THE CANCER LETTER

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National Cancer Act Of 1971 Commemorated In Symposium Marking Progress, Future Goals

The National Cancer Advisory Board marked the 20th anniversary of the National Cancer Act of 1971 with a one day scientific symposium that highlighted "Past Accomplishments, Future Goals" in cancer prevention, molecular biology, immunology, radiology and cancer imaging, biologic therapies, and clinical treatment.

The Act, signed by President Richard Nixon on Dec. 23, 1971, gave NCI enhanced authorities and a major budget increase, established the President's Cancer Panel to advise on areas of progress and impediments

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In Brief

Baltimore Resigns As Rockefeller President; Perry Named Medical Director At Ellis Fischel

DAVID BALTIMORE, Nobel prizewinner and key figure in one of the longest scientific fraud investigations, last week resigned as president of Rockefeller Univ., saying the controversy had created "a climate of unhappiness among some in the university that could not be dispelled." Baltimore served for less than two years in the post. The controversy stemmed from a 1986 "Cell" paper co-authored with Tufts Univ. researcher Thereza Imanishi-Kari. Though he was never accused of misconduct, Baltimore's defense of Imanishi-Kari was criticized. Later, he asked "Cell" to retract the paper and made a public appology. . . . **MICHAEL PERRY** has been appointed medical director of Ellis Fischel Cancer Center, which is now part of the Univ. of Missouri-Columbia Health Sciences Center. Perry is also senior associate dean for the university's School of Medicine. . . . **"TOBACCO CONTROL:** An International Journal," will begin publication next spring by the British Medical Assn. It is the first scientific journal to be devoted exclusively to issues related to smoking, tobacco, and tobacco use control. Its editor is Ronald Davis, chief medical officer, Michigan Dept. of Public Health and former director of the U.S. Office on Smoking and Health. . . . **JUDITH WHALEN,** NCI planning officer, has left NCI after 22 years to become chief of the Office of Science Policy & Analysis at the National Institute of Child Health & Human Development. She began her new job earlier this month. . . . **RESEARCH SYMPOSIUM** to honor NCI's departing Radiation Oncology Branch Chief Eli Glatstein is scheduled for Jan. 8 at Masur Auditorium in the NIH Clinical Center, 8:30 a.m.-4:30 p.m. Further information, contact NCI Clinical Director Gregory Curt, 301/496-4251.

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NCAB Symposium Marks Progress At Cancer Act 20th Anniversary

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to the National Cancer Program, made the NCI director a presidential appointment, and allowed NCI to submit a bypass budget directly to the President.

"The passage of the National Cancer Act in 1971 signaled the beginning of an escalated war on this disease," NCAB Chairman Paul Calabresi said at the Nov. 26 symposium. "Considerable progress has been made, but the struggle continues. At this time, it is appropriate that we temper our celebration with cautious optimism by observing the landmark and rededicating our efforts until final victory is achieved."

Calabresi noted that, "One of the most significant accomplishments of the National Cancer Act has been to transfer expeditiously the new scientific discoveries of research laboratories to the clinical setting. This has occurred by implementation of a number of important initiatives whose essential elements we must never allow to compromise. First, a substantial increase in funding for cancer research, accompanied by reduction of bureaucratic obstacles, has generated immediate enthusiasm and revitalization of the field. This resulted in a much needed increase in physicians and scientists dedicated to clinical and investigative oncology.

"Another contribution was establishment of additional comprehensive cancer centers, which have grown from three in 1971 to 28 in 1991. These coupled with specialized clinical research centers, the clinical cooperative groups, and the Community Clinical Oncology Program, has greatly expanded the number of patients to derive rapid betterment from experimental therapeutic advances.

"Finally, the development of the Cancer Information Service, supported by an extensive computer database, PDQ, provided more than half a million callers a year with information regarding treatment and advances in clinical oncology."

Diagnosis Was 'Synonymous With Death'

"Nevertheless," continued Calabresi, "there are some who may be discouraged by what they perceive as a slow rate of progress. And, due to improvements in mortality from cardiovascular disease, it is predicted that cancer will be the number one killer in the United States by the turn of the century.

"However, those of us who cared for patients at a time when the diagnosis of cancer was almost always synonymous with death, greatly rejoice in seeing our outpatient clinic filled with increasing numbers of healthy survivors. Today, more than 50 percent of patients with cancer are cured."

