THE CANCER LETTER

Vol. 16 No. 12
March 23, 1990


Price $195 Per Year US, Canada
$220 Per Year Elsewhere

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

## Flat Centers Budget Irks House Subcommittee; Porter Repeats Call For Funding Bypass Budget

Members of the House Labor, HHS, Education Appropriations Subcommittee sharply questioned NCI Director Samuel Broder about the nearly flat funding for the cancer centers in the President's FY 1991 budget, which Broder was compelled to defend until asked for his "professional opinion." The line of questioning at the subcommittee's

(Continued to page 2)

*In Brief*

## Monaco, Yarbro Named To Pharmacopeial Board; Gene Therapy Trial For ADA Clears First Hurdle

**KEY ADDITIONS** to the U.S. Pharmacopeial Convention: **Grace Monaco**, Washington D.C. attorney, elected to a five year term on the Board of Trustees; and **John Yarbro**, Univ. of Missouri (Columbia) professor of oncology, elected to a five year term on the Committee on Revisions. Monaco, a founder and chairman of the Candlelighters, specializes in health care reimbursement issues and is president of Emprise Inc., a health education company. Yarbro is the only oncologist at the Committee on Revisions and chairs the panel on hematologic and neoplastic disease. The committee is charged with annually updating the USPDI, the primary source of drug information for physicians, which also plays a key role in determining third party reimbursement. Yarbro takes over the oncology seat from **B.J. Kennedy**, who held the position for years. Among others elected to the Board of Trustees was **Richard Crout**, former director of what was at that time FDA's Bureau of Drugs, now vice president of Boehringer Mannheim Pharmaceuticals. . . . **NIH INSTITUTIONAL** Biosafety Committee has approved a joint NCI/National Heart, Lung & Blood Institute study to treat children suffering from adenosine deaminase deficiency with gene therapy. The study now faces six more federal regulatory panels. In the proposed trial, French Anderson of NHLBI and Michael Blaese of NCI plan to correct the deficiency by inserting a human gene for the ADA enzyme into a mouse retrovirus, which infects the patient's cultured T cells. The cells are transfered back into the patient. The Human Gene Therapy Subcommittee, part of the Recombinant DNA Advisory Committee, will consider the proposal March 30. . . . **TWO YOUNG** cancer researchers won scholarships in the 1990 Westinghouse Science Talent Search for their investigations. Soojin Ryu, 18, of Bronx High School of Science, won $10,000 for her research on HLA class 1 molecules, which may activate T cells. Bianca Santomasso, 17, of New York's Stuyvesant High School, won a $7,500 for an in vitro investigation of the role of thrombospondin in metastasis.

See P. 3 of Comm Economics section

## Center Directors Draw Attention Of Congress To Lack Of Funding

(Continued from page 1)

hearing on the FY 1991 budget last week probably was prompted by more than 50 letters cancer center directors sent to subcommittee members and other members of Congress calling attention to the paltry $159,000 increase for the Cancer Centers Program. The Assn. of American Cancer Institutes had encouraged center directors to write to subcommittee members.

Throughout the hearing, both Democratic and Republican subcommittee members expressed dissatisfaction with the President's $1.694 billion budget for NCI. They listed several areas in which more funds are needed, including research project grants (RO1s, PO1s), cancer prevention and control, public education and information services, and construction funding.

Rep. William Natcher (D-KY), chairman of the subcommittee, started the questioning on the centers program by asking Broder whether he was "satisfied" with the $104 million the President's budget allocated for cancer centers.

"We will face a difficult choice of phasing out core grants or having downward negotiations," Broder said. "What I hope we can do is achieve some measure of flexibility to maintain excellence in our grants portfolio." He said NCI is concerned about "excessive downward negotiations," and indicated that phasing out some core grants may be preferable.

Rep. Joseph Early (D-MA) asked Broder whether NCI had implemented the recommendations made in the Institute of Medicine report last year, "A Stronger Cancer Centers Program."

