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NCI To Cut Smoking Intervention Study By 20%, Says Chemoprevention Accrual Has Priority

Exactly one year after launching the federal government's largest single antismoking program, with promises of support at the highest levels of the Department of Health & Human Services, NCI announced that it plans to cut $5.1 million from the program and an NCI official said the program is not the Institute's first priority in cancer prevention and control this year.

NCI's Div. of Cancer Prevention & Control expects to make a 20 percent cut in the American Stop Smoking Intervention Study, reducing

(Continued to page 2)

In Brief

Thomas Jefferson Univ. Wins $5 Mil. P01; Former NCI Administrator Sentenced

THOMAS JEFFERSON Univ. Jefferson Cancer Institute has received a $5 million program project grant from NCI to study the genes and mechanisms involved in acute leukemia and non-Hodgkin's lymphoma. Principal investigator of the five-year study is JCI Director **Carlo Croce.** "Through this grant, we are deciphering the genetic changes going on in aggressive leukemias and lymphomas and are beginning to develop genetically based approaches to diagnose, monitor and treat the diseases," Croce said. The center will coordinate two research consortia and three projects using researchers from Jefferson and the Hospital of the Univ. of Pennsylvania. . . . **PREM SARIN**, former deputy to NCI Laboratory of Tumor Cell Biology Chief Robert Gallo, was sentenced to two months in a work-release facility for embezzling $25,000 in AIDS research funds that was provided by Degussa Corp., a German research firm. Sarin returned the money and said he was careless in combining it with personal funds. Baltimore U.S. District Judge Marvin Garbis said he wanted Sarin to be able to continue his consulting work. . . . **CANCER AND AGING** position paper has been published by the Oncology Nursing Society. The paper charges oncology nurses to establish a formal framework within which nursing care can be augmented or modified to meet the unique needs of elderly persons with cancer. Goals are to heighten awareness of cancer and aging, stimulating professional interest. The publication is available for $2 to members and $3 for nonmembers. Contact ONS Publications, 501 Holiday Dr., Pittsburgh, PA 15220, phone 412/921-7373. . . . **DENNIS AHNEN** was named associate director of cancer prevention and control at Univ. of Colorado Cancer Center. He is associate professor of medicine at UC Health Sciences Center and a clinical investigator at Denver Dept. of Veterans Affairs Medical Center.

NCI To Cut ASSIST By $5 Mil. In '93; DCPC Board Objects In Resolution

(Continued from page 1)
the budget for fiscal 1993 from $23.3 million to $18.2 million.

The DCPC Board of Scientific Counselors passed a resolution at its meeting last month urging that ASSIST not be subjected to a cut disproportionate from that of other DCPC programs.

Last October, NCI awarded contracts to 17 state health departments for smoking prevention and cessation activities. The American Cancer Society agreed to add the support of thousands of volunteers and cash of about $25 to $30 million.

NCI planned to spend $135 million over seven years on ASSIST. The study was designed to reach 18 million smokers, convince 4.5 million of them to quit, and pursuade 2 million youth never to smoke. The Institute spent $6.4 million and $9.7 million on ASSIST in FY91 and 92.

"We went out to these communities, we organized them, we promised them funds, and now we are doing the typical government two-step," DCPC board member Helene Brown said. "We go in, we ask for cooperation, they all put their wallets, time, and effort on the table, and we come back and say, 'Sorry, we have to pull back.'"

Brown, of Univ. of California at Los Angeles, Jonsson Comprehensive Cancer Center, wrote the resolution that was passed by the board with one nay vote and two abstentions.

DCPC Director Peter Greenwald said ASSIST is not taking a disproportionate cut and that it remains a high priority for the Institute. "We think it is a very important program and whatever you can do to reduce smoking in the U.S. will have a major public health impact," Greenwald said to **The Cancer Letter.** "The problem is we have to make choices in our budget. Overall in prevention and control, ASSIST is even with other programs."

NCI received the smallest budget increase in a decade this year. Earlier this year, the Institute estimated it would have to cut ASSIST by 40 percent under the Administration's proposed FY93 budget, which cut cancer prevention and control by $15 million (**The Cancer Letter,** March 20).

Congress restored the $15 million cut and urged NIH and the Administration to submit a budget request next year "which reflects the critical role that prevention and control should have in our National Cancer Program." However, Congress emphasized funding for women's health, breast cancer, and prostate cancer. Smoking cessation was never mentioned in this year's appropriations committee reports as an important mission of NCI.

