of significant fiscal constraints in which many government programs serving low and middle income families are being reduced, it is not justifiable to spend such a large amount of scarce biomedical research funding on international travel. The committee notes that this episode has the potential to erode public confidence in the wisdom of investing in biomedical research at the NIH. The committee has, therefore, directed the Secretary of the Department of Health & Human Services to reduce the number of attendees and to certify to the committee by July 15, 1991, the number who attended this particular meeting at government expense.

"This matter has also caused the committee to review more carefully the budget request for travel throughout the Public Health Service. Section 513 of this bill reduces funds available for travel by $8,000,000, which is approximately 20 percent of the amount requested."

Immediate Implications For Site Visits

Though Congress was concerned about international travel, the practical implication of the expense cut will be to severely limit domestic travel of NCI staff and its outside reviewers.

Thus, while NCI this year with a $1.95 billion operating budget is enjoying increases in most major program areas and is planning program expansions and encouraging grant submissions, the institute has to drastically limit travel of staff and reviewers to meetings designed to help implement some of those expansions.

NCI Director Samuel Broder said he argued with NIH and the appropriations committees that patient travel should take a share of the cut as well, and that the institute should be allowed to "reprogram" money from other programs for necessary travel. "We feel that we lost [that argument]," he told the National Cancer Advisory Board last week. However, he noted that NCI "is being fairly treated" in the NIH-wide cuts.

NCI's Div. of Extramural Activities said it would begin immediately to implement the following procedures for review-related travel:

"For the May 1992 National Cancer Advisory Board meeting, all project site visits in connection with the peer review of cancer centers (P30s), program projects (P01s) and clinical cooperative groups (U01s) will proceed as scheduled.

"For the September 1992 NCAB meeting (Feb.1/March 1 receipt dates), we will continue to allow project site visits for centers and groups, but will discontinue automatic site visits for the review of program project applications. [A footnote notes that, In every case, the decision to hold a site visit will be based on appropriate consideration, by review and program staff, of the actual need for on-site evaluation.] Instead, P01s will be reviewed by ad hoc initial review groups meeting in committee here in Bethesda, augmented, when appropriate, by 'reverse site visits,' i.e. conference calls or teleconferences. Reviewers will be reminded that deferral for a site visit is among the recommendations that they can make. In such cases, DEA will schedule the recommended project site visit as expediently as possible, and NCI will attempt to avoid discontinuity of funding for ongoing programs by providing some level of interim support. (This latter procedure will be in effect for the January 1993 Board, since review-associated travel by our staff would ordinarily take place during FY 1992.)

"During this transition period, it is in the best interests of all applicant P01 principal investigators to contact the DEA scientific review administrator assigned to his or her application to determine whether the application, as submitted, requires additional information or materials that might assure both its administrative completeness and its adequacy for peer review. The NCI/DEA SRAs will work with PIs to establish a reasonable time frame within which additional or supplementary materials might be submitted for distribution and adequate appraisal by the reviewers. This interaction could be of particular importance to the Feb. 1 program project applicants."

NCAB Resolution

The NCAB last week unanimously approved a resolution calling on Congress to "remove the restrictions imposed on domestic travel at the earliest possible time."

Broder said he was especially concerned about the participation of NCI intramural scientists in meetings of professional societies, including the annual American Society for Clinical Oncology and American Assn. of Cancer Research meetings.

"We're not talking about arcane meetings. These are important for professional standing and credibility," he said. "I'm extremely concerned about the potential impairment of the ability of scientists to exchange information one-on-one."

President's Cancer Panel Chairman Harold Freeman said the panel might consider taking up the issue of scientific travel.

"I'm not so concerned about the senior [NCI] people, who possibly don't need to travel to so many meetings," Broder said. "I am concerned about young people missing opportunities for career development."

ODAC Oks IV Melphalan As Palliative; Says Amifostine Needs More Study

FDA's Oncologic Drugs Advisory Committee recommended approval of melphalan for injection, a new formulation of a very old drug, for use as palliative treatment of multiple myeloma in patients who cannot tolerate the oral form of the drug.

Burroughs Wellcome Co., which sells melphalan under the trade name Alkeran, also sought approval of the drug for use in hyperthermic isolated limb perfusion as an adjunct to surgery for locally advanced malignant melanoma to the extremity.

However, a majority of committee members said there were serious design and methodical flaws in the two clinical trials attempting to prove the efficacy of melphalan for that use. The committee found that the trials could not be considered supportive of efficacy claims for use in limb perfusion for any stage of melanoma.

The committee said IV melphalan should be approved for "use in myeloma when oral medications are not indicated," but voted 9-0 against approval for first-line therapy.