"We have also learned that the enemy is far more fierce and wily than we had assumed," Calabresi continued. "The problem of cancer cell heterogeneity has revealed the complexity of tumors, and the fundamental advances in molecular genetics have identified the deep seated nature of the lesion. These findings have also given us a better insight into the pathogenesis of the disease and allowed us to focus on new preventive strategies and therapeutic priorities.

"The exhilarating explosion of knowledge that has occurred during the past two decades was fueled by funding provided through the National Cancer Act and sets the stage for exciting clinical advances in the future," Calabresi said. "We cannot afford to weaken our resolve and must continue to attract and support bright young basic scientists and clinical investigators who will maintain the momentum to translate the fundamental knowledge effectively to the patient afflicted with cancer."

Calabresi concluded: "Today, in 1991, as we mark these milestones toward the millennium, we sincerely hope that we will see the day when it will no longer be necessary to have future commemorations of the National Cancer Act of 1971."

HHS Secretary Louis Sullivan said the "cancer challenge of the next decade is staying focused on our primary goal of saving the lives of cancer patients through ever-better therapies and more effective prevention and screening strategies."

In 1971, Sullivan said, "the watchword was 'winning the war on cancer.' Under this mandate, thousands of America's best and brightest medical talent, backed by millions of dollars, targeted for eradication some of the most insidious diseases to

THE CANCER LETTER

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have afflicted mankind. We knew we were tackling a tough, elusive killer. Just how tough, and how elusive, I don't think anyone really understood at the time.

"I think it is very fair to say we have made tremendous strides forward. In 1971, surgery was the cancer treatment of choice. Radiation therapy was still developing, and chemotherapy was still controversial. Today, although surgery remains one of the most effective ways to treat tumors, its success rate has been dramatically improved with the addition of adjuvant chemotherapy, radiation, and more recently, biotherapy.

"Equally exciting are the positive results we're seeing as bone marrow transplants give new hope to many cancer patients. But perhaps most dramatic is the potential fore the discovery of 'silver bullets' for which we're all hoping; breakthroughs in basic research that will identify chinks in the molecular armor of cancers through which we can destroy them--or force them to destroy themselves.

"Such is the thrust of some of the most intense research ever performed--much of it right here at the National Cancer Institute and among NCI grantees around the country. From cell biology to biological response modifiers to gene therapy, the potential for dramatic, revolutionary advances in the way we treat cancer patients are occurring more rapidly than ever before, thanks to biomedical research--research that has resulted in clinical improvements, providing remission and cures that would not have been possible previously.

"Already, we're seeing the results of some of this basic research paying off in clinical trials. But, in a curious, ironic twist, as desperate as most doctors are to find cures for their cancer patients, we're finding that too many beds in some clinical trials remain empty. Many physicians across the country aren't taking advantage of the Physicians Data Query. Which means that some of their patients are not receiving the latest technology in cancer treatment. That's a shame. We must find a better way to get qualified patients into these trials. Or, if we can't get patients to the trials, then we need to find a way to get the trials to the patients, for they are the ones suffering and dying."

[Editor's note: Southwest Oncology Group Chairman Charles Coltman gave a presentation at the NCAB meeting a day before the symposium, describing the cap on patient accrual to SWOG trials due to lack of adequate funds. Other NCI funded clinical cooperative groups also have had funding difficulties and some, including SWOG, turned to the pharmaceutical industry for cash donations. NCI plans to increase funding for cooperative groups this fiscal year. Regarding Sullivan's call to "get trials to the patients," it must be noted that there are currently only about 50 funded CCOPs; the program originally called for 200 to make clinical trials available to most cancer patients treated in their communities.]

Sullivan also discussed gains in cancer prevention, especially prevention of cancers caused by tobacco. "Simply put, in the war against cancer, step one is for the general population to stay away from the war zone," he said. "The good news is that lung cancer could be virtually eliminated if people would stop smoking. Yet, although the antismoking message seems to be taking effect, too many Americans--more than 50 million--still smoke. Indeed, in a deadly ironic twist, lung cancer rates among some segments of our population, especially minorities, have risen dramatically. Worse, many young people are taking up the smoking habit. This is unconscionable. Smoking must stop; for the benefit of the smoker, for his or her children, spouse and co-workers, and because lung cancer patients add a significant strain on our hospitals and an additional burden on our health care system."

Sullivan concluded: "I hope and pray we will look back on today's symposium as the beginning of the end in our successful war against cancer."

