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Poverty Plays Key Role In Excess Cancer Deaths Among Minorities, President's Cancer Panel Hears

People who live in poverty are at a greater risk of dying from cancer due to cultural factors such as substandard living conditions, lack of information, risk promoting lifestyles, and diminished access to health care, experts told the President's Cancer Panel this month. Among blacks, poverty, rather than race, can explain much of the excess cancer death rate, according to an NCI study presented at the meeting. New Panel

(Continued to page 2)

In Brief

Harkin Proposes To Add Another $400 Million To NCI Budget, Money To Come From Defense

SEN. TOM HARKIN (D-IA) announced this week that he plans to introduce an amendment to the Senate's Labor, HHS, Education appropriations bill that would add $400 million to the Senate's proposed NCI budget of $2 billion. In a July 23 press conference, Harkin said the amount would bring the cancer budget to the "full professional judgement level." (NCI's Bypass Budget, its professional needs budget, calls for $2.6 billion in FY92, $200 million more than Harkin's proposal, but cancer program advocates at the press conference didn't quibble.) The Harkin amendment calls for adding a total of $3 billion to the bill for "several vital domestic programs," Harkin said, including, besides the $400 million for NCI, additions of $170 million for Alzheimer's research, $50 million for breast cancer screening efforts by the Centers for Disease Control, $100 million for mental illness, $150 million for education initiatives and $270 million for Pell grants, $100 million for the Ryan White AIDS Care Act (bringing the total to nearly $400 million), $100 million for CDC sponsored immunization program, $900 million for Head Start, and $800 million for home assistance and state grants. **HARKIN PROPOSES** to offset the spending by rescinding budget authority for unobligated balances in the Defense Department account from FY88-91. The amendment will not affect military personnel, operation and maintenance, training, readiness, family housing, National Guard or Reserves, Harkin said. **"WE DO A LOT OF TALKING** about priorities around here, and my amendment offers a choice," Harkin said. "Should our priority be funding programs created to combat a now nonexistent threat of the Warsaw Pact, or should we be investing in human resources here at home?" Cancer program advocates are asking their allies to write, call or fax their Congressional representives to support this measure, and the Senate bill that adds $200 million to the President's request for NCI (**The Cancer Letter,** July 19).

Poverty Is 'Powerful' Predictor Of Cancer Death, Cancer Panel Told

(Continued from page 1)

Chairman Harold Freeman, Harlem Hospital and former president of the American Cancer Society, said the Panel intends to examine issues such as poverty and access to health care--issues that go beyond NCI's role in cancer treatment, prevention, and basic research.

"I think NCI has done an incredible job over the past 20 years. But it is a mistake to think the effort is limited to what NCI can do," Freeman said in concluding remarks at the July 9 meeting at NIH. "NCI could do its job 100 percent and the American people will still get cancer. So the charge of the President's Cancer Panel is broader than that of NCI. It gets us into areas such as access.

"What we have shown in the research presented today is that the poor are at greater risk of dying from cancer," Freeman continued. "The culture in which people live is a major determinant of the diseases people will get. It is a complex set of issues that combine economics, culture, and our political will to solve a problem."

HHS Secretary Louis Sullivan hailed a "new beginning" for the Panel, which was newly appointed by President Bush earlier this year. Besides Freeman, the members are Nancy Brinker and Geza Jako. They replaced the late Armand Hammer, and former Panel members William Longmire and John Montgomery.

Sullivan said NCI has produced "some of our most creative and productive scientific work," however, "one out of every eight Americans can access these great miracles with great difficulty."

For example, five year survival from cancer is 52 percent for Americans overall, but only 38 percent for blacks.

"The reasons are many and complex," Sullivan said. Poor people are focused on "day to day survival," with little opportunity to seek medical care or cancer screening. "Poverty is a complex issue, a vicious cycle, perpetuated in generation after generation of disparity. I believe this cycle can be broken and with education and support those in poverty can assume a role in their own care," he said.

Sullivan called for a "culture of character" in which individuals would take responsibility "for their lives, for their health, and their children's health."

HHS last year published a report, "Healthy People 2000," that lists 20 priorities for health in America, including those for cancer prevention and reduction of tobacco use. Sullivan said some HHS priorities are smoking cessation in rural and inner city areas, improved diets, and availability of cancer screening methods. Other goals are smokefree workplaces, state laws prohibiting and enforcing the sale of tobacco to minors, and cancer screening for poor women in urban areas. "We can do a lot," Sullivan said, pointing out that in 1965, 40 percent of American adults smoked, while now about 20 percent smoke, the result of "massive public education." The goal for the year 2000 is less than 15 percent.

Sullivan concluded that, "The war on cancer is not over. Everyone knows we have a long way to go. The magnificent advances we have made so far belong to everyone. Sophisticated health care is not the sole province of the rich. We must address unemployment, poor housing, inadequate health care, and everything else that puts this group of Americans at a disadvantage. We must treat the whole problem with whole solutions."