If FDA follows the committee's recommendation, which it usually does, the company will not be allowed to advertise melphalan for first-line therapy, a fact that was a consideration in the committee's deliberations.

The trial that supported the drug's efficacy for this indication was performed by the Cancer & Leukemia Group B.

The oral form of the drug was approved in 1964.

ODAC also dealt with extensive methodological questions concerning studies of amifostine, also known as WR-2721, trade name Ethyol by U.S. Bioscience. The firm requested approval of the drug for protection of patients at risk of serious toxicities from conventional doses of cyclophosphamide and less than 100 mg/m^2 of cisplatin. The firm agreed two weeks prior to the meeting to limit claims of the drug's efficacy to these conventional doses.

The company's original New Drug Application, submitted last Sept. 30, requested approval of amifostine as "a chemoprotective agent that selectively protects against serious toxicities associated with intensive regimens of platinum and alkylating agent chemotherapy."

The committee agreed with FDA that data was not sufficient to warrant approval of the drug even as a protectant from conventional chemotherapy, and recommended that a study by Donna Glover, Presbyterian Univ. of Pennsylvania Medical Center, continue to accrue patients.

The committee voted 7-1 that the results of Glover's study "provide preliminary assurance" that amifostine does not decrease the antitumor effect of chemotherapy, and decreases hospitalization for febrile granulocytopenia. The committee said there was not enough data on the drug's effect on more serious toxicities such as neurotoxicity and ototoxicity.

FDA reviewer Gerald Sokol said Glover's trial had "multiple protocol violations" including three interim analyses rather than the one specified in the protocol, and has "poorly defined" study endpoints.

Those comments prompted ODAC member Steven Piantadosi to note, "It is striking how effective WR-2721 appears in preclinical studies and how difficult it has been for the sponsor to show clinical efficacy."

Piantadosi said the additional data from continuing Glover's trial "will be helpful," but will not provide the statistical rigor necessary to prove the drug's efficacy.

"You're suggesting we start with a new study?" committee member Nancy Kemeny asked.

"Yes, I'm suggesting that," Piantadosi said. "We've botched it, we've blown it. We've used an interim analysis that we can't justify."

"The message is that multiple looks may cost approval," ODAC Chairman Craig Henderson said.

Two other studies did not provide enough information on the drug's efficacy in decreasing the toxicity of cytoxan, the committee found.

The committee split 4-4 on the question of whether additional studies are needed to show that amifostine decreases the neutropenia related toxicity of cyclophosphamide, and voted 7-1 to require more data on the drug's effect on cisplatin-related toxicities.

NIH Consensus Panel Finds Narrower Margins Curative For Early Melanoma

An NIH consensus conference on diagnosis and treatment of early melanoma has concluded that narrower margins of surgical excision offer better cosmetic results without compromising survival.

Melanoma in situ may be cured by excision of the lesion or biopsy site with a 0.5 cm border or clinically normal skin and layer of the subcutaneous tissue.

Invasive melanoma previously was treated by removal of up to 5 cm margin of normal skin, requiring skin grafting procedures for reconstruction. The consensus panel concluded, however, that recent clinical trials suggest that these superficial melanomas can be removed with narrower margins.

"For melanomas <1 mm thick, a 1 cm margin of clinically normal skin and underlying subcutaneous tissue down to fascia is recommended as an

appropriate excision. This excision often can be performed with a primary closure of the margins without the need for reconstructive procedures."

However, the panel noted that, "Currently, there is not enough clinical experience utilizing microscopically controlled excision (Mohs surgery) for the treatment of primary melanomas to recommend it as an alternative approach. Mohs surgery may prove a useful technique for certain types and locations of melanoma, but more data are needed."

The panel noted that results of a 1 cm margin of excision for early melanoma are "excellent," with about a 95 percent eight-year survival. Prophylactic regional lymph node dissections should not be performed in these patients, the panel said, and extensive diagnostic studies are not indicated.

Following are the "conclusions and recommendations" of the consensus panel:

▶The diagnosis of early melanoma (melanoma in situ and invasive melanoma < 1.0 mm measured depth) is important because:

--Melanoma in situ is a distinct diagnostic entity effectively treated surgically with 0.5 cm margins with a resulting greater than 99 percent cure.

--Thin invasive melanoma, < 1.0 mm in measured depth, has the potential for cure in more than 90 percent of patients after a surgical excision with a 1.0 cm margin.

▶Minimal criteria for an acceptable pathology report for melanoma include diagnosis, depth of invasion in malignant melanoma, and status of margins.

