THE CANCER LETTER

PO Box 9905 Washington DC 20016 Telephone 202-362-1809

Vol. 24 No. 13 April 3, 1998

© Copyright 1998 The Cancer Letter Inc. All rights reserved. Price \$275 Per Year US \$295 Per Year Elsewhere

Black Men Face Disparate Cancer Burden; Minority Rates Vary, Klausner Tells House

The problem of cancer in minorities is not monolithic, and instead varies by ethnic group, gender and disease site, with some ethnic groups having lower rates of some cancers than the population overall, NCI Director Richard Klausner said in his testimony at the House Labor, HHS & Education Appropriations Subcommittee last week.

Klausner said African Americans, particularly men, experience a high rate of cancer incidence and mortality.

"The disparity in terms of cancer burden, overwhelmingly, is a disparity not between not all minority communities, but in this case very (Continued to page 2)

In Brief:

Sporn Wins BMS Cancer Research Award; Dana-Farber To Try To Affect Teen Health

MICHAEL SPORN won the 21st annual Bristol-Myers Squibb

Award for Distinguished Achievement in Cancer Research in recognition of his work in the development of the first recognized class of chemopreventive agents. Sporn, the Oscar M. Cohn '34 Professor of Pharmacology and Toxicology and professor of medicine at Dartmouth Medical School, will receive the \$50,000 award April 15. Sporn published his research on retinoids and their activity in pre-malignant and malignant lung cancer cells in 1976 while chief of the NCI Lung Cancer Branch. His research led to development of chemopreventive drugs that target retinoid receptors in epithelial cells, including tamoxifen and finasteride. ... DANA-FARBER CANCER INSTITUTE will receive a \$200,000 grant from the Bristol-Myers Squibb Foundation's Better Health for Women: A Global Health Program. Dana-Farber plans to use the award to develop a job-site intervention program to change unhealthy teenage behavior. . . . MARGARET KRIPKE was named vice president for academic programs at M.D. Anderson Cancer Center. Kripke, former chairman of the department of immunology at M.D. Anderson, and a former president of the American Association for Cancer Research, has held the position on an interim basis for several months. . . . ROBERT W. FRANZ Cancer Research Center at Providence Portland Medical Center received a gift of \$1.5 million to establish the Walter J. Urba Chair in Cancer Research. Urba is director of the Franz center. The center said the endowment will support trials of vaccines for the treatment of breast cancer, melanoma, and kidney cancer, and to expand the center's (Continued to page 8)

In Congress:
Could NCI Make Use
Of Increase? Porter
Asks; "We Can Handle It
Well," Klausner Replies

... Page 2

Regulatory Agencies:
HCFA Proposes
Physician Transfer
Of Drug Discounts
To Medicare, Insurers

... Page 5

NCI Programs:
NCI Drug Screening
To Take More Targeted
Approach; BSA Okays
Plan To Support
New MA Contracts

... Page 6

NCI Could Put Budget Raise To Good Use, Klausner Says

(Continued from page 1)

much in the African American community," Klausner said at the March 25 hearing on NCI appropriations.

"Overall, cancer burden in Hispanics and Asian Americans, Native American men, is lower than in the majority community," Klausner said. "We need to learn from that. However, in the African American community, we are very concerned and very disturbed about this disparate burden of cancer both in incidence and mortality."

Klausner's overview of the question of race, ethnicity, and cancer comes at a time when an umbrella group of organizations concerned about the problem of cancer in minorities is challenging the validity of NCI statistics on cancer in minorities and the underserved. The Intercultural Cancer Council said NCI statistics included too few minorities, a view that was disputed by Institute officials and other experts (**The Cancer Letter**, March 20).

Klausner made his remarks on cancer in minorities in response to a question by Rep. Louis Stokes (D-OH). Stokes, who is retiring from Congress at the end of his current term, has been asking questions about disparity of cancer mortality and incidence in African Americans in the course of appropriations hearings every year for a number of

THE CANCER LETTER

Member, Newsletter Publishers Association

World Wide Web: http:// www.cancerletter.com

Editor & Publisher: Kirsten Boyd Goldberg

Editor: Paul Goldberg

Staff Writer: Catherine Fiore

Editorial: 202-362-1809 Fax: 202-362-1681 PO Box 9905, Washington DC 20016

E-mail: kirsten@cancerletter.com or paul@cancerletter.com

Customer Service: 800-513-7042 PO Box 40724, Nashville TN 37204-0724

Subscription \$275 per year US, \$295 elsewhere. ISSN 0096-3917. Published 48 times a year by The Cancer Letter Inc. Other than "fair use" as specified by U.S. copyright law, none of the content of this publication may be reproduced, stored in a retrieval system, or transmitted in any form (electronic, mechanical, photocopying, facsimile, or otherwise) without prior written permission of the publisher. Violators risk criminal penalties and \$100,000 damages.

