THE CANCER LETTER

P.O. Box 2370 Reston, Virginia 22090 Telephone 703-620-4646

Vol. 15 No. 15

April 14, 1989

Price $185 Per Year North America
$200 Per Year Elsewhere

Cullen To Leave NCI, Will Become Director Of AMC Cancer Center; Nixon May Join ACS

The exodus of many of NCI's "best and brightest" continues. Joseph Cullen, deputy director of the Div. of Cancer Prevention & Control who has led the federal government's highly successful antitobacco campaign, will

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In Brief

Survivors Day Scheduled For April 30; Miami Center Name Changed; NCI's Adamson Honored

NATIONAL CANCER Survivors Day is scheduled for April 30. This will be the second annual observance of the day, which is cosponsored by the American Cancer Society and "Coping" magazine. Typical of programs to be held around the country will be an event at Ohio State Univ. Hospitals featuring Ivy Gunter, model and TV personality who resumed her career after losing a leg to cancer; John Minton, professor of surgery at OSU and president of the ACS Ohio Div.; David Schuller, director of OSU's Arthur G. James Cancer Hospital & Research Institute; and James, professor emeritus of surgery at the university. . . . **SYLVESTER COMPREHENSIVE** Cancer Center is the new name of the cancer center at the Univ. of Miami. Formerly the Papanicolaou Comprehensive Cancer Center, the new name recognizes the "historic gift of $32.5 million from the Sylvester Foundation" to the center, according to Gordon Zubrod, director emeritus. Nathaniel Berlin continues to serve as acting director while a search continues for a permanent replacement for Zubrod, who retired as director last year. . . **RICHARD ADAMSON**, director of NCI's Div. of Cancer Etiology, received the Arnold J. Lehman Award from the Society of Toxicology at that organization's recent annual meeting. The award went to Adamson "for his multidisciplinary research and management skills which have contributed to the application of sound scientific principles in regulatory activities". . . . **RICHARD GELB**, chairman and CEO of Bristol-Myers Co., has received the Distinguished Service Award from the Yale Comprehensive Cancer Center. The award honors individuals who are not scientists but whose accomplishments have made a major impact in cancer research and care in Connecticut. . . . **DOUGLAS ARMSTRONG** has been elected vice president for scientific liaison of the La Jolla Cancer Research Foundation. He has been serving as the Foundation's administrator since joining the organization in 1987.

Cullen To Become Director Of AMC Cancer Center; Nixon May Join ACS

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leave within two to three months to become director of AMC Cancer Research Center in Denver.

Cullen has been Peter Greenwald's deputy since 1981, his second tour at NCI. He had previously worked there during the 1970s, participating in the early development of the Cancer Control Program.

In what would be another major loss to DCPC, Daniel Nixon, associate director and director of the Cancer Prevention Research Program, probably will be named vice president for professional education of the American Cancer Society. He would replace Diane Fink, who is now with the ACS California Div. as vice president for cancer control and professional services.

Nixon is a Georgian and would be returning to Atlanta, where he was with Emory Univ. for 13 years before joining NCI. He told **The Cancer Letter** this week that he is "98 percent certain" he will accept the ACS offer, but that details had not yet been worked out with the Society.

Nixon's departure would leave Greenwald with three of his four associate director positions in the newly reorganized division either vacant or being filled on an acting basis. Donald Fox is acting director of the Centers & Community Oncology Program, and Edward Sondik is acting director of the Cancer Control Science Program. Sondik is also technically "acting" director of the Surveillance Program, but his permanent appointment to that job is virtually assured. He has been chief of the Operations Research Branch, was melded into the newly created Surveillance Program.

Greenwald, lamenting the loss of two more of his top people, blamed government salaries at least in part. "The pay situation is really hurting NIH," he told **The Cancer Letter**. "It is crucially important that the medical retention bonus include people in prevention." The bonus is available to MDs in some subspecialties (nothing resembling prevention), but not to PhDs.

Cullen is a PhD but probably would not have passed up the AMC offer even if the 50 percent pay raise had not died in Congress. "I've always wanted to be a center director," he said. "AMC has an opportunity to become a model cancer prevention and control center. People there have the right attitude and we've been promised the support we need."