▶Elective lymph node dissections and extensive staging evaluations are not recommended in early melanoma.

▶Patients with early melanoma are at low risk for relapse but may be at high risk for development of subsequent melanomas and should be followed closely.

▶Some family members of patients with melanoma are at increased risk for melanoma and should be enrolled in surveillance programs.

▶The use of "dysplastic nevus" as a clinical and histologic diagnosis is discouraged. The clinical lesions should be described as "atypical moles." Lesions with the appropriate constellation of microscopic features should be reported as "nevi with architectural disorder" accompanied by a statement describing the presence and degree of melanocyte atypia. The biologic significance of these nevi must be determined by the clinical features and family history of each case.

▶The familial atypical mole and melanoma syndrome (FAM-M) is clinically recognizable. Individuals with this syndrome have an increased risk of developing melanoma. Careful surveillance of the patient is necessary.

▶Education and screening programs for melanoma have the potential to decrease morbidity and mortality.

▶The public should be made aware of (1) the increased risk of melanoma related to sunburn, particularly in childhood; (2) the clinical appearance of early melanoma; (3) the excellent prognosis associated with detection of early melanoma; and (4) the need for regular skin examinations by themselves and by their physician.

The panel said future directions for research should include:

▶Determine the significance of histological regression in melanoma.

▶Develop specific serologic tests and tissue tests for early melanoma, extending beyond the epidermis to characterize radial and vertical phases.

▶Determine the optimal margins for primary melanomas deeper than 1 mm.

▶Determine the genetic basis of the FAM-M syndrome.

▶Determine the role of optical and computer technology for following patients with atypical moles.

▶Examine alternative therapies for primary melanomas where normal tissue conservation is critical (e.g., Mohs and cryosurgery).

▶Determine the effect of UV radiation on the formation and progression of melanoma and on the immune system by: Determining the effect of UV induced immune suppression on melanoma; and contrasting the effect of high-dose intermittent ultraviolet B light on human melanocytes with chronic UVB exposure.

▶Define the basic biology of melanoma. Some examples of needed studies include: Determining the cellular characteristics associated with malignancy, invasion, and metastases, including growth factors, growth factor receptors, gangliosides, karyotypic analysis; Developing cell lines for melanoma of different biological potential; Developing new markers for early stages of melanocytic neoplasia.

▶Perform meta-analysis on data on margins and risk of recurrence.

▶Determine the characteristics of those who neglect changing skin lesions so education campaigns may be improved.

▶Determine the optimum frequency of skin screening for individuals of varying risk for melanoma.

▶Develop better means to determine population-based incidence and prevalence data for melanoma.

Cancer RFAs Available

RFA CA-92-13

Title: Implementation grants for gene therapy programs in cancer treatment

Letter of Intent Receipt Date: April 3

Application Receipt Date: May 15

NCI's Div. of Cancer Treatment invites program project grant applications from interested investigators to establish interactive Gene Therapy Programs with the goal of conducting gene therapy clinical trials for cancer treatment. The purpose of this RFA is to promote the design and implementation of clinical trials of gene therapy, to support the requisite preclinical studies establishing the scientific and technical basis for human studies, and to foster the development of interactions between basic scientists and clinical researchers necessary for bringing gene therapy to patient trials. The program project grant mechanism will support establishment of broadly based, multi-disciplinary, multi-institutional research programs centered around this goal. For the purposes of this RFA, gene therapy will be defined as the transfer of a functioning gene(s) into somatic cells to treat disease.

Applications may be submitted by domestic non-profit and for-profit organizations, public and private. Applications may be submitted from a single institution or may include arrangements with one or more additional institutions if appropriate. Applications from minority individuals and women are encouraged.

The total project period may not exceed four years. The anticipated award date will be Sept. 30, 1992. Approximately $5 million in total costs per year for four years will be committed to fund applications submitted in response to this RFA. It is anticipated that six to eight awards will be made.

The Cancer Therapy Evaluation Program is seeking applications for research program project grants (P01) to establish interactive GTPs with the goal of conducting gene therapy clinical trials for cancer treatment. The applications must be focused on a specific clinical therapeutic approach. These awards are envisioned to serve as implementation grants for the development of a collaborative effort between a multidisciplinary and possibly multi-institutional group of investigators to rapidly move forward new approaches in gene therapy of cancer into the clinic. Funds are to be used to conduct the necessary preclinical studies to prepare a clinical product or procedure for human trials and to gain regulatory approval to conduct such trials.

CTEP will provide assistance in applying for regulatory approvals. NCI is encouraging investigators to forge new collaborations with other research institutions and private industry to obtain the necessary expertise in all aspects of the research program.