Founded Dec. 21, 1973 by Jerry D. Boyd

years.

"In the overall statistics, the group in whom the percentage fall in overall mortality is highest is in black men," Klausner said. "So, in our statistics this year, there is about a 1.4 percent per year drop in mortality among black men. The next group is white men, which is about a .9 percent. If that continues, that can eventually reduce what is a significant gap between mortality rates in African American men in particular and majority men."

Responding to a question by Rep. John Porter (D-IL), chairman of the subcommittee, Klausner said that if Congress were to double the NCI appropriation, the Institute would be able to make good use of the increase.

"I believe that we can handle it well," Klausner said. "We know cancer is a complicated puzzle, but I actually believe we know what we need to do to push us much further to knowing what the puzzle looks like. I don't know how long it will take to finish, and I don't know what we'll find, but we really do know what to do."

The President's budget proposal for fiscal 1999 will allow NCI to support the following initiatives, Klausner said:

- —Develop chemistry-biology centers to capture new approaches to the generation of millions of small molecules and to couple this with smart assays to target these newly defined cancer circuits.
- —Build a new program for Rapid Access to Interventional Development, which will make it possible to accelerate clinical testing of new preclinical ideas in cancer intervention.
- —Build a redesigned, informatics-based clinical trials system to expand access to prevention, detection, and treatment trials, to improve the speed and value of the trials, and to allow a growing number of ideas to be rapidly tested.
- —Build a new imaging research network to evaluate emerging technologies is tumor imaging for early detection, staging, and image-guided therapy.
- —Fund clinical training pathways and fund mid-level and senior clinical investigators to protect their time to engage in both clinical research and mentoring.
- —Improve the cancer surveillance system to gain a better understanding of the burden of cancer and guide special efforts to control cancer.

Under the President's proposal, NCI would receive \$2.536 billion, an increase of \$215 million (9.27 percent) in fiscal 1999. With AIDS programs

included, NCI would receive \$2.776 billion, an increase of \$229 million (8.99 percent) over the current year.

The excerpted transcript of Klausner's testimony follows:

Ethnicity and Cancer

KLAUSNER: The disparity in terms of cancer burden, overwhelmingly, is a disparity not between all minority communities, but in this case very much in the African American community. Overall, cancer burden in Hispanics and Asian Americans, Native American men, is lower than in the majority community. We need to learn from that.

However, in the African American community, we are very concerned and very disturbed about this disparate burden of cancer both in incidence and mortality. Once again, as with anything in cancer, it varies from cancer to cancer. It's not all cancers. There are some cancers where the mortality rates are lower among the African American community.

Unfortunately, for many cancers, and some of the most common, incidence rates are high and mortality rates are way too high. Are we making progress? In the overall statistics, the group in whom the percentage fall in overall mortality is highest is in black men. So, in our statistics this year, there is about a 1.4 percent per year drop in mortality among black men. The next group is white men, which is about a .9 percent. If that continues, that can eventually reduce what is a significant gap between mortality rates in African American men in particular and majority men.

What's really very important is that we look at each of these cancers, that we have good statistics so that we can begin to understand the why. We are committed to having those numbers and to acting on them to try to understand why they are different.

Maybe I can use one cancer as an example. Breast cancer mortality rates are about 20 percent higher overall for African American women than for Caucasian women. That disparity is even higher for younger women.

Why is that? First of all, mortality rates are falling for all white women under the age of 80. Actually, mortality rates are either flat or falling for all black women under the age of 70. But above 70 it continues to rise.

What's the explanation? Well, it's correlated with two facts: one—the percentage of women diagnosed with breast cancer at later stages remains

higher for African American women than for white women. 51 percent of white women are diagnosed with localized disease versus only 35 percent of black women.