"We have done what we can within the available funds," Broder said, noting that last year four core grants were phased out, leaving 56 cancer centers.

Early pressed Broder on his use of the term "within available funds," noting that the downward negotiations that will be required for research project grants, and, probably, cancer centers, will have a major effect on research. "Don't we have to make a decision that we can't keep downward negotiating at this rate?" Early asked.

"There's no question that downward negotiations do have an effect," Broder said. "There are many opportunities we could pursue."

After repeated questioning on funding for research project grants, information services and other topics, during which Broder had to defend the President's budget, Rep. John Porter (R-IL) finally broke the tension with a comment on the budget process.

**'A Strange Procedure'**

"This is a strange procedure," he said to Broder. "You submit what you really want in the bypass budget, and then NIH scales it down, and Office of Management & Budget scales it down more and then you have to defend that budget to us and you get beat up."

(Porter neglected the fact that the bypass budget, NCI's professional estimate of the funding it needs to take advantage of scientific opportunities, does not go to NIH, it is submitted directly to the President, though every president since Richard Nixon has routinely ignored it. NIH prepares another, significantly smaller, budget request for NCI, which is submitted to HHS and OMB, and that is the budget that is finally incorporated into the President's request.)

"The salary is compensation for that," Broder quipped.

In response to Porter's request, Broder went on to discuss the FY 1991 bypass budget, which requested a total of $2.4 billion. That amount would allow NCI to fund over 1,500 new and competing grants, double the number that can be funded now.

The bypass budget includes a total of $144 million for cancer centers, $41 million more than the President's budget, which would restore the four centers that were phased out this year, restore recommended funding levels for all centers and would add five new centers, Broder said.

The bypass budget also includes a total of $94 million for cooperative groups, $35 million more than the President's request; $388 million for intramural research, $75 million more than the President's request; $156 million for cancer prevention and control, $82 million more than the President's request; and $60 million for construction, which is $58 million

**THE CANCER LETTER**

*Editor:* **Jerry D. Boyd**
*Associate Editors:*
**Kirsten B. Goldberg, Patricia Williams**

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

ISSN 096-3917. Published 48 times a year by The Cancer Letter Inc., also publisher of The Clinical Cancer Letter and AIDS Update. 

more than the President's request.

"We could do all this if we could forego one B-2 bomber," Porter said. "For $750 million more (than the President's request) we could double the number of grants. We need to rethink our priorities and move funds to address biomedical needs. I hope we can get to your bypass budget sometime soon."

Porter has become perhaps this year's most outspoken advocate of NCI in Congress, making strong statements in support of the bypass budget. In an January address to the Sixth International Cancer Symposium in Brazil, Porter said he would work to shift money from the defense budget to NIH, and would work to achieve NCI's bypass budget. It was the first time in years that any member of Congress has publicly committed to the bypass budget.

"I am going to work hard for a very substantial increase for this year, and for the full bypass budget in 1992," Porter told **The Cancer Letter** after his Rio De Janeiro address (**The Cancer Letter,** Jan. 19).

In response to a question from Rep. Steny Hoyer (D-MD), Broder said that the five new centers were included in the bypass budget because NCI is "concerned that we need to have diversity in centers. Some areas of the country, especially the Midwest and Southeast, are underserved." The bypass budget also would fund one or more minority demonstration centers.

"Assuming you don't get the $144 million for cancer centers, what is the impact?" Hoyer asked.

Broder said NCI would have to phase out three or four centers in 1991 or engage in severe downward negotiations.

**What compelled center directors** to write letters to congressmen was an NIH budget justification that claimed that the $159,000 increase in the President's FY 1991 budget for the Cancer Centers Program will "avoid a further decline in the number of centers" funded by NCI. That claim was contrary to the statements Broder has made since last year that without a significant increase, three to four core grants would have to be cut in FY 1991.