Initial approaches to gene therapy would involve the alteration and administration of human somatic cells. Future techniques may include approaches such as the direct administration of genetic material to patients. Examples of gene therapy for the treatment of cancer include: (1) implantation of tumor cells transfected with functioning cytokine genes to elicit an immune response; (2) insertion of genes into host effector cells that will enhance their ability to recognize and bind tumor specifically and/or will potentiate the inflammatory response of the host at the site of tumor; (3) insertion of genes into normal cells of the host such as bone marrow stem cells that will increase their resistance to the toxic effects of chemotherapy; (4) in vivo introduction of genes into cancer cells that will restore suppressor gene function or neutralize the function of activated oncogenes that maintain the neoplastic phenotype. Investigators are not limited to the above studies; however all studies must be therapeutic in intent and not solely diagnostic.

Copies of the complete RFA are available from, and letters of intent should be sent to: Diane Bronzert, Program Director, Cancer Therapy Evaluation Program, NCI, Executive Plaza North Rm 734, Bethesda, MD 20892, phone 301/496-8866, fax 301/480-4663.

RFA CA-92-08

Title: Quantitation of tumor response to treatment: a three-dimensional approach

Letter of Intent Receipt Date: April 21

Application Receipt Date: May 21

The Radiation Research Program in NCI's Div. of Cancer Treatment announces the availability of a Request for Applications that advances current methods of imaging-based tumor volumetric analysis for optimization of response assessment in oncology. The objective of this RFA is to support meritorious research in the development of a three-dimensional (3D) approach to serial quantitation of tumor volume. The proposed research is expected to improve clinical management in oncology and to facilitate the development and evaluation of anti-neoplastic drugs and other treatment modalities in cancer patients.

Applications may be submitted by domestic and foreign, for-profit and non-profit organizations. Support will be through the NIH individual research grant (R01). Approximately $500,000 in total costs per year for three years will be committed to fund applications submitted in response to this RFA. It is anticipated that three awards will be made. The total project period may not exceed three years. Earliest feasible start date for the initial awards will be March 1, 1993.

The specific goal of this initiative is the development and optimization of a quantitative analysis of tumor response to treatment based on 3D medical imaging. The proposed research will stimulate the achievement of optimal tumor volumetric analysis by means of the development of advanced approaches to two critical basic computer science topics, automated image segmentation and multimodality image registration, and their validation and testing.

Copies of the complete RFA are available from, and letter of intent is to be sent to: Dr. Faina Shtern, Chief, Diagnostic Imaging Research Branch, Radiation Research Program, NCI, Executive Plaza North, Suite 800, Bethesda, MD 20892, phone 301/496-9531, fax 301/480-5785.

RFA CA-92-04

Title: Cancer prevention and control research small grant program

Application Receipt Date: May 6

NCI's Div. of Cancer Prevention & Control announces the availability of the above named RFA. This program is designed to aid and facilitate the growth of a nationwide cohort of scientists with a high level of research expertise in the field of human cancer control intervention research. New and experienced investigators in relevant fields and disciplines (e.g., disease prevention and control, medicine, public health, health promotion, epidemiology, social work, nursing research, nutrition, health policy, health services research, and behavioral sciences, such as social psychology, health education, sociology, and community organization) may apply for small grants to test ideas or do pilot studies.

Investigators are eligible to apply for a small grant to support research on a cancer control topic if they are interested in conducting exploratory studies in cancer control research. Eligible applicants include established researchers, new investigators, qualified staff of public health departments and collaborating agencies, and predoctoral investigators currently enrolled in an accredited doctoral degree program. Applications from minority individuals and women are encouraged.

The only INELIGIBLE applicants are: 1. those individuals who

are or have previously been a Principal Investigator on an NCI funded cancer control grant or contract for more than two years; 2. previous recipients (Principal Investigators) of a DCPC Small Grant; 3. foreign institutions.

Support of this program will be through the NIH small grant (R03). Anticipated award date is March 1, 1993. Approximately $500,000 in total costs for two years will be committed. Direct costs maximum is $50,000, and the duration of support is two years maximum. Up to seven awards will be made.

The program is designed to encourage investigators from a variety of academic, scientific, and public health disciplines to apply their skills to scientific investigations in the field of human cancer control intervention research. The research may occur in a variety of settings, such as communities, schools, health departments, and work sites. These investigators will become part of the new nationwide group of scientists pursuing cancer control research goals.

Within this small grant program, investigators may choose any of the full range of scientific approaches in their work. Many studies and research designs may contribute to the design, implementation or evaluation of future phase III-V studies, e.g., descriptive baseline surveys, testing, modification and validation of surveys or program materials for use in the proposed population groups, and testing of recruitment or compliance procedures for participants.