NIH Director Bernadine Healy said the Act was "a triumph in timing. The time was right. America's needs were being sorted out. We knew we had to do something. Information was accruing about the genetic basis of cancer." The Act, she said, "has been a strong but highly flexible law."

NCI Director Samuel Broder presented some of his research on HIV and singled out for praise NCI's Viral Cancer Program, which was highly controversial.

AIDS is a global pandemic "with no end in sight," Broder said. AIDS research is one component of NCI, which is appropriate given the Institute's history of basic immunology research, and the fact that as AIDS patients live longer, they are developing more cancers. Non-Hodgkin's lymphoma is a major complicating factor in AIDS, he said.

Broder also discussed the importance of CD4 as a marker for progression of AIDS. In his studies, he said, "Nobody died unless their CD4 was less than 50."

Despite the development of AZT, ddI and other antiretroviral drugs, "we do not have curative therapy" for AIDS, and until "the process of rational drug design leads to effective therapy," NCI's role will be to continue to search for effective drugs and to develop therapies for AIDS related cancers, Broder said.

Vincent DeVita, Benno Schmidt chair in oncology at Memorial Sloan-Kettering Cancer Center, was one of two former NCI directors present at the symposium. The other was Carl Baker, who headed the Institute in the years immediately prior to the Cancer Act's implementation.

DeVita came to NCI as a clinical associate in 1963 and worked to develop the MOPP treatment for Hodgkin's disease, "proving that systemic solid tumors can be cured with drug therapy," said Div. of Cancer Treatment Director Bruce Chabner in his introduction.

DeVita noted that the advances in chemotherapy in 1970-71 played an important role in the passage of the Act. He also discussed the importance of basic research. "When we used to tell Congress in the 1970s and 1980s that we were investing a great deal of money in basic research, we were met with some skepticism. We were right, the answer was molecular biology and molecular biology in fact will make a difference," he said. During that time, NCI's budget was 23 percent of the NIH budget, but supported 50 percent of NIH molecular biology research.

"What the Cancer Act did for cancer research, it did in an unusual way. The Act had a mandate to support basic research, and also to apply the results. There are two ways of development in the clinic. One was the discovery of new technology, and we had five fold increase in laboratory investigators. Now, just now, this molecular medicine is reaching the clinic. The second is the expansion of improvement of existing technology." He noted that before 1971, groups like the National Surgical Adjuvant Breast & Bowel Project were hurting for clinical trials funding, because trials were considered "too expensive, too high risk."

DeVita noted several milestones in cancer research and its application that were the direct results of the Act. In 1972, NCI expanded the cancer centers program, clinical trials, and cancer training. The Cancer Control Program was begun. In 1974, the Cancer Information Service was begun to disseminate information about cancer research and treatment. In 1975, the Surveillance, Epidemiology & End Results program was begun to track cancer incidence and mortality. In 1978, epidemiology research was expanded. In 1981, DeVita proposed the Community Clinical Oncology Program, or CCOPs, to expand the network of clinical trials and state of the art cancer treatment. 1983 marked the beginning of the prevention clinical trials program. In 1984, the Physicians Data Query system was begun to provide on-line access to the latest treatment information.

DeVita pointed out that many advances in molecular biology came as a result of the much-maligned Viral Cancer Program, including DNA hybridization, DNA sequencing, recombinant DNA techniques, hybridomas and monoclonal antibodies.

The "scientific yield" of the Act in late 1970s and 80s, DeVita said, included the oncogene cascade, suppressor genes, signal transduction systems, genetic control of metastasis, split genes, and gene regulation.

The "clinical yield" included the cure of a fraction of some advanced cancers, leading to interest in large scale clinical trials; adjuvant therapy, increased availability of cancer doctors, information systems such as PDQ; biologic tests and products such as monoclonal antibodies, IL-2, colony stimulating factors, molecular probes, and PCR; CT, MRI, and PET scanning techniques, combined modality treatment, decreased acute treatment toxicity, decline in mortality from lung cancer in white males, decrease of 63 percent in mortality for pediatric tumors, and decrease in morality in all other tumors below age 65, and if lung cancer is excluded, up to age 85.