For distant disease, about 22 percent of black women are diagnosed with distant disease versus only about 11 percent of white women. In addition to that, even within every stage, the tumors tend to be more aggressive, and the outcome tends to be poorer. So why is this?

We certainly are concerned that the use of screening, the use of early detection, is not as high, and historically that has been true. That could, in part, explain the difference in the stage of diagnosis. However, by 1992, our numbers show that for the first time, African American women are using mammographic screening at the same rate as white women.

Now, we don't expect to see the benefit of mortality for that for seven or eight years. We should see the effect of screening in the African American community now begin to fall. There had been disparities in delay between symptom and diagnosis, and, in terms of aggressiveness of treatment for African American women and white women. Our latest data suggest that those differences are being reduced. We will be following that carefully.

The final thing is that the biologic characteristics may be different. Does that mean that it's genetic differences? I suspect not, although there may be some of those.

Let me just point out one issue—we know that obesity is associated with later diagnosis, with poorer outcome at any stage, and with a greater risk of recurrence. And we know that there is a significantly different rate of being overweight or obese among African American women than men.

Quite significant—52 percent versus 34 percent.

We have several studies specifically aimed at understanding dietary patterns and attempting to produce educational materials aimed at the individuals, schools, workplace, and the community, to deal with this issue. I don't know if it's obesity, but that's one example where there might be a biologic difference that relates to cultural differences and behavior such as diet.

So that just gives you a flavor of how we're analyzing it, and what we're doing.

We do know, for example, that when black women and white women with breast cancer are in the same clinical trial, and we look for a particular stage and characteristics of their tumors, when they receive the same treatment, they do equally well. We know that from NCI clinical trials. That's very important, what we need to figure out is why the tumors are being diagnosed at a later stage and why they appear to be larger or more aggressive even within stage.

STOKES: Last year, you told us that African American men had the highest rate of prostate cancer in the world. Is that still the situation?

KLAUSNER: That is still the case. Prostate cancer incidence rates, because of the PSA phenomenon, are now dropping in African American men as fast as they had been dropping in whites, although the drop is delayed by about two years.

There are real changes going on in prostate cancer. Probably the most dramatic change we have seen in cancer in terms of these numbers is in prostate cancer.

One of the most significant things is over the last three to four years there has been a 50–60 percent drop in the diagnosis and detection of distant disease. Not percentage, but absolute numbers. And that drop is the same, and this is one example where we are finally seeing it the same between the African American and the majority community.

We are very anxiously watching those numbers to see if they translate over the next few years to a significant drop in mortality. But that's a very dramatic drop—50-60 percent of distant disease.

One of the things is that there is still a disparity in the nature of treatment between the African American community and the white community, and we are working very hard to understand that through, for example, the prostate cancer outcomes study, and are working with a variety of black organizations to get the word out both to physicians and to individuals about treatment options to make sure that everyone is being treated optimally.

Underneath all this is an issue not of race, but of poverty. Poverty rates are significantly higher among the African American community, and the issues that relate to access to care and quality of care that relate to poverty is not something we're going to solve by our studies. This is something we need to continue to talk about.

The \$5 Billion Plan

PORTER: You are now spending about \$2.5 billion at NCI. That's more than the budget of many

countries in this world. We are talking now about doubling the research expenditure over five years. If we were able to do that six or seven years from now, you will be dealing with a \$5 billion budget. Can you reasonably handle that amount of money and get good results from it?

KLAUSNER: I believe that we can, and I believe that we can handle it well. There are four ways that we would deal with that.

First of all, we know cancer is a complicated puzzle, but I actually believe we know what we need to do to push us much further to knowing what the puzzle looks like. I don't know how long it will take to finish, and I don't know what we'll find, but we really do know what to do.

That's coupled with something quite extraordinary—I think that for the first time in history, not only do we know that, but we have the technology to actually do it, and do it in a way that's much faster, more efficient, and more complete than was ever imaginable even a few years ago.

We need to do that so that we can actually really get answers to the nature of cancer, how it develops, and new answers to what causes it. That's one thing. I think we can do that. I think we have laid out the types of investments that are significant, that we can very productively spend in order to achieve that.