NIH Director Bernadine Healy commended the new Panel members for undertaking a "very serious responsibility." The Panel, she said, "intends to tackle issues of great national importance." Cancer is a major component of the trans-NIH Healthy Women's Study, and the study results will be applicable to all women and all interventions in the study must be "culturally sensitive and applicable."

NCI Director Samuel Broder called poverty "one of the most powerful and underestimated factors in the U.S. and throughout the world" in relation to cancer incidence and mortality. "We hope this meeting will mark an additional acknowledgement of poverty as a cause of cancer. For individuals on the edge of poverty, cancer in one member often leads them down the slippery slide to poverty," he said. "Though our topic today is cancer, it would be possible for any of

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the institutes to hold a meeting on poverty and disease; it is not unique to cancer."

One third of the American black population lives in poverty, compared to 10 percent of the white population. What Broder called "poverty driven lifestyles" may partly account for the higher mortality rate among low income blacks. Studies have found that 40 percent of black males had never heard of the digital rectal examination for prostate cancer, and half of black women had never heard of a mammogram. NCI is targeting information campaigns to those groups, he said, and is trying to include educational materials on cancer in Spanish.

Low income populations also have a heavier use of alcohol and tobacco, and unhealthy diets. What's more, "it is difficult for a woman to go for a mammogram, when she has a significant concern about paying for that evening's meal. It is difficult for young people to worry about the effects of smoking when they fear murder in streets," Broder said.

NCI is "committed to see that all of the people" benefit from advances generated by cancer research, Broder said. "We need to make sure the knowledge we generate doesn't lead to more disparity."

Broder highlighted several NCI programs that are useful for combatting cancer in the poor: the Surveillance, Epidemiology & End Results Program which provides cancer survival and incidence rates, the ASSIST smoking cessation demonstration program, the Cancer Information Service and the 1-800-4-CANCER phone number, NCI sponsored clinical trials, and the NCI designated comprehensive cancer centers, which now must conduct community outreach and prevention efforts. NCI also supports the National Black Leadership Initiative on Cancer and is replicating that effort in the Hispanic community. In addition, Broder stressed the importance of encouraging young minorities to pursue careers in science, the goal of NCI's Science Enrichment Program, which brings minority high school students to work with NCI scientists over the summer.

"I personally think cancer is a curable disease," Broder concluded. "The research supported by NCI will lead inexorably to progress in cancer. One should begin to address how the knowledge of NCI will be utilized."

An NCI study found that the disproportionate number of blacks at lower socioeconomic levels can explain much of the excess cancer burden blacks suffer compared to whites, said Claudia Baquet, director of the Cancer Control Science Program in NCI's Div. of Cancer Prevention & Control. The study matched cancer incidence and mortality from 1978-1982 with 1980 census information on socioeconomic status within individual census tracts in the metropolitan areas of San Francisco/Oakland, Detroit, and Atlanta.

Before adjusting for income level, education, and population density, blacks showed a 7 to 10 percent greater risk of developing cancer than whites. Cancer at only one site, the colon, showed no association with race, according to the study, published in the April 17 issue of the "Journal of the National Cancer Institute." When the data were adjusted for the three factors, the risks reversed: whites showed an elevated risk of cancer, 6 percent greater than that of blacks. However, the excessive rates for development of cervical, stomach and prostate cancer did not disappear, said Baquet, the lead author on the article.

"For all sites, for blacks and whites, the risk of cancer increases as education and income decrease and as population density increases," Baquet said. "Low income areas" showed excessive cancer incidence of 20 percent.

Further analysis of the study is being conducted to flesh out information on survival, but Baquet said preliminary data appear to show that survival is similar across racial lines; what matters most in survival is the level of income and education. "Upper income blacks survive better than lower income blacks; the same thing happens for whites," Baquet said.

"These analyses give support to the hypothesis that poverty does contribute to cancer incidence and survival outcome," Baquet said. But she cautioned against a "simplistic approach--an increase education or a check won't boost the outcome."

The "JNCI" article offered some suggestions: "Based on the findings of this study, it appears that several areas could be targeted for interventions in low income, high population density black and white populations. For example, low income women should be specifically targeted for Pap screening programs. Clearly, there is a need for developing stop smoking programs in these populations, which should contain appropriate, culturally sensitive programmatic components. Specific targeting of interventions to high risk population groups would enable more efficient utilization of available cancer intervention resources."

Freeman suggested that NCI and other government agencies examine how the data collection could be modified to allow for ongoing collection of the information that Baquet's study compiled. SEER does not collect socioeconomic status data due to privacy issues.

George Lundberg, editor of the "Journal of the American Medical Assn.," told the Panel that 36

million Americans are uninsured, and Medicaid covers only 40 percent of those in poverty.