According to the NIH budget justification, "This request for an increase in the FY 1991 budget will avoid a further decline in the number of centers throughout the nation which receive NCI core grant support, and will permit a level of funding necessary to ensure that the critical role of cancer centers in the National Cancer Program is maintained and fully realized in the future."

In a letter to Rep. Silvio Conte (R-MA), the ranking Republican on the Natcher subcommittee, Marc Lippman, director of the Vincent Lombardi Cancer Research Center, wrote that the statement is "incorrect and inconsistent. He noted that Lombardi "is in the awkward position of having submitted a new cancer center support grant application that was favorably reviewed ... but may not be funded because the cancer center (program's) budget has remained virtually static for the past three years."

Richard Steckel, director of the Jonsson Comprehensive Cancer Center, called the NIH statement "manifestly false" in his letter to Sen. Arlen Specter, a member of the Senate Labor, HHS, Education Subcommittee, which has already held its hearing on the NCI budget (**The Cancer Letter,** March 2).

"The Administration's FY 1991 budget proposal would constitute a disaster for the NCI Cancer Centers Program, accelerating the decline in this program which has occurred over the past several years as a result of continued flat budgets," Steckel wrote. As a result of inadequate NCI funding at Jonsson, he wrote, "we have had to delay the development of excellent research and related patient care programs that could otherwise take advantage of exciting new leads in cancer research."

**Natcher broke a tradition** at this year's hearing by not asking a question he used to ask former NCI Director Vincent DeVita, and had asked Broder last year: "Doctor, what can you tell us this year that you couldn't tell us last year," a pointed request for information on the progress made against cancer.

"Dr. Broder, I won't ask you the same question I asked Dr. DeVita every year," Natcher said. Instead, he asked Broder to give his prepared statement. "Tell us what you are doing now, we'll be glad to hear from you."

However, the first question Natcher after Broder had read his statement noted that since 1971, NCI has received $18 billion. "Are the American people wrong to expect more progress than there has been up to this time?"

"The American people are correct in expecting a high standard of performance from government officials," Broder said. "I would argue that there are some areas of significant progress against the death rate for cancer. We have made significant progress for people under age 65."

Broder listed the following mortality statistics: Since 1973, there has been a 15 percent reduction in the death rate of colon cancer; 25 percent reduction in death rate from ovarian cancer; 28 percent reduction for stomach cancer; 32 percent reduction for bladder

cancer; 37 percent reduction for cancer of the uterus; 39 percent reduction for cervical cancer; 20 percent reduction for oral cancer; 26 percent reduction for thyroid cancer and 52 percent reduction for Hodgkin's disease.

"For a number of common tumors for those under age 65 I believe there has been significant progress," Broder said. "For people over age 65, I believe nobody can be satisfied with the amount of progress."

Natcher requested overall mortality statistics. Since 1973, Broder said, there has been a 5.4 percent increase in the death rate of cancer. The number of new cases of cancer has gone up 14.6 percent. About 1 million Americans will get cancer in 1990 and approximately half a million will die this year from cancer.

Natcher also asked for the overall change in the cancer survival rate. Broder said that in the early 1970s, the chances for five year survival was 49 percent. This has gone up approximately 2 percent in 10 years.

Natcher noted that a few years ago NCI announced the goal of a 50 percent reduction in cancer mortality by the year 2000. "In your professional judgement, what are the chances of meeting this goal?"

"I think the jury is still out on this," Broder said. "The death rate for women of lung cancer has gone up 100.2 percent since 1973, so in some areas we need to redouble our efforts. But I would like to express one point. Some states, for some common tumors, have met or exceeded the Year 2000 goal. For example, Utah has a lung cancer death rate more than 50 percent below the national average. Wyoming and Utah, for cervical cancer, have a 50 percent or greater reduction compared to the national population. So I think these goals are achievable. They are not pie in the sky types of goals."

Switching from statistics, Natcher asked about the concentration of grants among investigators and institutions. "How much grant funding goes to the same investigators and how much ends up at the same institutions year after year?" he asked.