"Our first priority this year is to get our major prevention trials underway," Greenwald said to **The Cancer Letter.** "We don't have any flexibiltiy in funding them. You can't neglect accrual issues. One of the things driving our resource allocation is that I have to make sure our major trials are sound and on track--like the Breast Cancer Prevention Trial [testing tamoxifen in healthy women]."

Other trials beginning this year are the prostate cancer prevention trial testing finasteride and the Prostate, Lung, Colorectal and Ovarian cancer screening trial testing various screening modalities.

NCI's estimates of FY93 funding by and within each division were not available by this writing, but Greenwald said he was not optimistic that any funds could be added to ASSIST.

"I don't see a lot of flexibility in the budget figures I've seen thus far, so I dont want to promise anything," he said.

At a press conference last year announcing the 17 state health departments who were selected to receive contracts to implement ASSIST, HHS Secretary Louis Sullivan said, "If we could only do one thing to improve the health of our citizens and decrease health care costs, it would be to get people to stop smoking" (**The Cancer Letter,** Oct. 11, 1991).

ACS: 'Never Assumed There Would Be Cuts'

Joseph Patterson, ACS director of tobacco control and liaison to NCI on ASSIST, told **The Cancer Letter** he is scheduled to meet with NCI officials next week to discuss the program. "Without knowing the nature of the cut, I don't know what impact it would have," he said.

"When we went into this, we had the idea it would be fully funded, so I think any cut is something that

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we don't look forward to," Patterson said. "Part of our commitment was based on NCI's commitment. Everyone got into this game not assuming there would be cuts."

ACS agreed to commit 15 percent of NCI's contract amount at each ASSIST site. That amount "is not necessarily 'hard' money," Patterson said. It includes one full time position, travel expenses, and materials. It does not include the time its national staff spends on the program, or the work of volunteers at the local level. Several other organizations have committed volunteers to ASSIST as well.

Other ACS executives have been more disparaging in their comments. "We made a commitment to our people," said one, who asked not to be identified by name. "If NCI reduced its commitment, it could pose some serious problems."

Following is the text of the DCPC board's resolution:

Recognizing that, after more than a decade of important work validating that reduction in tobacco use can be acheived, NCI-DCPC announced the largest public health effort in the world--American Stop Smoking Intervention Study--ASSIST;

That, through ASSIST, NCI took the leadership in tobacco control from the NIH in an extremely visible program;

That the ASSIST program has been approved at a level of funding which provided for staging of planning and implementation over a seven year period;

That the 17 contract state health departments in collaboration with the 17 divisions of the American Cancer Society have employed staff, formed community based coalitions and partnerships based on this specific level of ASSIST funding through 1998;

That estimates made by NCI project that 1.2 million premature smoking related deaths could be avoided as an end result of ASSIST;

That the potential for reduction in mortality and morbidity from cancer is greater through the elimination of tobacco use than any other preventive measure currently available;

Therefore, be it resolved that should budgetary modifications be necessary in the DCPC and/or NCI budget, the ASSIST program not be subjected to a disproportionate adjustment from its original projected budget requirements.

Board member Arnold Kaluzny voted against the resolution, saying he favored budget flexibility.

Breast Cancer Funding

Uncertainty Lingers After DOD-NCI Meeting; Activists Offer Advice

Call it the $210 million question: What will the Department of Defense do with its windfall of breast cancer research funds?

After an initial meeting between NIH and Department of Defense officials, observers and insiders alike are hesitant to venture predictions.

However, several sources noted that DOD has not exhibited any inclination to make an interagency agreement to distribute the funds through the NIH peer review system.

Sources said a great deal of uncertainty remained following the initial meeting between DOD Assistant Secretary for Health Affairs Enrique Mendez and NIH Director Bernadine Healy and NCI Director Samuel Broder late last month.

The meetings between the agencies are expected to continue.

Observers also point out that the breast cancer appropriation is a potential land mine for Defense. For one thing, Defense did not seek the funds, and received them as a result of rushed dealmaking in the final days of the 102nd Congress, as legislators sought creative ways to increase breast cancer funding and thereby please the politicized breast cancer patients.