"I believe we are now poised on the brink of a medical system meltdown, by 1996 if there are no changes," he said. "JAMA" devoted a recent issue to proposals for health system reform. "Surely we in this rich and successful country can provide health care to all because it is the right thing to do. It is no longer acceptable morally or ethically for so many of our people to be medically uninsured or underinsured."

Lundberg said he believes that "proper organization of existing resources" would solve the problem. "We have to have real, significant cost control. We have to get primary care medicine back into the curriculum in medical schools." Government, he said, "finds the money for what the people tell it to find it for." In that respect, he said he has been encouraged by the recent response on Capitol Hill to the problem of health insurance. "There's a tremendous feeling that we have to do something," he said.

Lundberg was asked to further explain what he meant by a health system "meltdown." "What will happen is compromise, starting with patients not being able to get every glitzy new thing and doctors not being able to get what they want. I do not think it will be patients rioting to get into hospitals, but it might be hospitals closing in large numbers, though that might be a good thing. . . . The big winners are going to be the people who don't have access to care, and the industry itself. The money grubbing doctors who shouldn't have come into medicine in the first place--those are the losers."

Freeman asked Lundberg to comment on the nation's "war on cancer" begun with the National Cancer Act of 1971. "I was cheering at that time," Lundberg said. "I think it was a marvelous thing to declare war on, but don't think it is something we can win right away." Not all the basic scientific information was available at that time, he said. "Probably early on, there may have been more money spent on basic science than on prevention. If we could use what we already know, we could be doing a whole lot better," he said.

Broder took issue with that statement, emphasizing "the importance of science and the scientific method," and pointing out that NCI's budget has 6 percent less buying power than it had in 1980. Some basic science, he said, "is ripe for translation from bench to bedside." He stressed that NCI is "a scholarly organization."

"Second, I do not agree with the statement that doctors are responsible for the problem, but this is a national or even global difficulty," Broder said. "I do not endorse the view that physicians are to be singled out. Physicians are not responsible for poverty."

Freeman suggested that NCI's next target for study might be the rural populations of Appalachia, which have a higher proportion of cancer risk and are geographically isolated from prevention and control services. "We recognize need to look at appalachia," Baquet said.

Gilbert Friedell, director of cancer control for the Lucille Markey Cancer Center at Univ. of Kentucky, presented data from the Kentucky Cervical Cancer Study. The study found the incidence of invasive cervical cancer among white females in rural Kentucky from 1986-87 was 15.1 per 100,000, nearly twice the rate among white females nationwide. In Kentucky, the cervical cancer rate is the same as the national rate for black females, and nearly the same as the rate in "inner city Chicago," he said. Mortality was twice the rate of U.S. white females. Poverty, not race, explained the findings, Friedell said.

The Panel has scheduled its next meeting for Sept. 20 in Atlanta, GA.

Under the National Cancer Act of 1971, the President's Cancer Panel is charged to "monitor the development and execution of the National Cancer Program and report directly to the President. Any delays or blockages in rapid execution of the Program shall immediately be brought to the attention of the President. In addition, the panel annually evaluates the efficacy of the Program and makes suggestions for improvements, and shall submit such other reports as the President shall direct."

NCI Plans Cancer Vaccine RFAs, Approved In Concept By Advisors

Advisors to two NCI divisions have given concept approval to two complementary new grant programs to encourage research on cancer vaccines. The programs together would provide $4 million per year for approximately 20 grants, for four to five years.

The RFAs, approved in concept recently by the Boards of Scientific Counselors of the Div. of Cancer Etiology and the Div. of Cancer Biology, Diagnosis & Centers, grew out of an NCI workshop last fall on cancer vaccine research. Congressional interest in vaccine research had prompted the workshop.

Following are the two concept statements:

Vaccines for human cancers of viral etiology. Proposed RFA, $8 million over four years; first year funding $2 million; 9-10 grants (Div. of Cancer Etiology).

The possibility of developing cancer vaccines is complicated by the fact that cancer is a diverse set of diseases, some of which are associated with specific etiological agents, such as

viruses, and others of still unknown etiology. The conventional vaccine approach depends on the ability to identify specific antigens associated with ar particular disease entity or neoplasia and to elicit an appropriate protective host immune response to those antigens. Thus, for those cancers in which a viral disease plays a major role, a conventional vaccine approach could be feasible. Such a vaccine should be designed to prevent initial virus infection, and could additionally prevent the cancers assoicated later in life with that virus. Alternately, a therapeutic vaccine approach could be used in which tumor antigens and/or modified cellular substances appearing during the neoplastic process are reintroduced into the patient to stimulate antitumor activity and prevent the spread or recurrence of the tumor.