Broder noted that approximately 10 percent of grants in NCI's grants portfolio are committed to the FIRST award system for new investigators, or about 3 percent of all grants funding. However, he said there are "a significant number of grants which go to highly distinguished investigators who compete in the system every year and certain institutions that have a high probability of success."

Natcher asked Broder what changes he has made in NCI's "overall approach" in the past year.

"I believe we need to give a greater emphasis on prevention, control, community service outreach and knowledge dissemination," Broder said. "We need to do a more aggressive job of transferring the knowledge that we have.

He noted that NCI had increased funds for the Cancer Information Service, from $4.8 million to $8 million this year.

**Natcher was the only subcommittee member** to bring up the subject of construction funding, noting that the President's budget includes nearly $1.5 million for construction, all of which is slated for repairs at the Frederick Cancer Research Facility.

"I think there are very significant construction needs in the country," Broder said.

Natcher asked how much money Broder would allocate for construction if he had that authority. Broder was reluctant to name a figure, saying that it would be necessary to "balance all competing needs," but when pressed, said that, within available funding, $5 to $10 million would be a range.

"But there are competing requirements and I hope that's not taken as a promissory note," Broder said.

The exchange indicated that the subcommittee might propose giving NCI the authority to move funds from other areas to construction.

Natcher also asked Broder whether he was "satisfied" with the 1 percent increase for cancer prevention in the President's budget.

"We will be significantly challenged at that level," Broder said

**Downward negotiations** was a subject that Early pressed Broder on. He noted that downward negotiations necessary for grant recipients in FY 1991 are an estimated 20 percent for new and competing grants and 4 percent for noncompeting grants.

"We need to come to grips with this irresponsible downward negotiation," Early said. "Wouldn't you say downward negotiation threatens good science?"

"I think 20 percent downward negotiations compromises scientific review," Broder said. "It is possible to downward negotiate so that it negates any effect of a grant to do its job."

Hoyer asked about the level of grants funding and whether new cancer researchers are being discouraged from entering the field.

"In my professional opinion, we are at that point," Broder said. He noted that NCI tries "to give new researchers every possible break" in the FIRST award system.

Rep. Carl Pursell (R-MI) said NCI should spend more on information services.

"Something is out of balance in terms of good research," he said. "NCI has gotten $18 billion since 1971, but you allude the public education sector is way behind." He asked why the President's request for areas such as cancer prevention and control "are so low."

Broder said some public education and information services are not listed as such in the budget. For example, cancer centers do some public education.

"I promise that within available funds, I will make information services a priority, Broder said.

**Rep. John Myers (R-IN),** a member of the full House Appropriations Committee, sat in on the hearing though he is not a member of the subcommittee. He said he has developed an interest in cancer research since his wife was diagnosed with breast cancer in January. He said he and his wife consulted with NCI, and she is now receiving treatment at the Lombardi Cancer Research Center at Georgetown Univ. Myers told Broder he was concerned about the training of radiologists who read mammograms, since the early detection of breast cancer depends on accurate readings.

Broder said NCI has gotten involved in setting standards and recently held a conference inviting representatives of the electronics industry to come up with better equipment.

Conte asked questions mainly about scientific matters, including the potential of PCR technology, suramin for prostate cancer treatment, gene therapy, and pediatric AIDS. Early also said he thought "the real cures for cancer" are going to come from proton beam research, lasers and other energy-related technologies. Early was instrumental last year in appropriating $500,000 for NCI funding of proton beam "referral centers."

## USC, Wisconsin Get Construction Grants Totaling $1.5 Million

NCI's first construction grants since FY 1987 will go to the Univ. of Southern California Norris Cancer Center and the Univ. of Wisconsin Clinical Cancer Center.