Cullen will replace Marvin Rich, AMC director since his predecessor, Solomon Garb, died in 1982. **The Cancer Letter** was unable to obtain a comment from AMC officials by press time this week on why Rich left, nor was the newsletter able to locate Rich.

Cullen said that "Marvin built a superb basic science facility there. I hope we can take that very good basic science group and build a cancer control program around it."

Between his stints at NCI, Cullen developed the cancer control program at the UCLA Jonnson Comprehensive Cancer Center.

Cullen has headed NCI's antitobacco activities, most of which are managed by DCPC. He also has served as the Dept. of Health & Human Services' coordinator for smoking and tobacco programs, and was instrumental in work that led to actions based on effects of smokeless tobacco and passive smoking.

Cullen declines to take credit for all the progress achieved in the past few years. But it was during his watch that smoking was banned from most federal buildings; new and stronger warning labels were required for tobacco products, including smokeless tobacco; limits were placed on smoking aboard commercial airlines; the federal cigarette tax was doubled; state and local government enacted anti-smoking laws in increasing numbers and some levied stiff new tobacco taxes; and the percentage of American adults who smoke dropped from just under 40 to less than 28, and is still dropping. He planned and initiated major smoking cessation and education projects, including the latest one known as ASSIST, which he feels will deliver the most solid blow yet to smoking incidence in the U.S.

"Joe made a tremendously valuable contribution to cancer research," Greenwald said. "He

THE CANCER LETTER
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Published forty-eight times a year by The Cancer Letter, Inc., also publisher of The Clinical Cancer Letter and AIDS update.

has headed the best smoking research program ever undertaken."

Cullen is confident that program will continue its momentum. "We have a superb team. I have no concerns that the accomplishments will continue. I wouldn't leave if I thought otherwise." He credited the strong commitment and support from Greenwald, NCI Director Samuel Broder and former Director Vincent DeVita for much of the program's success.

Government pay was a significant factor in Nixon's decision to look elsewhere. "I might have stayed if the raise had gone through," he said. That was not the only factor, however.

"The hiring freeze has crippled new programs. That and budget restrictions have been generally frustrating." Nixon joined NCI in 1987 and had planned to stay longer. "We built a house and put down roots," but the frustrations became too much to contend with.

The ACS position will give Nixon the opportunity to work with physicians and other health professionals in advancing early detection and prevention activities, he said.

Painkillers Not Given Often Enough, Neuro-Oncologist Tells ACS Seminar

Many cancer patients needlessly suffer pain because their physicians refuse to prescribe enough narcotics out of fear of interference from regulatory agencies or that patients will become addicts, according to a pain specialist at M.D. Anderson Cancer Center in Houston.

Physicians need better training in the treatment of pain and state regulations need to be changed for this "opiophobia" to be overcome, said Stratton Hill, director of pain service in the Dept. of Neuro-Oncology at M.D. Anderson. Hill spoke at the annual Science Writers' Seminar, sponsored by the American Cancer Society, held in Irvine, CA, earlier this month.

Hill's was one of 34 presentations on a variety of studies selected by ACS for the conference. Nearly 50 science writers were in attendance.

The presentations ranged from a Swedish scientist's use of electricity for cancer treatment to the discovery of a fatty acid in beef that appears to inhibit carcinogenesis in mice.

There was research on a new method of predicting breast cancer risk, autologous bone marrow transplantation, use of colony stimulating factors, psychological aspects of cancer therapy, three presentations from NCI intramural scientists on their ongoing work and a biotechnology company's method of turning tobacco plants into factories for interferon, interleukin-2 or other products.

Treatment of Pain

Hill, who has been at M.D. Anderson since 1963, charged that despite the wide availability of pain relief medication, a large number of cancer patients are inadequately treated.

"This is especially true in the patient with advanced cancer in whom the pain is diffuse, and the cause of pain cannot be removed or otherwise treated," Hill wrote in a paper presented at the seminar.

"In spite of an adequate array of narcotics available, capable of providing optimum analgesia for these patients, only a minority of them receive adequate pain relief."