Before any cancer vaccine studies could be carried out, a number of basic issues needed to be addressed. An NCI workshop on cancer vaccines was held in Bethesda on Oct. 29-30, 1990. Myron Essex, Harvard Univ. School of Public Health and a member of the DCE Board of Scientific Counselors, chaired the workshop. Among the observations made at the meeting:

a) The importance of isolation and identification of common antigens for several types of cancer, penetration of antibodies into tumors and the choice of appropriate populations in which to test cancer vaccines.

b) The need to keep the goals simple, and not to try to solve problems that do no really exist, since successful vaccines have been developed in the past from a base of meager knowledge and an almost total void of understanding.

c) The importance of both humoral and cellular responses in developing possible cancer vaccines, and the role of T-cells and their ability to react with antigens which may not be expressed on the cell surface.

d) The importance of major histocompatibility complexes in antigen processing and presentation, and the availability of new techniques and procedures to identify immunodominant epitopes and to produce polypeptides containing a variety of these epitopes in order to increase the likelihood of an immune response.

e) The necessity to avoiding tolerance or the production of enhancing antibodies, and the difficulty of achieving successful immunotherapy in patietns with already established cancers, particularly solid tumors.

f) The presence of a defined viral etiologic agent which often, but not always, simplifies the production of vaccines, since the identification of viral antigens which elicit a protective response is somewhat more straighforward than identification of protective antigens in tumors of unknown etiology.

g) The importance of testing vaccines in a manner which approximates the realistic patterns of natural exposure, appreciating the diverse nature of the protective immune responses for difference diseases, and the difficulties of post exposure immunotherapy.

h) The significant problems of dealing with viral systems such as papillomaviruses, where the oncogenci potential in humans is strain specific and could require multiple vaccines to protect against a disease such as cervical cancer.

i) The important role of the Epstein-Barr virus in nasopharyngeal carcinoma, Burkitt's lymphoma, B-cell malignant lymphoproliferative diseases in immunodeficient individuals, Hodgkin's disease, CNS lymphoma, malignant lymphoproliferative disease of large granular lymphocytes, and certain T-cell lymphomas, which appear to justify efforts to produce an EBV vaccine.

j) The prospect that the hepatitis B virus vaccine, by preventing the establishment of the chronic carrier state of HBV in newborns, could prevent an extremely large percentage of the worldwide cases of primary hepatocellular carcinoma and thus, a vaccine for a specific human cancer of known viral etiology is already available and in use.

k) The possible association of viral agents other than HBV (e.g., non-A, non-B hepatitis or hepatitis C) in Japan, and perhaps in other countries, with liver cancer.

The thrust of this proposed RFA is to stimulate basic and applied research leading to the development of vaccines for human cancers of known, or strongly suspected, viral etiology, including cancers associated with HPVs, EBV, and HCV. Identification of protective viral or viral induced antigens which form the basis for vaccine preparation, development of antimal models to determine host immune response to viral induced tumors and to test the safety and efficacy of proposed vaccines, and the development of prototype therapeutic vaccines for viruses whose malignant sequelae occur as the result of chronic infection are all encouraged.

Development of a vaccine for HPV is made more difficult by the fact that there are no simple infectivity assays, no clear indication of the presence of a neutralizing antibody for HPV associated carcinoma in humans, and no suitable animal model or tissue culture system for viral propagation. Examples of research on HPVs would include 1) addressing the problem of multiple HPV types associated with human cancers and whether a polyvalent vaccine would be required, 2) identification of the relevant immunological determinants and defining if they are virion proteins, 3) developing other ways of expressing viral proteins since in vitro replication of the virus is presently impossible. This could be a significant problem if the expression of viral proteins in bacteria is not sufficient to develop good immunogens, 4) the possible importance of nonstructural viral proteins in mediating either prevention or regression, 5) development of animal models of infection and oncogenesis and development of bioassays for infectious virus, 6) development of immunoassays that correlate with resistance.

EBV has been associated with Burkitt's lymphoma, nasopharyngeal carcinoma, B-cell lymphoproliferative diseases in immunodeficient individuals, and several other malignancies, as well as with infectious mononucleosis. Nasopharyngeal carcinoma appears to represent a replicative infection, since those patients have high titers of secretory antibodies to EBV. B-cell lymphomas in immunocompromised individuals may represent the result of latent infection, a stage where few EBV genes are expressed but lymphocytes are altered and can proliferate indefinitely. EBV appears to play a variable role in a number of malignancies.

Examples of research objectives for EBV would include: 1) studies of the pathogenesis of EBV induced lymphomas in the SCID mouse, and the use of immune reconstitution by selected human lymphocyte populations to control the lymphomas, 2) development and assessment of EB viral mutants as inactivated vaccines, 3) development and assessment of glycoprotein vaccines as purified components or incorporated into replicating viruses, 4) studies of the association of EBV with various malignancies, particularly the incidence and importance of B-cell malignancy in immunodeficient patients and the relationship between EBV and Hodgkin's lymphoma, and 5) studies of the immune mechanisms which control EBV replication and the proliferation of transformed B-cells, particularly in patients recovering from mononucleosis.