The awards will be funded from the allocation ordered by Congress, taps from each of NIH's institutes. That amount totaled $14.8 million, with $10 million designated for the competitive replacement of Jackson Laboratory's mouse facilities. NIH gave NCI $2 million of the balance, with $2.8 million to be awarded through a new RFA (**The Cancer Letter**, March 2).

NCI's Research Facilities Branch has collected several high quality applications for construction/renovation since the last awards. They were reviewed and awaiting availability of funds. The USC and Wisconsin applications were among those with the highest priority scores.

The USC grant is $1.2 million, which will provide new laboratories in shelled space, on one floor of a new $16 million building. The center is matching the NCI funds for the laboratories, and the university is raising the major cost of the building from other sources.

The Wisconsin grant is $385,000, which will provide office space for the center's biostatistics group. The NCI money amounts to a about 40 percent of the total required for the biostatisticians. The center is in the process of raising another $1.8 million for additional shell space.

The entire module that includes the new space, which will include other health research facilities, will cost $5 million, of which $1 million is being provided by the National Eye Institute. NEI, along with NCI and the National Heart, Lung, & Blood Institute, are the only NIH entities with the authority to award construction grants. UW has a strong eye program.

The two grants total only a little more than $1.5 million, leaving nearly a half million dollars which NCI will not be able to award. Brian Kimes, associate director of the Div. of Cancer Biology, Diagnosis, & Centers told **The Cancer Letter** that the extra money will go back into the NIH pool because NCI was prohibited from making partial awards.

That means that the amount available in the NIH competition is now $3.3 million. Institutions involved in cancer research, along with the constituents of NEI and NHLBI, may compete for those funds. Those who had previously submitted construction grant applications to NCI have been advised to apply under the new RFA.

## Becker, Brown Testify On Need For Greater Biomedical Funding

Two prominent cancer center representatives were invited to testify before the Human Resources Task Force of the House Budget Committee last week on the need for greater biomedical research funding.

Frederick Becker, vice president for research and scientific director of the Tumor Institute at Univ. of Texas M.D. Anderson Cancer Center, and Helene Brown, director for community applications of research at Jonsson Comprehensive Cancer Center at Univ. of California (Los Angeles), testified before Rep.

Barbara Boxer (D-CA) on a panel that included John Sherman, executive vice president of the Assn. of American Medical Colleges and Sheldon Wolff, chairman of the Dept. of Medicine at Tufts Univ. School of Medicine.

Boxer said the task force is concerned "that our country just isn't doing enough" to support biomedical research and development and was using the hearing to "enter into a dialogue" with "the experts."

Brown's theme in her testimony was that medical research "is not charity" and does not deserve the "remnants" of the budget. Medical research "is one of the best investments that can be made by governmental funds seeking returns in gross national product, production of goods and services, the creation of taxable income and return on investment," Brown said.

After World War II, there were two approaches that could have been taken on the polio epidemic, she said. One was to build more hospitals, manufacture more respirators, train more therapists and "prepare for the onslaught of the dead or permanently handicapped." The other approach was to try to produce a vaccine. Fortunately, the second route was chosen.

In the first six years after the vaccine was available, from 1954 to 1960, 154,000 cases and 12,500 deaths were prevented, averting the loss of $6.3 billion in income, and hospital costs of $2 billion a year. The total cost of the vaccine and its field trials was $41 million. "Now it's 30 years later," she said.

"We have a tendency to put science and research on the back burner," Brown said.

Boxer said the example of the polio vaccine was "excellent."

Becker discussed the cost of care of cancer patients versus the costs of research to prevent cancer. "The failure to prevent and cure cancer is enormously costly in monetary terms. Cancer treatment is one of the major forms of catastrophic medical care," he said.

"Our aging population, the continued exposure to carcinogens in tobacco and our lifestyle predict that the number of cancer patients will increase. Thus, an investment in prevention and in research directed towards cure bears the possibility of a savings in dollar terms."