DeVita also presented his thoughts on tumor response to chemotherapy. He said he believes that, "There may be two populations of cells in reference to responsiveness to systemic cancer chemotherapy. That is, there may be cells that have some signal system left that can still hear cell talk between cells, and these cells may be the ones that are more difficult to treat with chemotherapy and may be logical candidates for treatment with other types of therapy, biologicals, monoclonal antibodies, etc. The success that we had with chemotherapy--and I suspect this is true, there is a lot of data to suggest it is--is really on the cells that have totally slipped the leash, they no longer respond to any of the signal systems at all, and they are very vulnerable. One looks at differentiated versus undifferentiated cells in any type of tumor that is responsive, the undifferentiated tumor always responds better in terms of cure rate.

"I think you can use this type of information with suppressor genes, in such a way you might be able to redefine populations to treat. I think there is a decision to become a cancer, and a decision to metastasize. We need to be able to tell whether the tumor has made that decision or not, and we cannot continue to use as we have in the past, prognostic factors as things that predict cell metastasis. We want to be able to find and detect the exact genetic effect that has control over the metastatic process. I think this molecular information will change how we approach cancer treatment.

DeVita also discussed "the major limitations of cancer treatment as of today:

--"The inability to determine whether an apparently

localized tumor has metastasized.

--"Overcoming specific and "permanent" resistance to anticancer drugs. The presence of the expression of the MDR protein is probably one of the major barriers to success of cancer chemotherapy. Most tumors we treat require combination chemotherapy. Most effective combinations require at least one natural product. And expression of the MDR protein is probably the reason we are able to treat diseases like acute leukemia, lymphoma, and breast cancer, and there are clinical studies underway to try to bypass it or overcome the problem. This is the most exciting exploitation of current technology, using molecular biology to overcome a limitation of current technology.

--"The inability to easily and reliably detect minimal residual disease. We are now in a position to do something about this.

--"The inability to monitor the impact of the treatment on cancer cells in vivo.

DeVita also emphasized the role of cancer centers in technology transfer. "I think we are facing a problem now which is two waves set in motion by the National Cancer Act which may wash over each other. We need to sort out and ask the appropriate questions. We need a viable and free standing clinical trials and clinical research program."

Research questions are "not unique to any institution. They are universal questions. To answer them we need to use our clinical material wherever there is cancer. Usually one clinical research program resonates with a laboratory program in some ways which allows the strength of laboratory program to be expressed. Unfortunately in this country more often we have dislocation between two. We either have a laboratory program that controls the clinical program. so there needs to be some universality to the questions, that we pose for clinical trials."

DeVita, who was the last speaker, closed with an appeal on behalf of the National Cancer Program: "I can say this now that I'm not a member of the government staff. It's unfortunate that although the cancer program basically did what it was supposed to do and accomplished major things that people really did not expect it to accomplish, that the budget for it has really washed out. All that network [clinical trials groups, CCOPs, centers] was put together by 1984 and by that time the budget was already flat. It seems to me that Congress ought to have had the opportunity to be in the audience today and hear what has happened to the cancer program and refuel the revolution started by the cancer program. It will make no difference if they do or they don't in terms of whether it will be a success, it already is a success."

AHF Honors NCI On Anniversary Of National Cancer Act Of 1971

The American Health Foundation, commemorating the 20th anniversary of the National Cancer Act, honored the National Cancer Institute "for its vital work in promoting research, improving treatment, and providing a more hopeful outlook for cancer patients nationwide" at the Foundation's recent awards dinner in New York.

NCI Director Samuel Broder accepted the award "for the magnificent men and women who work at NCI." Broder said he and his colleagues at the Institute "are striving to put ourselves out of business," through cures and prevention. "That day will come, and then we can turn our attention to other diseases."

Broder praised Mary Lasker, who was present, as "the living embodiment and spirit of the National Cancer Act."

After briefly describing areas of progress, especially gene therapy, Broder noted that developments in molecular biology and genetics were legacies of the Virus Cancer Program of the 1970s. "That was very controversial then, but it has proven to be one of the most successful biomedical research programs in history."

Alluding to the American Health Foundation's emphasis on disease prevention, Broder said, in quoting his Div. of Cancer Etiology Director Richard Adamson, "Prevention suffers from an absence of grateful patients."

Broder received the award from Harold Freeman, chairman of the President's Cancer Panel. Freeman said that the "war on cancer is now a ground war, being fought out in hand to hand combat in neighborhoods and communities, in the prevention of cancer."