Hill's comments drew support from other seminar participants, including Benjamin Byrd, clinical professor of surgery at Vanderbilt Medical School. Byrd noted that 23 physicians in Tennessee recently had their licenses suspended, allegedly for the improper use of drugs.

"Even if the physicians are proven innocent of wrongdoing, there is a great deal of expense involved in the defense, and the negative effect of publicity resulting in possible loss of patients," Byrd said. For this reason, physicians view regulatory agencies with alarm, he said.

Hill said the inadequate treatment of pain is the result of three factors:

--Cultural and societal pressures that influence the physician's and patient's concepts about pain and narcotics.

--Physicians' lack of knowledge about pain, narcotics and their side effects.

--Fear of action by state and federal drug regulatory agencies which may result in loss of license.

"It has been suggested that physicians have become phobic about the use of narcotics," Hill said. "Treatment of phobias often defy rational therapy. Small, almost one on one, sessions will probably be required to change these attitudes and concepts."

A common problem, Hill said, is the practice of prescribing a dose of narcotic inadequate to effectively relieve the pain, and for a time interval that exceeds the duration of action for the drug.

"The inadequately relieved patient then becomes a 'clock watcher' waiting in eager

anticipation for the next dose, which at least will give some modicum of additional relief."

However, the "clock watcher" is in danger of being labeled a drug addict by physicians, Hill said.

"The culture fails to distinguish between a patient who has a legitimate need for the pain relieving, or other pharmacological action of a narcotic, and an individual who takes narcotics for recreational purposes and ultimately becomes a drug abuser."

Laws intended to keep drugs out of the possession of drug abusers reflect this lack of distinction, Hill said.

"In essence, narcotic treatment of pain is often suspected of being a criminal activity. Any action on the part of the patient which seems to the observer to be atypical becomes suspect, and often he or she will be treated as a drug abuser, and access to narcotics will be very restricted and therefore inadequate for pain relief."

Medical training does little to educate physicians about pain, Hill said. "Pain is perceived simplistically as a single entity, easily controlled by narcotics.

"Narcotics, however, are perceived as 'bad,' no matter what the reason for their use, therefore they should be used in doses as small as possible for as short a period as possible."

Too often, narcotics are reserved for pain relief "as close to death as possible," Hill said. Patients may suffer for long periods before physicians consider them terminal, justifying the use of narcotics.

Physicians learn little about the difference between acute pain in a patient with an intact nervous system and chronic pain in a patient with a damaged nervous system. Acute pain responds in a predictable manner to narcotics, while chronic pain often does not, Hill said.

"Failure to appreciate this leads to frustration on the part of the physician, who may then classify the patient as a drug seeker or abuser," Hill said.

Many physicians have been under the belief that small doses of a narcotic such as morphine can be injected, but that large doses of morphine are dangerous due to respiratory depression and possibility of addiction.

According to Hill, recent studies of cancer patients in pain have found that belief to be mistaken.

"These studies show the pharmacology to be different in two major aspects: respiratory depression and their addictive potential. In the first instance, patients who become tolerant to the analgesic action also become extremely tolerant to the respiratory depressant effect.

"However, many patients in pain are given inadequate doses of narcotics because of fear of causing respiratory depression."

Hill said he had given cancer patients doses of morphine as high as 400 mg. The usual dose for a morphine injection to control severe pain in cancer patients is 10 to 15 mg.

"No dose is too large for a patient who is increasingly tolerant" to the medication, he said.

Since the patient's interest in the drug subsides as soon as he or she is adequately relieved of pain, addiction "is of no consequence to these patients," Hill said.

A major factor in treatment of pain is that physicians are not familiar with regulations on the medical uses of narcotics, Hill said. As a result, they are fearful and overly cautious.

But state regulatory agencies often set arbitrary parameters to judge a practitioner's actions.

"Some boards have simply stated that a certain practitioner is prescribing 'too many' of a particular narcotic without regard to the diagnosis," Hill said. "Regulatory agencies can have a chilling effect on the practitioner."

Seven states require physicians to file triplicate or multiple prescription forms when prescribing narcotics, Hill said.

In California, for example, those forms must be issued to each physician. One copy is given to the pharmacist, one is for the physician's records and the third is for the state narcotics agents.