Congress raided Defense funds in such a way that the appropriation could not be scored as domestic spending. That, in turn, meant that breast cancer funds had to be kept in Defense with no provision for an interagency agreement with NCI (**The Cancer Letter**, Oct. 16).

As a result, Defense will outspend NCI by $73 million on breast cancer. The program will be administered through the Army Medical Research and Development Command, headed by Maj. Gen. Richard Travis.

"This was a windfall that came unexpectedly to them, and they were not sure they wanted it," said one Congressional source.

It is not entirely clear whether Defense realizes the extent of monitoring and political pressure that will accompany this windfall, sources said.

The breast cancer patient activists have vowed to ensure that, in the words of Fran Visco, president of the National Breast Cancer Coalition, "not one cent of that money is wasted."

The activists, represented by the NBCC, have scheduled a meeting with Mendez in mid-November. Similar meetings were scheduled by the National Coalition for Cancer Research, a group that represents the cancer specialties, and by the Susan G. Komen Breast Cancer Foundation.

These players have their own plans for DOD's breast cancer money and, more importantly, they have clout on Capitol Hill.

"We are going to continue to work with the Army to make sure the money is spent for the purposes intended and would contribute to prevention and treatment of breast cancer," Sen. Tom Harkin (D-IA) said in a statement to **The Cancer Letter**. "We intend

to use all the means at our disposal to carefully monitor the manner in which the money is spent."

"Very Preliminary"

Days after learning that it would have to hand out $210 million in breast cancer research funds in just two years, DOD made its first stab at developing a plan of action.

Under that plan, outlined in a memo that circulated internally and on Capitol Hill, the funds were to be spent on "relatively short-term, high technology, innovative research with specific goals and endpoints."

According to the memo, DOD planned to emphasize digital mammography, radiochemistry, thermography and genetic, cellular and hormonal markers. In treatment, the goal was to achieve "early intervention and minimal or no disfigurement of the breast."

Overall, the memo said the objective would be to avoid duplication of research performed at NCI.

"That was very preliminary," NBCC's Visco said to **The Cancer Letter.** "That was before they spoke or met with any of us."

One Capitol Hill source characterized DOD's original plan as an attempt to minimize work by handing out a small number of short-term, sizable grants. Considering the intensity of scrutiny that will accompany the breast cancer funds, observers said the Army is likely to be forced into some kind of a cooperative relationship with NCI.

Advising DOD

At a meeting with DOD's Mendez later this month, the Susan G. Komen Breast Cancer Foundation is expected to recommend that all research financed through DOD be fully funded at the outset.

This way, DOD would not be saddled with carry-over obligations, giving Congress the leeway to consolidate all breast cancer research at NIH.

The Komen foundation is also expected to ask that DOD finance basic research in breast cancer, create additional Specialized Programs of Research Excellence and include the underserved populations in its clinical trials.

At a separate meeting, NBCC is expected to ask DOD to emphasize development of genetic, cellular and hormonal markers, primary and secondary prevention and identification of the role of environmental factors in the development of breast cancer.

Further, the coalition is expected to ask that research into treatment modalities be limited and directed at primary and secondary prevention and novel treatments for metastatic disease.

According to a statement by the coalition, a team overseeing the grantmaking should include representatives of the Army, NCI, and the NIH Office of Research on Women's Health. According to the statement, "there should be a nongovernmental ad hoc advisory committee to work with the management team. This committee should be made up of representatives from basic epidemiologic, clinical, prevention and psychological research and advocacy organizations. Oversight should be by a government management oversight committee of which NCI provides at least one member."

Mendez has also received a number of letters from cancer groups.

▶From Clara Bloomfield, member of the NCI Div. of Cancer Treatment Board of Scientific Counselors and head of the Dept. of Medicine, Roswell Park Cancer Institute:

"The members of the [DCT] Board of Scientific Counselors unanimously and emphatically urge that the $210 million Congressional appropriation to the DOD for the study of breast cancer be committed entirely for research of the very highest scientific priority and quality, as determined by peer review.

"We hope that this money can be made available through the established peer-reviewed NIH programs, where its is most likely to be utilized effectively and productively to decrease the incidence of breast cancer and to improve the survival and quality of life of women with this disease."

▶From Lee Wattenberg, president of the American Assn. for Cancer Research:

"AACR is eager to collaborate with [DOD] and would welcome the opportunity to explore with you how our scientific membership could be of assistance... Specifically, we offer the expertise of our researchers involved in basic and applied breast cancer research to work in the program planning and in the peer review of the research that will be supported by these funds."