AHF President Ernst Wynder called for mandatory health education programs in school, starting in kindergarten. "I hope the government will find the will to support these programs, and not just with the so called peace dividend. We should be able to give our people a life dividend. . . Our goal should be to help people die young, as late in life as possible."

The AHF 1991 Lifeline Award was presented to the American Cancer Society, with acceptance by the Society's chairman of the Board of Directors, Stanley Shmishkiss.

Lee Wattenberg, Univ. of Minnesota, received the 1991 Naylor Dana Award for his work in cancer prevention, particularly chemoprevention and biomarkers.

The dinner was chaired by Brenda Johnson,

member of the National Cancer Advisory Board, and Irwin Lerner, president and chief executive officer of Hoffman-La Roche.

Several national leaders, including President George Bush, and cancer center directors sent letters to AHF congratulating NCI and acknowledging the National Cancer Act's anniversary.

Bonadonna, Hsu, Sullivan Receive Medal Of Honor From ACS

The American Cancer Society's most prestigious award, the Medal of Honor, was presented to Gianni Bonadonna, T.S. Hsu, and Louis Sullivan at the Society's annual banquet last month.

Bonadonna, director of medical oncology at the National Tumor Institute in Milan, was honored "for developing and supervising clinical trials successfully using combination chemotherapy as adjuvant treatment to surgery for breast cancer patients and confirming randomized trials as an important research method."

Hsu, geneticist and professor emeritus of cell biology at M.D. Anderson Cancer Center, revolutionized research by devising a way to study the chromosomes of cells. His technique enabled others to develop such initiatives as the Human Genome Project, genetic screenings for diseases, and a molecular understanding of DNA.

Sullivan, secretary of the Dept. of Health & Human Services, was honored for "bringing public attention to the importance of tobacco control and for steadfast leadership in the fight to protect Americans from the health consequences of tobacco use.

The Society's Distinguished Service Award was presented to B.J. Kennedy, Univ. of Minnesota, for his "45 years of distinctive and compassionate care of cancer patients and his vision in pioneering the field of oncology;" Jesse Steinfeld, former U.S. surgeon general and former deputy director of NCI, who was the first surgeon general to call for social action supporting the rights of nonsmokers; Betty Lea Stone, 92 year old ACS volunteer who has served on the Massachusetts Div. board for 40 years; and Linda Nan White, director of cancer prevention and detection at M.D. Anderson, for "her development and energetic delivery of cancer prevention programs which have trained thousands of nurses."

Armin Willig, of Prospect, KY, former chairman of the ACS Board of Directors, received the Humanitarian Award.

The Society's Volunteer Leadership Award was given to Harold Amos, Harvard scientist, past president of the Massachusetts Div., and a former member of both the National Cancer Advisory Board and President's Cancer Panel; Norma Hayman, honorary life member of the New Jersey Div. and its delegate to the ACS Board; Allan Jonas of Los Angeles, former chairman of the ACS national Board; and Cyril Schulman, clinical professor of medicine emeritus at George Washington Univ. and a 42 year ACS volunteer.

Among the actions and reports at the Board meeting:

--The Board approved the phase 1 feasibility trial of the New York diet and breast cancer study in which volunteers will carry out most of the tasks in determining if a very low fat diet and reduction in calories can improve survival of breast cancer patients. The trial will be carried out through five centers throughout the state. A volunteer physician will be in charge of the study at each center, aided by volunteer nutritionists and data collectors. Ninety patients in the very low fat arm will be placed on a diet in which no more than 15 percent of calories will be from fat. Patients on this arm will be closely monitored and counseled. The control arm will include 90 patients who receive initial counseling, a copy of the ACS diet recommendations (30 percent of calories from fat), and no further intervention. If the phase 1 study is successful, a phase 2 trial will be implemented to include 900 patients in each arm.

More details on this trial and a discussion of some of the controversies involved appears in the December issue of **The Clinical Cancer Letter.**

--Daniel Nixon, ACS vice president for detection and treatment, reported on preliminary results of the Society's U.S. Navy dietary guidelines study. Two ships are involved in the study, one in which ACS guidelines are followed to achieve fat and caloric reductions, the other a control ship on the Navy's regular diet. The crew of the diet ship lost weight overall compared to the control ship, which showed a mean weight gain. Body fat content on the diet ship declined. Cholesterol levels declined or showed no change in those in low stress jobs, while crew members in high stress jobs showed a tendency to increase cholesterol levels. The majority of crew members on the diet ship said they liked the food, and 44 percent said they would try to maintain similar eating habits.