The second thing is, all of that information is going to have to be coupled to the development of successful interventions. I think we need a significant new investment in new types of chemistry, chemistry that is built on biology, new immunology, etc.—to bring in those areas and target them to the molecular opportunities for prevention and treatment that we are going to have.

I think we've begun that, but we've begun it on a very small scale. It's the type of thing that is very scalable, and in fact, can utilize well a fair amount of resources.

But all of that leads to a real significant demand on our clinical resource system. We are going to need a much better, much larger, much more rapidly responsive clinical trials system than we have now.

To answer the types of questions we are going to have, and to test what we know is going to be a dramatic increase in the number of good ideas for interventions—whether it's prevention, for detection, for new diagnosis, and for treatment.

We've seen over the last 10 years, going from 60 cancer drugs to well over 300. This is just going to increase based upon the science.

We need to be prepared for it. We have laid out a plan for expanding that system which is, again, especially with the changes in the health care system, we're going to need to step in to support our clinical trials system.

The fourth area is that we are going to need to make sure that once we have those trials done, that we have effective ways to apply what we have learned across the entire population, all of our communities, changing behavior, making sure that not only do we know what to do, but we act on it.

In those four areas we can accommodate such increases and accommodate them well.

Regulatory Agencies: HCFA Proposes Transfer Of Drug Discounts To Insurers

The Health Care Financing Administration has proposed regulations that would require physicians to transfer any discounts on drugs or services to Medicare and other insurers.

The proposed rule "would allow physicians to receive a discount based on the volume of their referrals to an entity, provided the discount is passed on in full to the patients or their insurers (including Medicare), and does not enure to the benefit of physicians in any way."

The wording of the proposed regulation has some observers wondering whether the language could be interpreted to mean that HCFA will eliminate the markup of drugs by office-based physicians.

HCFA is accepting responses to the proposed regulations, published Jan. 9 in the Federal Register. The comment deadline was extended to May 11.

Under the Balanced Budget Act of 1997, Medicare reimburses drugs at the Average Wholesale Price minus 5 percent.

HCFA's proposed change to Medicare reimbursement is part of a broader set of rules designed to regulate physician referrals to companies with which they have financial ties.

The regulations are intended to put into effect sections 1877 and 1903 of the Social Security Act, as amended by section 13562 of the Omnibus Budget Reconciliation Act of 1993—also known as the Stark law. The proposed HCFA rules, designed to incorporate the Stark law into Medicare regulations, would deny Medicare payment for services provided based on physician referrals.

Under the proposed HCFA regulations, the discount on pharmaceuticals that physicians purchase could be considered a form of remuneration. According to the proposal, discounted products would not meet the fair market value and would not be reimbursed unless the discount was passed on.

"We are aware of situations in which discounts enure to the benefit of referring physicians," the HCFA proposal said. "For example, physicians will sometimes purchase oncology drugs from manufacturers at a discount, yet mark the drugs up to eliminate the discount when billing Medicare. Such arrangements would not meet the standard."

The regulations include exceptions to the fair market value standard: If the product is sold through an arm's-length transaction; if the company offers the same discount to all similarly situated physicians regardless of the number of referrals the physician has made; and if the discount is passed on to Medicare and other insurers.

The American Society for Clinical Oncology called the proposal "ill-advised" and "inconsistent."

A draft of the ASCO response was obtained by **The Cancer Letter**.

"Some have interpreted this proposal as intended to require physicians to bill Medicare and Medicaid for drugs at the physician's acquisition cost—thus achieving through the Stark regulations the drug reimbursement policy that Congress rejected last year when the Administration presented it as a legislative proposal," the draft letter said. "If this is the intent, it would obviously be contrary to Congressional intent."

Rep. Bill Archer (R-TX), chairman of the House Ways and Means Committee, and Rep. Bill Thomas (R-CA), chairman of the House Ways and Means Subcommittee on Health, also responded to the proposed HCFA regulations.

"We are concerned that this proposal is intended to require physicians to bill Medicare for drugs at their acquisition cost," Archer and Thomas said in a letter to HCFA Administrator Nancy-Ann Min DeParle. "We would view any such attempt by HCFA to impose acquisition costs in direct conflict with Congressional intent and would strongly oppose such a measure."

Archer and Thomas were key opponents of a provision included in President Clinton's budget proposal last year that would have eliminated markups. The Ways and Means Committee wrote the current policy, a compromise between the President

and professional societies.