Equally disastrous, he said, is the cost in terms of new researchers. "Morale is terrible among established researchers, and worse among the young." The loss of new researchers will cause a gap in cancer research. Presently, the U.S. holds a lead in biomedical research, exporting technology abroad.

"Will we relinquish this lead to other countries whose investments in biomedicine increase daily, whose agents cruise our campuses and medical centers searching out viable and exciting prospects? If so, then let us bash no one but ourselves in later years," Becker said.

Brown and Becker both noted some major advances made in recent years, such as the discovery of oncogenes. There are tremendous scientific opportunies available that are only lacking funding, they said.

Becker noted that foregoing one Stealth bomber, estimated to cost $600 million, would go a long way towards funding the NCI bypass budget.

Boxer thanked Becker for the suggestion. "The days are over when people can come up here and ask for more money without telling us where to get the money. You have done that."

Boxer also said she recently learned a "new buzzword" (which has actually been in the NIH lexicon for many years), "downward negotiations."

"That's when NIH attempts to reduce the level of funding after a grant has been approved," she said. She said she hoped her colleagues "on both sides of the aisle will join together" to improve funding for biomedical research.

In their written testimony submitted to the task force, Brown and Becker included a discussion of NCI's FY 1991 bypass budget and resource needs of the FDA.

## DCBDC Board Approves Concepts For Two New Small Grant Programs

Two new small research grant programs, which could result in as many as 20 grants, received concept approval this week from the Div. of Cancer Biology, Diagnosis, & Centers Board of Scientific Counselors.

The awards, which can be for as much as $50,000 each, will be for three years. One will support small grants for research on the molecular and cellular biology of metastatic tumor cells; the other to stimulate development of animal models for research on the immunology of solid tumors.

The concept statements and board discussion follow:

**Small research grants on the molecular and cellular biology of metastatic tumor cells.** RO3 small grants, nonrenewable, one time solicitation. Total cost estimated at $600,000 a year for three years. It is anticipated that approximately 10 awards will be made at a direct cost of $40,000 each a year to provide salary support for the postdoctoral investigator only and a reasonable supply and travel budget.

The goal of this initiative is to provide funds to investigators very early in their research careers to begin projects on metastasis. These projects may form the basis for future grant

applications. The intent is to foster collaborative research between investigators with experience in the molecular biology of the cell and those skilled in metastasis research, and to increase the number of laboratories and investigators active in metastasis biology research.

The Cancer Biology Branch supports a broad spectrum of basic biological research on cancer cells in order to determine how they differ from normal healthy cells and why they progress to ever greater degrees of malignancy. The fundamental mechanisms behind cancer cell invasion and metastasis present an important challenge in cancer biology. A prerequisite to malignancy is the expression of the special phenotype responsible for the cancer cells' escape from the primary tumor, invasion of the structural matrix and entry into the vascular system, avoidance of host defense mechanisms and then adhesion, invasion and colonization at some other anatomical site. Currently, advances in our understanding of this metastatic phenotype depends on the rather limited number of basic biochemical, cellular, and molecular biological techniques being applied and the number of investigators involved in this research.

In recent years significant advances have been made in understanding the molecular properties of many elements involved in the behavior of malignant cells. Included are the extracellular matrix components, proteases, adhesion and homing receptors, chemotactic and growth factors, suppressor genes and oncogenes. It is unlikely that any one of these molecular entities, or any single cellular activity such as motility or growth, will turn out to be the master determinant of the metastatic phenotype. Rather, each of these elements must be considered in relation to one another. However, it is critical to establish a baseline of information on the molecular biology of these various elements within the context of the metastatic process.

Not long ago it would have been impossible to provide answers to such complex issues in molecular terms. Opportunities resulting from the advances in molecular and cellular biology are now numerous and the resources are available to address these issues in a meaningful way. In spite of this, progress toward understanding, at the molecular level, how these individual elements are involved in the intrinsic mechanisms of metastasis has been slow.