--The Board approved a resolution supporting the National Surgical Adjuvant Breast & Bowel Project's clinical trial to determine the worth of tamoxifen in preventing breast cancer. Sixteen thousand women 35 years of age and older, determined to be at high risk for breast cancer, will be randomized to receive

tamoxifen or placebo for at least five years. There was some discussion among Board members whether the Society should single out one clinical trial, among several hundred being conducted by NSABP and other cooperative groups, for emphasis. Since it is a study which must recruit from the general population, members agreed it needed endorsement from ACS and other organizations.

NSABP also receives a $100,000 a year grant from ACS.

--ACS was able to fund only 12 percent of the grant applications received and approved this year. President Walter Lawrence said he hoped that could be increased to 25 percent. Lawrence also said he hoped the number and quality of clinical trials grant applications ACS receives could be increased.

--U.S. military representatives reported that tobacco use in the armed forces declined from 51 percent in 1980 to 41 percent in 1988. The Dept. of Defense goal for the year 2000 is to reduce the rate to no more than 15 percent.

Interactive Research Project Grants PA Application Deadline Feb. 20

Following is the "final revised draft" of NCI's program announcement for Interactive Research Project Grants for Cancer. The program announcement has not yet been officially released and therefore has not been assigned a PA number. The official announcement is due out in a few weeks.

Title: **Interactive Research Project Grants for Cancer**
Application Receipt Dates: Feb. 20 and regular receipt dates thereafter.

Complex questions in cancer research often require investigative efforts that extend beyond the level practicable in a single project, or that require a mixture of technical approaches beyond the means of a single investigator. The perceived merit of individual research project (R01) applications sometimes may be limited by the lack of a comprehensive, interdisciplinary approach, or by limitations in resident technical expertise. There also may be areas of investigation that are under-represented in applications because they cannot effectively be exploited without a collaborative effort, yet local opportunities for such interactions are not available.

NCI seeks to encourage the coordinated submission of related research project grant applications where investigators wish to collaborate on a common cancer research theme, but do not require extensive shared physical resources or core functions. A minimum of three independent investigators with related research objectives are encouraged to submit concurrent, collaborative, cross referenced individual research project grant applications (R01) that share a common research focus. Applications may be from either one or a consortium of institutions. Applications will be reviewed independently for scientific merit. Meritorious applications will be considered for funding both as independent awards and in the context of the overall proposed collaboration.

Historically, NCI has relied on multi-component awards such as program projects (P01) and Cancer Center Support Grants (P30) to encourage interdisciplinary collaborations in areas requiring integration and central direction of basic and clinical research components. A hallmark of such awards is the provision for extensive core facilities/resources and appointment of a program director to manage the overall effort.

For many research areas it may be more appropriate to consider an intermediate level of collaboration, less extensive than that described above, but beyond that practical for single projects. For such intellectually driven collaborative efforts, the exchange of data, materials, ideas, rather than shared physical resources or central oversight, is the primary requirement. The concept of IRPGs put forth in this announcement is meant to address and facilitate this class of research activities. Typically, the IRPG approach will be suited to many basic research questions, as well as research to develop, apply and evaluate interventions for cancer prevention and control. The IRPG mechanism may also fit well with clinical applications that propose limited testable research questions; or with focused phase 1 and 2 therapeutic and related correlative laboratory studies.

Applicants will benefit from use of the IRPG mechanism by establishing a larger framework of reference for the proposed work, by facilitating formal collaborations tailored to achieving research objectives, by providing a record of independently acquired awards credited to each funded investigator, and by allowing retention of research autonomy by the named PI on each of the interactive grants. Each grantee will have the ability to submit on his/her own behalf competing supplements as appropriate to incorporate promising new directions of research as they evolve. The freedom to establish collaborations on an equal footing at separate sites (including foreign locations), and the improved transferability of awards made to individual principal investigators, also are significant benefits. In contrast, translational research programs that span a variety of disciplines and programs that require extensive co-located core resources would continue to be served best by traditional multi-component program award mechanisms.

NCI encourages qualified investigators to develop and submit concurrently coordinated research project applications that address areas of relevance to cancer where the interactive research project concept may be applied. Applications submitted as a package should be tightly focused and the interactions and benefits of the proposed linkages should be made explicit.