Investigators must address the specific aims and hypotheses, the background and significance of the proposed work, results of any preliminary studies, experimental design and methods including any relevant theoretical concepts that underlie the research, human subjects involvement and protection, and relevant literature.

Cancer Control program areas appropriate for human intervention research grant applications include:

o Prevention (chemoprevention, diet and nutrition intervention studies).

o Screening and early detection, e.g., pilot studies of new methods; application of the "NCI Guidelines For Early Detection." In the area of breast screening and detection, studies of breast self-examination as a single modality will not be accepted.

o Cancer Control sciences (studies to change current behaviors and/or institute new behaviors or health promotion interventions effective in reducing incidence, morbidity, or mortality from cancer).

o Smoking prevention and cessation pilot studies targeted at improving utilization of current technologies in target populations or organizations are encouraged. Minor enhancements of existing technology are not encouraged.

o Applications research in modifying, feasibility testing, and adopting proven, state-of-the-art intervention programs and strategies from other research projects (e.g., screening, smoking prevention) for use in special populations, State and local health agencies, or other organizational and community settings. In addition, planning, epidemiologic, and survey studies aimed at developing cancer control operations research and evaluation studies are appropriate for human intervention research grant applications.

o Community oncology (improving the application of patient management and continuing care research advances into community settings).

o Applied epidemiology studies (using epidemiologic methods to determine the association between exposure to an intervention and its impact on disease) are acceptable within the above program areas.

Although the specific study proposed may attempt only to obtain preliminary data and/or to conduct pilot studies in support of a future, more detailed study, it is important that a long term human cancer control hypothesis and supporting scientific justification be presented.

Exclusions: Studies to determine the efficacy of chemotherapy, surgery, radiotherapy, and other primary treatment interventions are not considered cancer control research under this RFA. Other laboratory animal studies are not allowed.

Copies of the complete RFA and other inquiries may be directed to: Dr. Sherry Mills, Program Director, Prevention and Control Extramural Research Branch, Div. of Cancer Prevention & Control, NCI, Executive Plaza North Rm 320, Bethesda, MD 20892, phone 301/496-8520.

AIDS RFA Available

RFA AI-92-04

Title: NIAID institutional training awards for clinical research on the acquired immunodeficiency syndrome

Letter of Intent Receipt Date: Feb. 28

Application Receipt Date: April 8

The National Institute of Allergy & Infectious Diseases announces the availability of NIAID institutional training awards for clinical research on AIDS. The purpose of this RFA is to solicit applications from established programs of excellence at institutions that are able to develop a clinical research program that provides training opportunities to outstanding new investigators who have shown an interest in, and commitment to, clinical research on HIV disease and AIDS. This program will target a variety of disciplines that work with patient clinical material or other clinical data in clinical research.

Only domestic academic, non-profit, private and public institutions are eligible to apply for this award. OnLy U.S. citizens or non-citizen nationals, and individuals admitted to the U.S. as Permanent Residents are eligible to become trainees. Minority individuals and women trainees are encouraged.

Awards for this program will be made as Institutional National Research Service Awards (NRSA) (T32). The total project period may not exceed five years. NIAID has set aside $750,000 in total costs for the first year of this RFA. The number of awards will be influenced by the availability of funds, the overall scientific merit of the applications, and reLevance to program goals.

The goals of the NIAID Institutional Training Awards for Clinical Research on AIDS are to:

o Increase the number of clinical researchers with a broad background in clinical research methodology working in the field of HIV disease.

o Provide support to post-doctoral fellows, advanced graduate students, and physicians for training in disciplines that are directly relevant to clinical biomedical research on HIV disease.

o Provide a training experience that integrates the range of disciplines necessary for the conduct of clinical research.

o Provide a training experience in an environment committed to interdisciplinary collaboration among faculty/investigators active in HIV research. Programs must include a range of disciplines requisite for the development of research skills in clinical studies on HIV/AIDS. These include: epidemiology, surveillance, natural history and transmission studies, biostatistics, theoretical fundamentals of clinical research design, protocol development, regulatory requirements, ethical considerations, clinical research execution, data collection, quality assurance, data management and analyses, clinical immunology, virology, microbiology, infectious diseases, molecular biology, pharmacology, biochemistry, scientific writing, and manuscript preparation.

Copies of the complete RFA are available from, and letters of intent may be sent to: Dr. Evelyn Rodriquez, Div. of AIDS, NIAID, Solar Bldg., Rm 2A23, Bethesda, MD 20892, phone 301/496-6177.