Impediments to progress in metastasis research include suboptimal utilization of existing technology and a limited number of qualified investigators actively working in this research area. These problems must be overcome before research in metastasis biology will begin to reach its potential.

Given the programmatic concern for advancing understanding of metastasis, the Cancer Biology Branch has determined that there are several clearly defined needs. These are: improved communication between the allied areas of basic molecular cell biology and metastasis research; opportunities for technical and intellectual interchange; and, increasing the size of the research community conducting research on metastasis.

To accomplish these goals, the Cancer Biology Branch proposes to encourage new investigators (with less than four years from receipt of a doctoral degree at time of application) [Ed. note: the board asked that this be changed to five years] to apply for small short term grants to conduct pilot studies. Predoctoral degree students may apply if they will have received their doctoral level degree by the time of award. Postdoctoral and other new investigators are also encouraged to apply. These studies should have the potential for forming the basis of future grant applications on metastasis. Recent doctoral researchers have been targeted to encourage the formation of a new cadre of metastasis researchers. Either the new investigator or the host laboratory (which must have its own PHS supported research project) must have demonstrated experience in metastasis research.

This initiative is not intended for support of new investigators who have metastasis research experience going to host laboratories that are engaged in metastasis research to any significant extent. The scope of the research may encompass any aspect of biochemistry, cellular or molecular biology as it applies to metastasis biology. Some representative topics might include the role of the vascular endothelium, homing and other adhesion receptors, cell-matrix interactions, growth modulators, tissue specific gene expression, cell motility, signal transduction, and chemotaxis.

Board member Harold Moses suggested that four years since obtaining a doctoral degree was too restrictive and recommended five years. Margaret Kripke added that with the four year limit, "you will miss the young professor who needs to develop collaborations." Michael Martin, program director in the Cancer Biology Branch, agreed to make it five years in the RFA.

Board Chairman Vittorio Defendi said that a $40,000 salary "is not much for an MD," but Moses pointed out that this did not have to be 100 percent of the investigator's salary.

Board member Albert LoBuglio questioned whether the restrictions would preclude paying technicians from the grant. Martin said the grants would be more flexible than that, but "What we want is for this to be the major focus for the individual. We don't want him to put in five percent of his time, dropping by once in awhile to see the technicians."

The concept was approved unanimously.

**Immunology of solid tumors: animal models.** RO3, maximum $50,000 in direct costs, three years. Total cost estimated at $700,000 a year.

Many commonly studied animal tumors are known to be poor models for human disease. Most models have used long establishes serially transplanted, spontaneous, chemical or retrovirus induced tumors. Some, particularly many of the virally induced tumors, induce much more vigorous immune responses in the most animal than are usually seen in humans. Other tumors are derived from cell types not commonly represented in human tumors. Still others have been propagated in vitro so long that the relationship of their properties to the original primary tumors is probably limited.

The congenitally athymic (nude) mouse has been the most widely used model for transplanting human solid tumors as xenografts. However, the species difference between the most immune system and the transplanted tumor confuses the interpretation of immunologic studies. Each of the existing models can be used for certain types of experiments, but each has serious limitations in its applicability to the study of current questions in the immunology of human cancer. Therefore, this request for applications is designed to promote the development and production of animal models of solid tumors that are more analogous to human cancers and can be utilized more effectively to study ongoing host responses to solid tumors at various stages of tumor development and progression.

During the past decade, many advances have been realized

in elucidating the complex biology of lymphocyte functions in the recognition of Self vs. non-Self. Among these advances were the deciphering of the molecular structure of the T cell receptor-CD3 complex for antigen recognition, the identification of cell surface lymphocyte function antigens, and the elucidation of B and T cell ontogeny.

In addition, new mouse strains have been developed which provide new tools for the immunologist to unravel the complexities of host-tumor interaction. The most notable examples of new animal resources are transgenic mice and the many strains of SCID (severe combined immunodeficiency) mice which can be reconstituted with a human immune system. Thus, opportunities now exist to apply these new findings and resources to the study of solid tumor immunology.