Non-A, non-B hepatitis virus recently has been designated hepatitis C virus. HCV causes an acute hepatitis which is somewhat milder than HBV induced disease, however, it has been estimated that at least half of the NANBH infections result in chronic hepatitis, which in turn results in cirrhosis in approximately 20 percent of these cases. Chronicity and cirrhosis carry increased risk of PHC. Up to 10 percent of transfusions in

the US are thought to result in hepatitis and more than 90 percent of the transfusion associated hepatitis in the US is associated with HCV.

Examples of research objectives for HCV would include: 1) development and/or use of sensitive and specific assays for blood born NANBH (HCV) to determine the etiologic role of this agent in PHC, 2) studies of pathogenesis of HCV infections and determinants of oncogenesis, 3) development of animal models for HCV infection/oncogenesis, 4) identification of protective HCV epitopes which could lead to development of vaccines, 5) determination, in transgenic antimals, of the oncogenic potential of specific viral gene products and 6) determination of the possible role of cellular oncogenes or antioncogenes in HCV induced PHC.

Board member Myron Essex said others might be "pessimistic" about the opportunities for vaccine research since little is understood, but he pointed out that, "We now have a very effective feline leukemia virus vaccine," which shows that the research opportunities are available. Other board members agreed, but questioned the concept's exclusion of HTLV research. NCI staff said the decision was made not to "muddy the water" of the RFA with inclusion of HTLV. DCE Director Richard Adamson said another workshop focusing on HTLV might be in order.

In his remarks, Essex concluded that, "This was suggested by Congress, but surprisingly, I think it was a very good idea. So sometimes it pays to listen to higher bodies."

"We always listen to them," Adamson said.

The concept was unanimously approved.

Immunologic recognition and control of tumors: a basis for cancer vaccines. Proposed RFA, total cost $10 million over five years ($2 million per year), 10-11 awards (Div. of Cancer Biology, Diagnosis & Centers).

The intent of this initiative is to accelerate the application of emerging immunologic concepts of antigen recognition and cellular effector mechansisms to the special problems of cancer immunology. The past five years have brought revolutionary changes in immunology. These changes have forced a reexamination of the theoretical basis of much of cancer immunology and have opened major new research opportunities. The goal of this proposed RFA is to encourage further applications in selected areas that seem ready for investigation.

These areas can be divided into two broad groups, dealing with initiation of specific immune recognition and improvement of an ongoing immune response, respectively. In the phase of initial recongition, the emphasis is on identification of tumor associated antigens recognized by T cells and development of novel methods to improve T cell recognition of tumors. For ongoing immune responses, the areas of emphasis include, but are not limited to, genetic manipulation of tumor or immune cells (not limited to T cells) with cytokine or other genes to improve the effectiveness of an antitumor immune response, approaches to increasing the number of antitumor immune cells and their capacity to reach sites of tumor growth, and identification of mechanisms (tolerance or suppression) that lead to downregulation of otherwise effective immune responses to tumors.

Tumor associated antigens were originally defined operationally by their ability to immunize against subsequent tumor challenge. In recent years, the overwhelming focus of cancer immunology has been on the identification of cell surface tumor associated antigens; as detected and defined by monoclonal antibodies. These studies were very successful in identifying important differentiation antigens. They produced some important diagnostic reagents and still have treatment potential through immunotoxin and radioconjugate approaches. What this type of study could not do was to identify epitopes of importance for stimulating the T cell limb of the immune system. The reasons for this limitation have now been illuminated by a series of fundamental discoveries in basic immunology.

Chief among these discoveries is the elucidation of the mechansism of T cell antigen recognition. The CD4+ (helper/inducer) T cells see fragments of antigen bound to class II Major Histocompatibility Complex antigens on specialized antigen presenting cells. The antigens are derived from the extracellular environment and fragmented by the antigen presenting cell. The CD8+ (cytotoxic/suppressor) T cells, in contrast, see antigen fragments bound to class I MHC antigens on target cells. These antigenic fragments are derived only from proteins synthesized within the cell, but they are not limited to proteins destined to be cell surface molecules. Following the intial antigen recognition event, the development of an effective immune response depends on proper communication between immune cell subsets.

Communication between the major subsets of immune cells is controlled by local secretion of cytokins, which is in turn dependent on specific intracellular signals generated in the T cell following antigen recognition. Changes in the cytokines produced can augment or depress the effector arm of the immune response. Certain patterns of recognition lead to tolerance, a long lived paralysis of the immune system. These discoveries have necessitated a new approach to cancer immunoloyg and provided a firm theoretical foundation of tumors by T cells and the identification of cellular interactions and/or patterns of cytokine secretion that can translate recognition into an effective, cytotoxic response to the tumor.