At least 30 percent of the state's physicians do not bother to keep the forms on hand, Hill said.

Sen. Daniel Inouye (D-HI) has introduced legislation in Congress that would legalize heroin for the treatment of pain in patients with terminal diseases.

But Hill said making the drug available would do little to change the way patients are treated.

"We could make heroin legal, but physicians wouldn't use it because they would be afraid of it," he said.

What is needed, Hill said, is change in state laws to give doctors more flexibility in prescribing narcotics without fear they will be targeted for investigation.

In addition, more effective education for physicians in the use of narcotics for pain relief is needed, Hill said.

Electrical Treatment Described

Another provocative presentation came from Bjorn Nordenstrom, professor emeritus of radiology at the Karolinska Institute in Stockholm. For the past 25 years, Nordenstrom has used electricity to treat patients with far advanced metastatic lung cancer.

Nordenstrom's work is "backed up by solid research," said Gerald Murphy, chief medical officer of ACS. "He has a theory and wants to apply it," but has had trouble getting ethics committees at his institute and other institutions to approve any protocols.

The electrical treatment, which Nordenstrom tested first in animals and then on patients whose cancers were inoperable or far advanced, involves placing a positive electrode in the main tumor and a negative electrode at some point outside the tumor.

An electric current is created, up to about 20 volts. In some cases the electrodes are kept in place for two to three hours. The tumor and any healthy tissue around the positive electrode is destroyed, Nordenstrom said.

As with surgery, the tumor must be able to be imaged before the treatment takes place, and 100 percent of the tumor is destroyed. However, the method destroys less healthy tissue than surgery, Nordenstrom said.

Around the negative electrode, a series of electrochemical changes take place which destroys some metastases, creating a secondary field effect.

Nordenstrom showed slides of a dog's lung before and after the treatment, demonstrating that the main tumor and the secondary metastases were cleared.

Nordenstrom said that out of 100 patients he has treated, two are in good health 10 years after treatment. One patient, now 29, had four lung tumors and had failed chemotherapy.

After treating the patient using the electrode method, all four tumors disappeared completely and the patient is in good health now, Nordenstrom said.

Other patients have shown regression of treated cancers, but died from nontreated tumors or metastases.

One patient, an older woman who could not be operated on due to age and a heart infraction, had two lung tumors which Nordenstrom treated.

Five years later, the tumors still had not relapsed. However, the cancer metastasized to the brain and the patient died.

"The method is not ideal, but it can be improved," Nordenstrom said. "I need other material to work with."

In 10 years, he said he has had three serious complications in patients as a result of the treatment, including one temporary heart arrest. He said that was due to a mistake he made in placing an electrode too close to the heart.

Nordenstrom said he recently has begun using adriamycin in combination with the electrical treatment since the drug is electropositively charged and can be accumulated in the cancerous tissue by electrophoresis.

He theorized that through this method, any cancer cell within the electrical field created could be killed.

Nordenstrom said he approached a U.S. institute, which he would not name, to conduct a protocol using the treatment. He proposed that the study involve two groups of patients with any type of localized tumor. The control group would get whatever treatment they were recommended to receive. The test group would be pretreated with the electrical method and then get their recommended treatment. The institute turned down the study.

"People are afraid of doing new things," Nordenstrom said. He said researchers in Italy, Japan and Great Britain were doing clinical studies with the treatment.

Fatty Acids In Beef, Cheese

A food researcher presented findings that he said showed that a substance found in fatty meats and cheeses protects mice against cancer.

The substance, conjugated linoleic acid, counteracts the damage made by rare forms of oxygen in cells, said Michael Pariza, director of the Food Research Institute at the Univ. of Washington. The results of the study "came as a complete surprise to us," he said.

Although CLA was discovered in milk about 20 years ago, Pariza said he and his colleagues discovered the substance in grilled ground beef about three years ago.

Unpurified CLA was found to prevent skin cancer in mice. More recently, the researchers purified the CLA and identified it as a mixture of fatty acid isomers, all derived from linoleic acid.

CLA has a molecular structure that attracts and holds free oxygen radicals, which have been thought to assist in the initiation of cancers, arthritis, heart disease and aging.