President Clinton's fiscal 1999 budget proposal again includes the provision to reduce Medicare reimbursements to the actual acquisition cost paid by physicians (**The Cancer Letter**, Feb. 6).

ASCO plans to submit a response to HCFA's proposal. The Association of Community Cancer Centers and the Oncology Nursing Society have begun letter-writing campaigns among their members.

The ACCC Executive Committee has authorized a budget of \$200,000 to campaign against the proposed regulations.

"If free-standing cancer centers and medical oncology practices are, in effect, driven out of the business of treating Medicare beneficiaries, the end result is not only bad policy, but bad medicine," ACCC said in a model letter for members to send to HCFA. "This measure is profoundly unfair to one of the nation's most vulnerable populations: elderly cancer patients who are battling the ravages of cancer, compounded by the afflictions of old age."

The elimination of drug markups is one of several issues in the proposed rules that ASCO and ACCC oppose. Included in the HCFA document is language that could prohibit oncologists from providing external ambulatory infusion pumps to patients, require physicians to be present in the office suite while any in-office ancillary services are performed, and prohibit physicians from receiving any free samples of drugs or chemicals or free training sessions from pharmaceutical companies.

If the professional societies successfully execute their letter-writing campaigns, HCFA will have thousands of responses it is obligated to review before implementing the new rules. The original law was passed in 1993, but did not go into effect until 1995. The 450-page HCFA document that would implement the regulations was not completed for another three years. Considering the pace HCFA has taken with Stark II so far, there is little danger of the provisions being enacted soon, sources said.

To respond to HCFA's "Proposed Rules on Physicians' Referrals to Health Care Facilities With Which They Have Financial Relationships" (Docket HCFA-1809-P; 63 Fed. Reg. 1659), send an original letter and three copies by May 11 to The Honorable Nancy-Ann Min DeParle, Administrator, HCFA, Department of Health and Human Services, Attn: HCFA-1809-P, PO Box 26688, Baltimore, MD 21207.

NCI Programs:

DTP To Take More Targeted Approach To Drug Screening

NCI's Developmental Therapeutics Program next year will not renew a \$1.4 million contract that tests compounds for anti-tumor activity in subcutaneous xenograft models of molecularly uncharacterized human tumors in athymic mice, because the method isn't targeted enough, Institute officials said.

Southern Research Institute, of Birmingham, AL, holds the current contract, titled "Model Development/Quality Control of Human Tumor Xenografts," which expires at the end of this fiscal year.

DTP plans to release a new Request for Proposals for master agreements that would provide \$50,000 a year to 10 academic or small business research groups that would evaluate drug leads "in disease-related in vivo models designed to assess effects on molecular targets as indicators of success, as well as 'mere' cytotoxicity or anti-proliferative effect," according to a concept statement.

The NCI Board of Scientific Advisors voted to approve the RFP concept at its meeting March 2.

The excerpted text of the concept statement follows: [Editor's note: Concept statements reflect NCI's plans for future grant or contract solicitations. Actual issuance of RFAs or RFPs, as well as funding levels, are not certain. For further information, contact the NCI staff member listed.]

In Vivo Efficacy in Disease-Related Models. Concept for a new RFP, Master Agreement, total \$3 million over five years. Project director: Richard Camalier, Developmental Therapeutics Program, Biological Testing Branch, tel: 301-846-5065.

This proposed Master Agreement would support the ability of the Developmental Therapeutics Program to assess candidate compounds for in vivo activity in models that have been created or characterized to represent a particular pathway relevant to human neoplasia, or which represent a particular histology but which possess a unique spectrum of biologic features, for example, hormone dependence, spectrum of invasiveness, capacity to metastasize, etc.