Recent developments in molecular biology have provided powerful tools with which to accomplish these new goals. There have been enough applications of new concepts and new methodology to cancer immunology to demonstrate enormous promise. What is needed now is an expansion of these efforts, which will involve not only established investigators in the field, but a new generation of scientists who have been trained in these concepts and methods, but who may not appreciate the opportunties that tumor systems have to offer.

Board member Margaret Kripke said she favored the RFA concept to "stimulate" this research; many in this field have a perception that study sections have not looked favorably upon this area, and investigators have "shied away" from this research, she said. DCBDC Director Alan Rabson said money probably would be available in FY92 to fund the RFA.

The concept was approved unanimously.

The DCBDC Board also approved an RFA concept titled, "Clinical Correlative Studies in Solid Tumors," which would provide $6 million over three years ($2 million per year) to fund cooperative agreements (U01s). The goal of the program is to promote "collaboration between basic researchers and clinical

investigators to advance research on clinical correlations that can improve therapeutic approaches," according to the concept statement. The program is funded in cooperation with the Div. of Cancer Treatment; the DCT Board approved the concept at its meeting in June. The text of the concept statement was published in the June 21 issue of **The Cancer Letter.**

The DCE Board also gave concept approval to a new grant program to stimulate research on domestic animal models for retrovirus associated human cancers. "Agriculture schools have the models, but they don't support reserach on the models," said Adamson. Following is the concept statement, which was unanimously approved:

Domestic Animal Models for Retrovirus-Associated Human Cancers. Proposed RFA, first year funding (FY92) $750,000, four years.

Animal retroviruses isolated from many mammalian species have the potential to provide valuable basic information on the etiology and mechanism(s) of cancer induction by viruses. Mammalian retroviruses have been isolated from humans, monkeys, mice, cats, cows, goats, sheep, pigs and horses. In some virally infected animals, neoplastic and Kaposi's sarcoma-like lesions have been observed, supporting the hypothesis that retroviruses may be directly or indirectly involved in the development of malignancies. Retrovirus animal models may therefore aid in investigations of the initiation and progression of neoplasia of viral origin and provide a better understanding of the role of viruses in the etiology of human cancer.

A NCI workshop entitled "Animal Models of Retrovirus-Associated Malignancies" was organized by the Biological Carcinogenesis Branch. The workshop focused on the current status of research on the role of retroviruses in the etiology of domestic animal cancers, including both lymphoid malignancies and sarcomas. The neoplastic potential of various retroviruses and the different molecular mechanisms by which viruses might be involved in the neoplastic processes were discussed. It was pointed out that retroviruses can transcriptionally activate host genes by cis- or trans-mechanisms or inactivate host genes by direct insertional disruption. In the avian and rodent system, it has been generally accepted that retroviral insertional activation (and, in one case, inactivation) of cellular oncogenes represents a key step in oncogenesis caused by nonacute retroviruses which do not carry their own oncogenes. A by-product of this process is the genesis of oncogene-transducing retroviruses. Workshop participants also noted that little is known about the ability of the host to restrict the replication of retroviruses, and thus it is not known which host factors determine whether a virus replicates lytically or might be involved in the initiation or progression of neoplastic sequelae. Some retroviruses, such as the equine infectious anemia virus in horses have not been shown to be involved in malignant sequelae, while other retroviruses, such as the feline leukemia viruses, are frequently involved in malignancies. The workshop participants concluded that studies on the pathogenesis of cancers of viral origin from animal models should result in additional information and knowledge relevant to human cancer.

Based on the recommendations from the workshop participants, the objectives of the RFA are designed to encourage basic research on retroviral pathogenesis in domestic animals. These studies will aid in understanding the properties of viruses and features of the host and its response that determine disease progression from initial virus infection to neoplastic sequelae. For the purposes of this RFA, domestic animals include cows, horses, sheep, goats, and pigs; specifically excluded are retroviruses of dogs, cats, primates and avian species. Collaborative efforts between scientists with complementary areas of research expertise will be encouraged. Specific research topics of interest to the NCI, include, but are not limited to:

1) Study of the oncogenic mechanisms in domestic animal retroviruses; 2) investigation of cancer etiology and viral pathogenesis from initial infection through the development of pre-neoplastic lesions and neoplastic sequelae with retroviruses of domestic animals; 3) the role of RNA and DNA viral co-factors in cancer etiology in animal models; 4) investigations to assess the role of the host immune system and host genetic factors in the control and limitation of virus replication, and the susceptibility or resistance of animals to oncogenic processes; 5) studies on the expression and regulation of viral and/or associated host cell genes in pre-neoplastic lesions and malignant tissues from retrovirus-infected domestic animals.