Since CLA, as a fatty acid, is incorporated into every cell in the body, it may be able to

act in situ to protect the cell's genome from attack. It may also be possible to develop anticancer drugs that are absorbed into cell membranes using CLA, Pariza said.

However, Pariza emphasized that it is far too early to make dietary recommendations based on the findings. Rather, the amount of cooked beef fed to mice was so high that people could harm themselves trying to eat enough beef to obtain any benefit from CLA.

The researchers conducted several experiments in which mice were given the substance by stomach tube four and two days before the administration of a carcinogen, benzopyrene. The cycle was repeated each week for four weeks. After 20 weeks, the mice were sacrificed.

The amount of CLA administered to each mouse was equivalent to that present in about two pounds of cooked beef, Pariza said.

In each experiment, the mice treated with CLA developed significantly fewer neoplasms than the control animals, which received only the carcinogen.

In the latest trial, the control mice developed an average of five neoplasms each, while the CLA treated mice developed less than two neoplasms each.

Pariza's research was financed by NCI and the Wisconsin Milk Marketing Board.

Mammographic Densities

A study presented by Audrey Saftlas, of the Epidemic Intelligence Service of the Centers for Disease Control, found a new method predict breast cancer risk by measuring the mammographic density of breast tissue.

Previous studies have shown that Detroit radiologist John Wolfe's classification of mammographic parenchymal patterns are indicators of breast cancer risk. But that method is difficult and differences in tissue can be "very subtle," Saftlas said. Wolfe was a participant in this study.

This method would make it easier for radiologists to identify women at risk than the Wolfe method, Saftlas said. It requires only brief training.

Under the new method, the radiologist only has to measure the percentage of dense breast tissue, not the type of density that is present.

The study evaluated mammograms from 266 subjects who had been diagnosed with breast cancer and 301 controls with no cancer diagnosis involved in the Breast Cancer Detection and Demonstration Project, a five year screening program sponsored by ACS and NCI.

The study found that breast cancer risk increased steadily with increasing breast density. Women who had 65 percent or greater mammographic densities had the highest risk, while women with densities less than 5 percent had the lowest risk.

"We suggest that physicians consider the percentage of mammographic densities in combination with other breast cancer risk factors to identify high risk subgroups of women in need of more intensive screening," Saftlas said.

Three NCI researchers presented data from their recent studies. They were Charles Evans, chief of the Tumor Biology Section; Michael Blaese, deputy chief of the Metabolism Branch; and David Segal, senior investigator in the Experimental Immunology Branch.

Evans reported on his ongoing research of leukoregulin, a lymphokine discovered in his laboratory in 1984. Leukoregulin or its future derivatives could be important pharmacologic agents for increasing the tumor killing ability of conventional drugs or other new biological agents, Evans said.

In the past year, the lab has developed the elucidation of transmembrane signals accompanying leukoregulin induced sensitization of the target cell to natural killer and lymphocyte activated killer cell cytotoxicity. Within one minute after introducing leukoregulin, the tumor cell's ionic calcium increases five to 10 fold, Evans said. In vitro, the introduction of leukoregulin has increased destructive ability of NK and LAK cells by two to 10 fold.

One stumbling point in the study of leukoregulin, Evans said, is that its gene has not yet been cloned. Until it can be cloned, there will not be enough of the agent available to do patient studies.

Blaese gave an update on the potential of gene therapy for cancer treatment, describing animal and patient studies using T lymphocytes and tumor infiltrating lymphocytes.

"The potential of gene insertion for the treatment of a wide variety of diseases is only now beginning to be realized," Blaese said. "We hope our experiments with TIL will help speed the use of the power of genetic engineering to benefit all areas of clinical medicine."

Segal reported on the potential role of targeted immune effector cells. Studies are underway using immunodeficient mice to determine the best way of treating a growing tumor in vivo with targeted cytotoxic cells, Segal said.

Other studies the laboratory has done have found that targeted human cytotoxic cells, when injected with human tumor cells into mice, are "highly competent" at blocking the growth of the tumor, he said.