Earlier last month, the American Society of Clinical Oncology urged an interagency agreement between Defense and NCI (**The Cancer Letter**, Oct. 16).

Breast Cancer Patient Advocate, Radiologist, Added To Commission

A patient advocate and a radiologist will fill two newly created slots on the President's Cancer Panel Special Commission on Breast Cancer.

The patient advocate seat will be filled by Fran Visco, president of the National Breast Cancer Coalition. The name of the radiologist has not been announced. The panel's membership was increased to 19 in response to unrelated protests from NBCC and mammography specialists.

The breast cancer coalition held a protest of a commission meeting earlier this year, demanding additional representation for patient advocates on the panel. The panel is chaired by Nancy Brinker, a patient advocate and a breast cancer survivor, and includes Zora Brown, founder of Cancer Awareness Program Services, a Washington, DC, patient advocacy group.

$3.2 Bil. NCI Bypass Budget Seeks Double Breast Cancer Funds

NCI's bypass budget asks for $448.7 million for breast cancer research, more than double the money sought last year.

Overall, the FY 1994 bypass budget requests $3.2 billion for the Institute, about $400 million above the FY 1993 bypass, and more than $1.2 billion over the current appropriation.

The request for increased funds for breast cancer appears to reflect political pressures that emerged in the 102nd Congress. The largest portion of the increase is a $95.5 million "trans-NIH" breast cancer initiative.

The bypass budget is required by law to be submitted directly to the President (bypassing NIH and HHS) and is supposed to indicate the NCI director's determination of the full funding needs of the National Cancer Program.

"The bypass budget reflects the professional judgement of the Institute and represents a realistic appraisal of the scientific opportunities currently available," NCI Director Samuel Broder wrote in the introduction to the 457-page document.

Even so, the document does appear to respond to political events. Last year's bypass sought $220 million for breast cancer research. During the time the FY94 bypass budget was prepared, a group of politicized breast cancer patients was lobbying Congress for an additional appropriation of $300 million for breast cancer research.

Breast Cancer Initiative

The proposed trans-NIH breast cancer initiative would include:

--Breast cancer research complex: an intramural laboratory to focus on all aspects of breast cancer research in addition to other hormonally sensitive tumors.

--NMR imaging studies: in conjunction with the National Institute of Diabetes and Digestive and Kidney Diseases to improve imaging techniques.

--Basic research and training: to be conducted in collaboration with the National Institute for General Medical Sciences. Research would focus on the abnormalities of molecular behavior at the genetic level.

--Psychosocial and rehabilitation studies: in conjunction with the National Institute of Child Health and Human Development and the National Institute on Aging, to evaluate quality of life in breast cancer patients, breast reconstruction, management in older women and pain management.

--Mastitis and non-malignant breast disease: funds would be provided to NICHD for studies on benign breast disease to develop new treatment and diagnostic methods.

--Environmental carcinogenesis studies: support for R01 grants for collaborative studies between NCI and the National Institute of Environmental Health Sciences on environmental and occupational exposures which may promote development of breast cancer, including pesticides and chemicals, dietary fat and heterocyclic amines generated by various cooking methods.

--Multidisciplinary center for the study of environmental carcinogenesis and occupational risk effects (EnCORE): a new center would be established in conjunction with NIEHS similar to NCI's SPOREs.

--Studies in breast cancer and aging, with increased funding to the National Institute on Aging.

--Breast cancer tumor genetics, in collaboration with the National Center for Human Genome Research.

--Animal models for breast cancer research, in conjunction with the National Center for Research Resources.

NCI proposes that the $95.5 million be available as multi-year funding authority.

The bypass budget cites the National Cancer Act of 1971 and the Public Health Service Act as the authority for NCI to coordinate all NIH activities relating to cancer.

NCI also proposes, with the higher bypass funding, to create additional SPOREs for breast cancer, and add funding to ongoing prevention clinical trials including the tamoxifen trial, dietary fat studies, and other dietary approaches.

Bypass Overview

Other areas emphasized in the bypass document are:

▶NCI participation in the NIH strategic plan--the bypass budget outlines how the Institute is addressing general themes identified in the NIH plan.