NCI Advisory Group, Other Cancer Meetings For Aug., Sept., Future

American Assn. for Clinical Chemistry Annual Meeting--July 28-Aug. 1, Washington, DC. Contact Nick Ryerson, 800/892-1400 or 202/835-8718.

Cancer Centers Support Grant Review Committee--Aug. 1-2, Hyatt Regency Bethesda, MD, One Bethesda Metro Center. Open both days from 8-8:30 a.m.

Enterostomal Therapy Nursing: Across the Life Span--Aug. 12-13, Cleveland, OH. Contact Cleveland Clinic Foundation, Dept. of Continuing Education, PO Box 94977, Cleveland, OH 44195, phone 216/444-5696 or 800/762-8173.

Oncology Nursing Certification Exam Review--Aug. 16-17, Tampa, FL. Contact St. Joseph's Cancer Institute, 813/870-4320.

Beijing Blood Cell Growth Factors Symposium--Aug. 21-24, Beijing, China, Beijing International Hotel. Contact Dr. Ann Murphy, Hipple Cancer Research Center, 4100 South Kettering Blvd., Dayton, OH 45439-2092, phone 513/293-8508 or fax 513/293-7652.

Primary Care Medicine--Aug. 23-25, San Diego, CA. Contact Laurel Steigerwald, Scripps Clinic & Research Foundation, phone 619/554-8556.

Breast Cancer Working Conference--Sept. 3-6, Leuven, Belgium. Contact EORTC Univ. Hosp. St. Rafael, Radiotherapy Dept., Capucijnenvoer 33, 3000 Leuven, Belgium.

Exercise, Calories, Fat & Cancer--Sept. 4-5, Pentagon City, VA. Ritz Carlton Hotel. Sponsored by American Institute for Cancer Research. Contact Rita Taliaferro, Conference Management Div., Associate Consultants Inc., 1726 M St. NW Suite 400, Washington, DC 20036, phone 202/737-8062.

International Conference on Human Tumor Markers--Sept. 8-11, Istanbul, Turkey. Contact Dr. Gurol Buyuk, Buyuk Laboraturari, Buyukdee Cad. 127, 80300 Gayrettepe, Istanbul, Turkey.

Arizona Cancer Center North American Conference on Cancer in Hispanics--Sept. 12-14, Tucson, AZ. Contact Nancy Rzewuski, Arizona Cancer Center, Tucson, AZ 85724, phone 602/626-2276.

Transrectal Ultrasound--Sept. 13-14, Chicago, IL. Contact DCMI, PO Box 2508, Ann Arbor, MI 48106, phone 313/665-2535 or 800/458-2535.

Benign & Malignant Bone Tumors--Sept. 14, Los Angeles.

Contact Beulah Anderson, American Cancer Society, 3255 Wilshire Blvd. Suite 701, Los Angeles, CA 90010, phone 213/386-6102.

International Congress on Hormones and Cancer--Sept. 15-19, Amsterdam, Netherlands. Contact Netherlands CAncer Inst., Plesmanlaan 121, 1066 CX, Amsterdam, Netherlands.

Cancer Epidemiology/Genetics of Cancer--Sept. 19-20, Turku, Finland. Contact Cancer Society of Finland, Liisankatu 21B, 00170, Helsinki, Finland.

President's Cancer Panel--Sept. 20, Atlanta, GA. Moorehouse School of Medicine, Basic Medical Science Bldg. Rm 104, 720 Westview Dr. SW, Atlanta, GA 30310.

Cancer Management Course--Sept. 20-21, Mayo Clinic, Rochester, NY. Contact American College of Surgeons, Cancer Dept., 55 East Erie St., Chicago, IL 60611, phone 312/664-4050.

Pheresis--Sept. 20-21, Houston, TX. Contact Jeff Rasco, Conference Services, Box 131, 1515 Holcombe Blvd., Houston, TX, phone 713/792-2222.

International Gynecologic Cancer Society--Sept. 22-26, Cairns, Australia. Contact Australian Convention Services, PO Box 468, Paddington NSW 2021, Australia.

National Cancer Advisory Board--Sept. 23-24, NIH Bldg. 31 Conf. Rm 6. Open 8:30 a.m. on Sept. 23. Complete schedule/committee meetings not available.

Current Topics in Lung Cancer--Sept. 23-25, Venice, Italy. Contact European School of Oncology, Via Venezian 18, 20133 Milan, Italy.

Methodology of Clinical Trials--Sept. 23-27, Venice, Italy. Contact European School of Oncology, Via Venezian 18, 20133 Milan, Italy.

Chlorinated Dioxins and Related Compounds--Sept. 23-27, Research Triangle Park, NC. Contact Office of Continuing Education, Unvi. of North Carolina School of Public Health, phone 919/966-4032.