"Although the in vivo mouse studies are promising, there are many studies to be done to determine which types of targeted cells and what modes of activation will result in the most effective antitumor therapy," Segal said.

Segal said that there are two clinical studies, one in Japan and one that is to begin soon in the Netherlands, using the targeted cells.

The Japanese study is using the method to treat glioma, and the Netherlands study will treat ovarian cancer.

In those studies, the tumors will be removed and targeted lymphocytes from the blood of the patients will be injected back into the tumor site.

A Good Use For Tobacco?

The president of a California based biotechnology company said his company has developed a way to use tobacco plants as factories to produce other products, even anticancer agents.

Robert Erwin, president of Biosource Genetics Corp., based in Vacaville, CA, said researchers from the company have developed a transient gene vector that can be sprayed on fully grown tobacco plants to convert them to "minifactories" producing immune system stimulants.

The method could be used to produce such agents as interferon, interleukin-2, tumor necrosis factor, sun blocking agents such as melanin, or any other agent that can now be produced by genetic engineering methods, he said.

The product can be harvested from the plants' leaves.

Vincent DeVita, physician in chief at Memorial Sloan-Kettering Cancer Center and former NCI director, said the irony of using tobacco plants to fight cancer is "kind of cute" and an "interesting idea" that should be pursued.

Erwin said the vector, an artificial plant virus, was made by combining genes from several plant viruses. The gene that is the blueprint for the desired product is then inserted into the virus. The virus is enveloped into a synthetic protein coat.

The virus enters the plant through cuts or abrasions on the plants leaves. The virus spreads within the plant, but it cannot escape to infect other plants because it cannot produce the protein coat.

The virus does not permanently change the plant's own genetic information, it only takes over the plant to produce large quantities of whatever protein for which it carries the gene, for example, interleukin-2.

The company will apply for a patent on the virus soon, Erwin said. If the method could be proven to be cost effective, it would provide an alternative source of income for tobacco farmers besides selling their crops to cigarette manufacturers.

The demand for other products also could drive up the price of tobacco, and, possibly, the cost of cigarettes.

The privately held company hopes to collaborate with other firms in licensing the virus for further studies of its potential, Erwin said.

He said that the company could field test the method within the next 12 months.

Other products that could be produced include industrial enzymes, or starches for use in cosmetics or food.

In another presentation, John Black, a senior scientist at Roswell Park Memorial Institute, proposed that fish be used as "sentinel animals" to detect cancer causing chemicals in the environment.

Epidemics of liver and skin cancer have been found among fish in areas where the bottom sediments are heavily contaminated with organic chemicals, some of which are suspected human carcinogens.

"Fish may have the capacity to warn man of unsuspected hazards," Black said.

Since fish are prisoners of their environment, "in some cases it may be possible to document the complex history of their environmental exposure by examining their tissues for the presence of carcinogens."

In addition, fish may provide less expensive alternatives to rats and mice for testing chemicals, Black said.

Small species can be raised in a simple, inexpensive aquarium. Cancers can be induced in relatively short amounts of time, using very small amounts of chemical carcinogens.

However, more data is needed on the similarities and differences between cancer in fish and that in humans, Black said.

Other studies presented at the seminar will be included in the April issue of **The Clinical Cancer Letter.**

RFAs Available

RFA 89-CA-12
Title: Therapeutic correlates of drug resistance
Letter of intent receipt date: May 15
Application receipt date: July 12

NCI's Div. of Cancer Treatment invites grant applications for a tightly focused, integrated research program at the interface of laboratory experimentation and concurrent clinical trials involving the correlation of drug resistance to clinical response and development of clinical treatment to overcome acquired drug resistance.

A formidable obstacle in cancer therapeutics is the emergence and growth of treatment resistant tumor cells. Recent research efforts concerning this phenomenon have utilized in vitro systems to elucidate the molecular and cellular mechanisms operative in resistance to chemotherapy. These efforts have resulted in the determination of a number of genotypic and phenotypic alterations which appear to correlate with the development of drug resistance in tumor cells.