▶Multi-year funds availability--$125 million of the bypass request is proposed to be available as a two-year appropriation.

▶Basic research--NCI would fund 50 percent of

1994 Bypass Budget Request

Breast Cancer Research

(dollars in thousands)

	1993 President's Budget	Breast Research Increase: NCI Increase	Breast Research Increase: Collab-orative Efforts	Breast Research Increase: Total Breast	1994 Request	MultiYear Authority Request
Research Project Grants	$72,057	$63,765	$26,000	$89,765	$161,822	
Cancer Centers			4,000	4,000	4,000	
SPOREs	6,000	19,000	5,000	24,000	30,000	$9,000
Subtotal	6,000	19,000	9,000	28,000	34,000	9,000
Other Research:						
Research Career Prog.		1,000		1,000	1,000	
Cancer Education Prog		2,000		2,000	2,000	
Clinical Cooperative Groups	10,987	22,000		22,000	32,987	10,000
Conference Grants	415	250		250	665	
Small Grants	560				560	
Subtotal	11,962	25,250		25,250	37,212	10,000
Total Research Grants	90,019	108,015	35,000	143,015	233,034	19,000
National Research Service Awards		2,500	2,000	4,500	4,500	
R&D Contracts	10,250	19,567	8,000	27,567	37,817	
Intramural Research	17,616	26,687	8,500	35,187	52,803	
Research Management & Support		1,500		1,500	1,500	
Cancer Prevention and Control	18,786	49,731		49,731	68,517	26,000
Construction		30,500	20,000	50,500	50,500	50,500
Total NCI	$136,671	$238,500	$73,500	$312,000	$448,671	$95,500

NIH Organizations in the Collaborative Breast Research Initiative

National Institute of Diabetes and Digestive and Kidney Diseases	$8,000
National Institute of General Medical Sciences	11,000
National Institute of Child Health and Human Development	7,000
National Institute of Environmental Health Sciences	11,000
National Institute on Aging	3,000
National Center for Human Genome Research	7,000
National Center for Research Resources	4,000
NIH Central Resources	22,500
Total	$73,500

* Multiyear authority requested within this Bypass Request level is $125,500, of which $95,500 is for collaborative breast research. Multiyear authority would be used in circumstances where an additional period of availability of funds would allow time to complete negotiations on complex procurements such as a multifaceted construction project.

Source: "NCI 1994 Budget Estimate." Copies are available from the NCI Financial Management Branch, NIH Bldg. 31 Rm 11A18, Bethesda, MD 20892, phone 301/496-5803.

competing research project grant applications and encourage the submission of applications in areas where cancer mortality rate has not improved significantly.

▶Cancer causation, prevention and control--NCI would initiate and expand chemoprevention studies, expand the Community Clinical Oncology Program, extend research on nutrition and dietary effects on cancer with an emphasis on persons over age 65, augment studies of cancer among the underserved and rural populations, construct an intramural cancer prevention research facility, exten activities related to intermediate endpoints for the early detection of cancer and premalignant lesions.

▶Women's health--expand the number of SPORES in specific cancer sites including breast cancer, increase breast, ovarian and cervical cancer research, expand accessibility and delivery of health care to medically underserved women, promote development and availability of new therapies such as taxol, promote the design and development of breast or ovarian cancer vaccines.

▶Prostate cancer--further identify factors than influence onset, detection, progression and management of prostate cancer, intensify research on prostate specific antigen, support prostate cancer research at $128.5 million, of which a portion would be two-year money.

▶Clinical trials--increase the number of patients accrued onto clinical trials to 45,000 with a focus on lung, breast, colon and prostate cancers, women's health, and underserved populations; expand high priority clinical trials including autologous bone marrow transplant for breast cancer; accelerate new trials involving natural products and biological response modifiers.

▶Oncologic imaging--support diagnostic imaging initiatives expanding novel research in the diagnosis, staging and management of cancer.

▶Cancer centers--support new senior leadership positions in comprehensive and clinical centers to focus on research relevant to regional needs; supplement centers for pilot and feasibility studies in high priority research areas, particularly in women and minorities; expand outreach and prevention and control initiatives; fund regional enhancement centers in geographically underrepresented areas; award planning grants; fund 66 core centers (P30 grants) and increase funding to those centers funded below peer recommended levels.