Aging and Cellular Defense Mechanisms--Sept. 23-27, Modena, Italy. Contact Marketing Dept., New York Academy of Sciences, 2 East 63rd St., New York, NY 10021, phone 212/838-0230.

International Symposium on Colorectal Cancer--Sept. 24-25, Turin, Italy. Contact Scientific Secretariat, Dept. of Oncology, Via Cavour, 31, 10123 Torino, Italy, fax 0039-11-8398477.

Cadmium in the Human Environment--Sept. 25-27, Gargnano, Italy. Contact IARC, 150 cours Albert Thomas, 69372 Lyon Cedex 08, France.

Society for Leukocyte Biology Annual Meeting--Sept. 26-28, Aspen, CO. Contact SLB, c/o Dr. Sherwood Reichard, Medical College of Georgia, 1120 15th St., Augusta, GA 30912, phone 404/721-2601.

Familial Cancer--Sept. 27-28, Lugano, Switzerland. Contact European School of Oncology, Via Venezian 18, 20133 Milan, Italy.

Pain: Diagnosis, Treatment & Management--Sept. 28, La Jolla, CA. Contact Laurel Steigerwald, Scripps Clinic & Research Foundation, phone 619/554-8556.

Future Meetings

International Nursing Research Conference/American Academy of Nursing Annual Meeting--Oct. 22-26, Los Angeles. Contact American Nurses Assn., 2420 Pershing Rd., Kansas City, MO 64108, phone 816/474-5720.

Current Issues in Pediatric Hematology/Oncology--Nov. 21-23, Orlando, FL. Contact Nancy Pollock, FAPTP, PO Box 13372, Gainesville, FL 32604, phone 904/375-6848.

Cellular Responses to Environmental DNA Damage--Dec. 1-6, Banff, Alberta, Canada. Contact American Assn. for Cancer Research, Public Ledger Bldg. Suite 816, 6th & Chestnut Sts., Philadelphia, PA 19106, phone 215/440-9300.

Current Concepts in Cancer Management: Symposium for Primary Care Physicians and Cancer Care Providers--Feb. 13-15, Newport Beach, CA, Hoag Cancer Center. Contact Meeting Management, Biotherapy of Cancer, 5665 Oberlin Dr., Suite 110, San Diego, CA 92121, phone 619/453-6222.

American Radium Society Annual Meeting--April 11-15, Walt Disney World Swan, Orlando, FL. Abstract deadline Oct. 31. Contact ARS, 1101 Market St. Suite 1400, Philadelphia, PA 19107, phone 215/574-3179.

Taxol Issue Prompts Questions From One Cancer Letter Reader

The complex and interesting problem of the procurement of the bark of the Pacific yew tree for the extraction of the promising anticancer drug taxol has been reported in **The Cancer Letter** recently (June 14 and July 5). Mike Kiley, director of the Interactive Reimbursement Information Service funded by Schering Laboratories, submitted the following letter in response to the June 14 article.

To the Editor:

Thank you for your reports. Most of what I know about the yew I learned in your pages. One question, though: What is the larger configuration of interests involving the yew?

The interests I see are (1) yew harvesting for cancer therapy, (2) timber harvesting, both per se and clearcutting as a method, (3) spotted owl habitat, (4) old growth forest preservation. Is the issue (1) versus (3)? Is there an issue of (1) versus (4)? Is there an issue of (1) versus (2)?

I can't see the conflict between (1) and (3), although you are reporting news and the news is of spokespeople supporting the spotted owl who oppose yew harvesting. It seems to me that yews can be cut without displacing the owl. But they would have to be cut selectively, and not clearcut. To me the real conflict with the owl is (3) versus (2), clearcutting. There is no question that preservation of the owl habitat and clearcutting are in conflict. I think (1) versus (3) is a straw man.

Similarly, I see the historical conflict as between (1) and (2). Historically, the practice of timber harvesting by clearcutting has treated yews as wastage. For decades, yews and other flora were tragically wasted to allow cheap harvesting of the Douglas fir. This conflict is, therefore, the conflict between economic practices involving botanical wastage and the selective harvesting of botanicals.

In the same light, there seems to be no issue of (1) versus (4), of yew harvesting versus old growth forest preservation. Only the method of timbering by clearcutting actually conflicts with preserving old growth forests. The yew can be harvested in old growth areas without destroying them, can it not?

So it seems to me that there is no fundamental conflict between either preservation objective (owl habitat and old growth forest) and taxol harvesting. It seems to me that there is a fundamental conflict and a historical anomaly between timbering by clearcutting and yew harvesting. I also think that a pseudo-conflict between conservationists and yew harvesting is a straw man, the result of which is to lend undue support to timber harvesting by clearcutting, the cause of a tragic history of wastage of a precious antineoplastic botanical.

The Cancer Letter welcomes letters to the editor. Letters may be sent to P.O. Box 15189, Washington, D.C. 20003, or faxed to 202/543-6879.