However, while there is a substantial amount of ongoing basic research there are relatively few current studies which will determine the clinical relevance of laboratory assays for drug resistance. Research directed at correlating the results of laboratory assays of drug resistance with results of clinical trials is an essential step in the development of effective regimens of cancer therapeutics. In defining the mechanisms of drug resistance, preclinical studies have resulted in the development of therapeutic strategies to overcome acquired clinical drug resistance. These new approaches need to be tested in the clinic and their efficacy correlated to laboratory measures of drug resistance.

The major focus of this RFA is to stimulate clinical trials using new therapeutic strategies to overcome or reverse acquired drug resistance. Studies should be proposed for an integrated research program of laboratory experimentation and concurrent clinical trials involving therapeutic correlates of drug resistance. Studies should be proposed for a clinical trial of antitumor agents which include obtaining malignant tissue to be assessed using measures of drug resistance. Drug resistance assays should include a correlate other than dose responsiveness to the drug in question. Data from the laboratory should be collected to permit statistical analysis so that the measure of drug resistance can be correlated with clinical outcome. Location of the assay laboratory and the target patient population for clinical trials may be at different/multiple institutions.

Examples of potential studies which would be appropriate for this RFA include:

A. A clinical trial which measures drug resistance of human tumor samples obtained prior to treatment and at the time of recurrence or progressive disease in those same patients.

B. A clinical trial involving studies of patients whose tumors are assessed in the laboratory as being drug resistant, and whose treatment includes a specific strategy directed at overcoming or reversing clinical drug resistance. Studies that are directed towards dose intensification or replacement by noncross resistant drugs are not the focus of this RFA.

This program will be supported through traditional research grants. Awards may be made to public, private nonprofit and for profit organizations. Approximately $1.5 million in first year total costs will be committed to specifically fund applications which are submitted in response to this RFA. NCI plans to make multiple awards for project periods up to five years. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. The earliest feasible start date for the initial awards will be April 1, 1990.

Copies of the complete RFA may be obtained from and written or telephoned inquiries directed to Diane Bronzert, Program Director, Cancer Therapy Evaluation Program, DCT, NCI, Executive Plaza North Rm 734, Bethesda, MD 20892, phone 301/496-8866.

Prospective applicants are asked to submit letters of intent which include a descriptive title of the proposed research, name and address of the principal investigator, names of other key personnel, participating institutions, and the number and title of the RFA. The letter of intent is requested in order to provide an indication of the number and scope of applications to be reviewed. The letter of intent does not commit the sender to submit an application, nor is it a requirement for submission of an application. Letters of intent should be directed to Bronzert at the above address.

RFPs Available

Requests for proposals described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Executive Plaza South room number shown, National Cancer Institute, NIH, Bethesda, MD 20892. Proposals may be hand delivered to the Executive Plaza South, 6130 Executive Blvd., Rockville, MD. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CP-95617-61
Title: Development and purification of peptides, oligodeoxynecleotides and monoclonal and polyclonal antibodies
Deadline: Approximately April 19

NCI is interested in receiving proposals from contractors who can develop, purify and provide 100-299 samples of purified synthetic peptides per year; 100-150 samples of synthetic oligodeoxynucleotides per year while supplying 1-5 mg of each of the purified synthetic oligodeoxynucleotides; and monoclonal and polyclonal antibodies against selected synthetic peptides or other proteins.

A three year award is anticipated. This will be a 100 percent small business set aside.
Contract Specialist: Charles Jackson
RCB Executive Plaza South Rm 620
301/496-8611

Program Announcement

Cancer Education Program (R25)

The next application receipt dates for the Cancer Education Program (R25) will be Oct. 1 for new applications and Nov. 1 for renewal applications. The June and July 1989 receipt dates will be skipped; therefor, any applications received on those dates will be deferred to the next cycle.

The timetable for all these applications will be as follows: initial review for scientific merit, February 1990; second level review by the National Cancer Advisory Board, May 1990.

Information on the program may be obtained from Dr. Robert Adams, Cancer Training Branch, Div. of Cancer Prevention & Control, NCI, Bethesda, MD 20892, phone 301/496-8580.

NCI Contract Awards

Title: Preparation of radiolabeled materials
Contractor: Research Triangle Institute, $1,931,081

Title: Radiotherapy treatment planning tools
Contractor: Washington Univ., $1,524,689