▶Specialized Programs of Research Excellence--expand and support additional SPORES in ovarian, colon, brain cancer, and melanoma.

▶Cancer and poverty--emphasize smoking and tobacco prevention among blacks, Hispanics and Asians, and improve technology transfer to impoverished populations.

▶Natural products--empasize acquisition of natural products.

▶Vaccine development--expand molecular biology and immunology research, solicit investigator-initiated proposals, and develop clinical trials of vaccine based primary and secondary prevention and treatment.

▶Construction--Use two-year money to begin renovation, modernization and construction of extramural cancer research facilities, with emphasis on facilities for breast cancer, vaccine development and prevention research, and high technology; provide $20 million for construction of proton beam or other heavy particle therapy facility.

▶Information dissemination--increase activities for underserved populations and expand the Cancer Information Service.

▶Rehabilitation and pain research--expand activities to promote quality of life, increase emphasis on behavioral and psychosocial aspects of cancer rehabilitiation, and support new research in pain management.

▶Over 65 population--expand efforts to determine survival/mortality differentials in persons over age 65.

▶Gene therapy--expand preclinical and clinical initiatives.

▶AIDS--NCI requests $225 million for AIDS research to expand identification of new active compounds, develop antiretroviral drugs, support studies to determine mechanisms of pathogenesis for AIDS related malignancies and develop treatment clinical trials, expand studies of cervical cancer in HIV infected women, and increase support for AIDS vaccine studies.

▶Human resource professional development--increase number of trainees in the National Research Service Award program by 50 percent, continue the Summer Science Enrichment Program, expand education programs on pain research, rehabilitation, psychosocial issues and community outreach, expand research career programs (K12 awards), expand intramural research training programs.

RFPs Available

Requests for proposals described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Executive Plaza South room number shown, National Cancer Institute, Bethesda MD 20892. Proposals may be hand delivered to the Executive Plaza South Building, 6130 Executive Blvd., Rockville MD.

RFP NIH-NIAID-DAIDS-93-15
Title: Core immunology laboratory for assessment of AIDS vaccines in primates
Deadline: Approximately Jan. 5

The National Institute of Allergy & Infectious Diseases has a requirement to provide for the centralized performance of immunological assays to support preclinical AIDS vaccine trials in primates. The purpose of this contract is to support the NIAID in its mission to stimulate research towards discovery and testing of prototype vaccines for AIDS. NIAID requires a primate core immunology laboratory to assay specimens from macaques, chimpanzees, or other primates for humoral and cellular immune responses induced by immunization with prototype Simian Immunodeficiency Virus and HIV vaccines. This effort will support the research of AIDS investigators, including three SIV vaccine evaluation units, a chimpanzee unit, the National Cooperative Vaccine Evaluation Group, the AIDS Vaccine Evaluation Group, and other programs initiated by NIAID.

Specifically, the selected contractor will be responsible for: 1) performing specific evaluations of cellular immune responses induced by vaccination, 2) performing specific evaluations of humoral immune responses induced by vaccination, 3) adapting, standardizing, providing quality assurance, and performing any newly developed immunological assays that may be identified during the period of the contract as offering potential for assessment of vaccine safety and immunogenicity, 4) receiving, cataloging, tracking, and maintaining an inventory of the specimens arriving for evaluation, and 5) maintaining test result database and transferring data to the AIDS Vaccine Clinical Trials Network data coordinating and analysis center.
Contract specialist: Kristi Hofacker, NIAID, Solar Bldg. Rm 3C07, 6003 Executive Blvd., Bethesda, MD 20892.

RFA Available

RFA CA-93-02
Title: **The regulation, function and specificity of proteins induced in mammalian cells exposed to ionizing radiation**
Letter of Intent Receipt Date: Dec. 10
Application Receipt Date: Feb. 10

NCI's Div. of Cancer Etiology invites grant applications from inteested investigators through the announcement of an RFA for studies of the function and regulation of expression of proteins differentially expressed in mammalian cells exposed to ionizing radiation. The focus of this initiative is the molecular discription of the function and regulation of radiation modulated proteins formed in mammalian cells in response to ionizing radiation. The RFA will emphasize direct analysis of the genes and gene products associated with ionizing irradiation of mammalian cells.