Recent review of experience by DTP leads to the conclusion that in vivo subcutaneous xenograft models of molecularly uncharacterized human tumors in athymic mice utilized in DTP's empiric drug screening program (after initial demonstration of drug activity in vitro) are flawed in their capacity to predict clinical activity in

corresponding tumor histologies. Thus, there is little rationale to screen for in vivo activity with diverse, molecularly uncharacterized tumors of differing histologies in the hope of clearly establishing a basis for activity in that histology. Nonetheless, if any degree of activity in vivo is demonstrable in some in vivo model, there is no worse than a 25 to 50% likelihood of demonstrating clinical activity at some organ site. This activity can then provide very useful information in choosing initial clinical trial designs. Reasons for the relative failure of xenograft models to predict accurately activity in specific clinical site scenarios after detection of anti-proliferative activity in empirical in vitro screening programs could include the artificial nature of such xenograft systems, with unnatural vasculature and poor tumor permeation by candidate compounds; lack of normal relation of tumor cells to stromal elements; poor correspondence of the in vivo subcutaneous models to processes promoting proliferation at "naturally" occurring metastatic sites, introduction into empiric in vivo screening programs of compounds that are not optimized for pharmacology or formulation, and unfaithful representation of molecular pathways relevant to common adult neoplasms.

This proposal would allow setting up of Master Agreements where the evaluation of drug leads occurs in disease-related in vivo models designed to assess effects on molecular targets as indicators of success as well as "mere" cytotoxicity or anti-proliferative effect. These would allow informed and focused initial in vivo evaluation of a candidate compound to occur. DTP views this approach as a qualitative improvement over the current empirical in vivo screening contract, which is not being re-competed. That contract took candidate compounds and tested them via intraperitoneal administration in a not necessarily optimized vehicle against the three most sensitive cell lines from the in vitro screen, but grown as an in vivo athymic mouse xenograft.

A current movement in cancer drug discovery and development leads away from empirical screening and development. This proposed Master Agreement would support that goal by developing a cadre of in vivo models to be practiced not at one large extramural site (as is the case for the current contract), but at extramural sites representing centers of excellence in diverse molecular pathways leading to neoplasia. Ideally, these models might be practiced at academic centers with established funding success and scientific expertise in the disease type or pathway to be the focus of the model. Examples might include models engineered to be relevant to cell cycle checkpoint control (Rb, pS3) apoptosis (bc12 family genes), molecularly defined but cell type-related (e.g., mutated androgen receptor in prostate cancer) or process-related (e.g., angiogenesis) disease endpoints. Spontaneous, genetically modified or induced (e.g., knockout), orthotopic and xenotransplanted models are all of potential interest, provided that their biological characteristics and correlation with relevant issues in the pathogenesis of neoplasia are clearly apparent.

Following the identification of appropriate candidate drug leads by the NCI Decision Network or similar governing bodies (e.g., RAID oversight or advisory group), and taking into account previously established pharmacologic and biological features of the test molecules, study in the in vivo model will be undertaken to define not only effects on cell proliferation as an endpoint, but also effects of the drug on its putative molecular target or cellular process of reference, e.g., level of expression or activity of a target, differentiation, apoptosis, cell cycle modulation, transcription factor activation, etc. The results of this project area would be evidence that a candidate compound could indeed affect a clearly defined molecular endpoint. This information would be of critical importance in designing initial clinical activities where the endpoint of the compound's action may not be classical cytotoxic effect, but for example, cytostasis or differentiation. This activity would support a new way of thinking about cancer drug action, which has modulation of important molecular targets or cellular processes as endpoints for early clinical trials, rather than merely pharmacology or anti-proliferative effects in very late-state tumor systems.

Preliminary Data: As an example of the type of interaction that this Master Agreement would attempt to make more general, workers at two academic centers recently expressed interest in pursuing a DTP lead compound which targeted the hsp90 chaperon molecule. DTP efforts to define in vivo activity in xenograft models selected only by the results of prior empiric in vitro screens had been negative, despite good evidence of biologic effect in the "hollow fiber" assay. However, a university-based researcher, funded by a small subcontract from the DTP SAIC contract at FCRDC, characterized modest but significant growth inhibitory activity in an in vivo xenograft model previously characterized in their center, but also documented clear modulation of hsp90 levels in tumor tissue. This result creates confidence that the compound can actually modulate hsp90 levels, and indeed provides a basis for a pharmacodynamic assay of drug effect in early clinical trials in humans. DTP would like to promote a series of academic or small business investigators who could be called into service as the need arises to evaluate the molecular effects of novel candidate compounds.

Objectives: First, to define the capacity of candidate compounds to affect molecular targets mediating compound efficacy in a series of in vivo models (which are ready for use) representing known important pathways in neoplasia; second, to validate methodologies that would assess molecular targets affected by drug candidates which would be readily "translated" to the clinical setting; and third, place these actions of the compound into the context

of conventional measures of tumor shrinkage or growth delay.