In 1989, following administrative consolidation of grants from the Organ Systems Program into DCBD, it became apparent that little research was being performed to study the host immune response to the most common human tumors, the solid tumors of nonhematopoietic origin. It was the unanimous conclusion of the participants in a recent workshop that new animal models were required to better apply new immunologic research findings to studies of solid tumors. The frustration was expressed that development of new models is time consuming and expensive, and it is difficult to obtain support for the initial developmental phases.

The need for new and/or improved animal models has been emphasized. Clinicians need models more predictive of clinical usefulness for studies leading to immunotherapy of solid tumors in humans. Little is known regarding the ongoing immune response during the natural evolution of tumors. The effective immune response may differ depending on stage of disease, and it is important to know the type and subsets of immune cells which have potential to eliminate tumor cells at the various stages of tumor growth and spread. Human tumors have usually progressed past the early stages when detected clinically, and cannot be studied serially in any case. Therefore, relevant animal models are necessary to provide basic scientific information which is needed as a foundation upon which new or improved immunotherapy approaches and cancer vaccine development can be based.

"I have a problem understanding what new models need to be developed," Defendi said. "Every model developed in the last 50 years has been used for solid tumors" in testing for viral and chemical carcinogenesis.

Faye Austin, DCBDC associate director for the Extramural Research Program, said that the immunology of those systems has not been investigated. "We would like to apply the model to understanding the immunology of the tumor after the carcinogenic event."

Kripke said that "you can't get an RO1 grant to develop an immunology model. They are considered boring [by the study sections]."

"All of the pressure has been for the opposite kind of model," LoBuglio said. "The most popular are the most distant from human tumors."

Kripke asked if the grants would be limited to small animals. "These grants will not go far with larger animals." Austin said that that would be left open.

The concept was approved unanimously.

## CTEP Director Adds To Article On New Minorty Initiative

Michael Friedman, director of NCI's Cancer Therapy Evaluation Program, has written a letter about a story in the March 2 issue of **The Cancer Letter** on the CTEP minorities activities. Friedman worte that the story "was accurate but not complete. A couple of important items to be added are:

"1. DCPC has a large Minority CCOP solicitation and applications are currenly being reviewed. Support to major minority academic centers may be forthcoming. We anticipate an important contribution to clinical trials through this Minority CCOP initiative.

"2. CTEP will be asking the group chairmen to devise other methods for increasing minority accrual to therapeutic studies. We anticipate that close collaboration will exist between new sites for minority accrual and established group members. However, we would not exclude other appropriate administrative structures. Pragmatically, any means likely to increase accrual of ethnic minorties to these studies would be considered."

## 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, Bethesda MD 20892. Proposals may be hand delivered to the Executive Plaza South Building, 6130 Executive Blvd., Rockville MD. RFP announcements from other agencies will include the complete mailing address at the end of each.

**RFP NCI-CO-03885**
Title: Pamphlet printing
Deadline: May 9

Single award for a fixed price contract. Production area, assumed 125 mile radius of zero milestone, Columbia, MD. Offerors outside area must furnish documentation of their ability to meet schedule. Inspection of source materials will be from April 26-27, 8 a.m.-5 p.m. at NIH Bldg. 31 Rm 10A30, 9000 Rockville Pike, Bethesda, MD. For an appointment contact Erin Lange one week prior to source review. Four pamphlets, 2,500,000 total copies. Printed with four color process plus black plus 1 PMS color (different for each pamphlet). Operations include saddle wire stitch, trim, printing, folding, binding, negatives, packaging, mailing and f.o.b. destination to Columbia, MD. Contractor furnish paper. Quality attributes level 2 for printing and finishing. Bid request on Standard Form 1447. Phone, telegraph, fax request not acceptable.

Contract specialist: Erin Lang
RCB Executive Plaza South Rm 608B
301/496-8628