Applications may be submitted by domestic and foreign for profit and nonprofit institutions, public and private. Approximately six grants will be funded, with total program costs not to exceed $1 million for the first year. This RFA will permit a wide range of research activities, including, but not limited to:

--Studies to determine the biochemical and molecular functions carried out by the uncharacterized RMPs, to relate them to porrly understood radiologic endpoints in mammalian cells such as radiation induced arrest of the cell cycle, repair of radiation damaged DNA, radiation induced mutagenesis, transformation, and cell survival.

--Research to identify the radiogenic lesions that trigger the differential expression of the uncharacterized RMPs.

--Analysis of the genetic organization of the uncharacterized RMP structural genes and the mechanisms of regulation that govern their expression.

--Determination of the effects of radiation quality on differential expression of the uncharacterized RMPs, specifically on the efficacy of high LET radiation should be compared with low LET radiation for inducing the uncharacterized RMPs.

Inquiries and letter of intent should be directed to: Dr. Richard Pelroy, Radiation Effects Branch, NCI Executive Plaza North Suite 530, Bethesda, MD 20892, phone 301/496-9326; fax 301/496-1224.

RFA AI-92-15
Title: **National cooperative drug discovery groups for the treatment of opportunistic infections associated with AIDS**
Letter of Intent Receipt Date: Jan. 15
Application Receipt Date: March 10

The purpose of this RFA is to invite applications aimed at the discovery of new, more effective, selective, and diverse therapeutic agents to treat AIDS-associated opportunistic infections caused by Mycobacterium tuberculosis, Mycobacterium avium, Cryptosporidium parvum, Toxoplasma gondii, Cryptococcus neoformans, Pneumocystis carinii, and Candida albicans. Applications that include research projects or core components from the private sector (e.g., pharmaceutical, chemical, or biotechnological companies) are encouraged.

Research in the following areas is needed to provide the foundation for improvements in therapeutics for the OIs: selective drug targeting; unique metabolic activities for drug targeting; structure-function properties of microbial proteins; biochemistry and molecular mechanisms of OI-host interactions; improved culture methods for conducting metabolic studies on parasite-host interactions; inhibitors of enzymatic and regulatory functions, and of biochemical pathways; mechanisms of drug resistance; and discovery and biochemical characterization of promising natural products or synthetic chemical compounds.

Applications may be submitted by domestic and foreign for profit and nonprofit organizations, public and private. Awards will be made as Cooperative Agreements (U01s). The applicant institution will provide a Central Operations Office for the Group.

NIAID has set aside $3.5 million for the initial year's funding of this RFA. Five to seven awards anticipated. No more than one Group each will be funded for drug discovery against M. tuberculosis, T. gondii, P. carinii, C. parvum, M. avium, C. neoformans, and C. albicans. Applications focusing on C. albicans must study novel drug targets; further study of triazoles or polyene antibiotics will not be supported. Awards are subject to a first year limit of $650,000 in total costs (direct plus indirect costs). Subsequent years will be funded at a level no greater than the first year plus four percent. Funding duration will be three years for new applications and up to four years for competitive renewal applications.

The goals of the National Cooperative Drug Discovery Groups for the Treatment of Opportunistic Infections are:

--The conceptualization, discovery, and preclinical development of drugs and strategies designed to effectively treat OIs in individuals infected with HIV.

--The conduct of biological, biochemical, and pharmacological studies leading to selection of potential therapies.

--The recommendation of therapies, entities or strategies for development in clinical trials.

Seven NCDDG-OIs were awarded in 1990, four were awarded in 1991, and four more are anticipated to be awarded in 1992. Five Groups are eligible for re-competition under this RFA.

Research should be directed toward discovery and preclinical evaluation of new entities with potential to control infections caused by the pathogens listed previously. It is not a requirement of this RFA that a complete development plan for new drugs be included, although applications which include research projects or core components from the private sector are encouraged. Projects focusing on the early phases of new drug target identification are appropriate. However, each application must clearly state in an introductory section how information from the proposed projects will directly accelerate new drug discovery and what therapeutic approaches are likely to ultimately derive from these studies. Priority will be given to therapies with potential for prophylaxis, practical administration to AIDS patients, and low toxicity.

Inquiries and letter of intent may be directed to: Dr. Barbara Laughon, Developmental Therapeutics Branch, National Institute of Allergy and Infectious Diseases, Solar Building, Room 2C10, Bethesda, MD 20892, phone 301/496-8197, fax 301/402-3211.