Following assignment by the Decision Network or RAID advisory committee, compounds which have previously been optimized with respect to formulation, route of administration, and pharmacology will be provided to Master Agreement holders, who have indicated through standard competition procedures for Master Agreement holders, an interest in working with the compound or compound class. The output of their work will be documentation of compound efficacy in modulating the molecular target which is the focus of the particular model, as well as measures of compound efficacy by conventional criteria. The data provided to the Project Officer would form a basis for more or less enthusiasm in promoting the development of the compound.

Methods: Transfection followed by xenotransplantation, knock-out, or transgenic approaches could be used to generate tumor cells or animals bearing tumors. The offeror will be expected to have already developed the model to be utilized; that is, this Master Agreement will NOT be used to fund developmental efforts to produce or validate the model. Each experiment will consist of appropriate control (vehicle-only) and drug-treated (dose-escalating) groups. Assessment of antiproliferative or growth inhibitory activity on the part of the test agent will be recorded according to published NCI, DTP standards.

Correlative studies, to assure that pharmacologically relevant concentrations of the test substance have been achieved, can be coordinated with other DTP contracts but will NOT be the focus of experiments to be conducted here. Instead, correlative pharmacodynamic studies utilizing immunohistochemistry, Westem blot, PCR or RNAse protection-based gene expression methodologies relevant to the molecular target of interest, and standard histopathology techniques will be an integral part of the operation of the Master Agreement, and should be clearly demonstrated to be within the skill and competence of the successful offeror. While it is assumed that drug treatments will be the major focus of the use of these Master Agreements, the offeror is encouraged to include capacity to examine other treatment modalities as well, including, for example, radiation therapy, photosensitization, inhaled or other special routes of delivery.

In Brief:

SSO Gives Ewing Award To Rep. John Porter

(Continued from page 1) research program. . . . **REP. JOHN PORTER**, chairman of the House Labor, HHS, and Education

Appropriations Subcommittee, will receive the James Ewing Layman's Award at the Annual Cancer Symposium of the Society of Surgical Oncology. The award is presented annually to a non-physician who has made a significant contribution to improving the care of cancer patients.... MARK COGGESHALL received the Leukemia Society of America Scholar Award of \$70,000 per year for five years. Coggeshall, assistant professor of microbiology at Ohio State University and a researcher at the Arthur G. James Cancer Hospital's Comprehensive Cancer Center, conducts research into the role of the SHIP protein in halting cell proliferation. . . . VINCENT DE VITA received the Commendatore Order of Merit of the Republic of Italy, presented by the Deputy Consul General of Italy, in recognition of contributions to the treatment and cure of cancer. DeVita is director of the Yale Cancer Center and former director of NCI. . . . FRANK HSU received a three-year, \$340,000 grant from the Gabriella Rich Leukemia Fund for basic research on lymphoma. Hsu is assistant professor of medicine/oncology, and codirector of the Immunology Research Program at Yale University School of Medicine. . . . DEBORAH MAYER received the Debbra Flomenhoft Humanitarian Award, presented by the Oncology Section of the American Physical Therapy Association. Mayer, a cancer counselor and educator, and a member of the NCI Board of Scientific Advisors, was recognized for her contributions to oncology rehabilitation and physical therapy. . . . EDWARD BEATTIE, medical director of the Beth Israel Cancer Center in New York, died earlier this month of skin cancer. He was 79. Beattie, a lung cancer specialist, was chief medical officer of Memorial Sloan-Kettering's Memorial Hospital from 1965 to 1983. In 1983, Beattie moved to the University of Miami, where he helped set up the university's cancer center. He moved to Beth Israel Medical Center in 1985, where he became chief of thoracic surgery and founding director of Beth Israel's David B. Kriser Lung Cancer Center. Beattie was named medical director of the Cancer Center in 1995.... WILLIAM MANNING HAENSZEL, an epidemiologist who was chief of the NCI biometry branch from 1962 to 1976, died March 13 at his home in Wheaton, IL. He was 88 and had Parkinson's disease. Haenszel retired from NCI in 1978 and became a professor at the University of Illinois. He began his career at NCI in 1947 as head of the biometrics section.