IRPG applications will be accepted in any relevant area of cancer research where this mechanism may be constructively applied. Some typical (non-exhaustive) examples are cited below:

--Immunobiology of specified cancers, such as breast, ovarian and prostate cancer. Since these cancers involve both immune and neuroendocrine responses, projects requiring expertise in various aspects of cancer biology, immunology and/or endocrinology will be needed for a comprehensive approach for these questions.

--Hormones and signalling pathways. Basic science proposals

may be combined that integrate multiple aspects of hormonal regulation of cancer from growth factors to receptors to signal transduction to genetic regulation.

--Detection and intervention studies in breast and other cancers. New methods are needed to promote the use of detection methodologies in populations at risk, and to measure the efficacy and compliance with recommendations. Studies to identify and overcome barriers to health promotion and to measure cost effectiveness may also be linked to such a program.

--Focused studies on phase 1 and 2 clinical trials. Projects designed to investigate promising combined therapeutic approaches to a single type of cancer may be linked with correlative laboratory investigations to investigate further the mode of action and/or biological effects of treatments.

--Related basic studies focused on multiple facets of common viral or chemical carcinogenic agents such as HIV or human papilloma virus that do not require extensive core resources.

--Basic drug discovery programs that focus on multiple aspects of a related class of compounds or on a single mechanism of action.

--Methodologically related applications that focus on development and/or application of specific methodologies to cancer research, where extensive shared physical resources are not required.

--Research on variations in control of the cell cycle which operate specifically in tumor cells. Projects might focus on unique enzymes or effector molecules, the role of protein modifications such as phosphorylation, activation of oncogenes, interactions with suppressor genes, etc.

Prospective applicants are encouraged to explore other areas of potential for the IRPG mechanism with NCI program directors.

Support of this program will be by the research project grant (R01). One principal investigator out of the group must be identified as the Program Coordinator and should be cited in all applications. Individual investigators may request funds for the time and effort contributed toward the coordination of the overall research and for collaborative resource activities.

To facilitate referral, all applications submitted under the IRPG mechanism must be submitted in one physical package. Each application must be complete in itself, with all appropriate approvals, budgets, and signatures. A cover letter must accompany the package identifying all principal investigators and project titles that are a part of the combined submission. The letter should be firmly attached to the face page of the top application. Each application must be identified by checking "yes" on line 2 of the PHS 398 face page and citing this announcement, "Interactive Research Project Grants for Cancer."

The use of the IRPG mechanism should be mentioned briefly in PHS Form 398, Sections A-D of the research plan. The goal of the collaborative efforts must be identified in the specific aims of each application, with he major rationale and explanation for the use of the IRPG mechanism to be given in Section G, Consultants/ Collaborators. A complete list of applications in the IRPG should be provided in Section G, as well as an indication of the specific collaborations to be established for the individual application under consideration.

Requests for limited shared resources, if any, should be proportionally budgeted in each application based on anticipated use, with a full explanation given in the budget. Personnel time and effort requests for management of shared resources are allowable. Where consortium arrangements between independent institutions are proposed that would make transfer of funds for required new equipment impractical, the entire equipment request may be budgeted by the responsible laboratory. This should be clearly justified.

Domestic and foreign nonprofit and for profit organizations and institutions, governments and their agencies are eligible to apply. Each application will be considered on its own merit as an individual research project. Therefore, applicants for IRPGs may not concurrently submit R01 applications that represent significant duplication of the efforts described in the applicant's IRPG. NCI will consider funding meritorious individual IRPG applications if it is not possible to fund the IRPG package as a whole. Concurrent submission of program project (P01) applications that request support for essentially similar work is also prohibited.

Applicants are strongly encouraged to consult with NCI program staff prior to submission to ensure that the application conforms to these guidelines, and that the IRPG mechanism is an appropriate choice.

Complete applications will be reviewed for scientific and technical merit by an appropriate peer review group convened by the NIH Div. of Research Grants. Insofar as possible, assignment of all IRPG applications will be made to standing DRG initial review groups, which may be supplemented by consultants with additional expertise as required. Investigators should be aware that applications utilizing widely differing approaches will not necessarily be reviewed by the same initial review group. Attention in selecting clearly related applications for submission will aid the process of assignment for review.

While there is no fixed set aside of funds committed to the IRPG mechanism, NCI will consider for funding all IRPG applications in a cohort if all are rated by peer review as having significant and substantial scientific merit.

Written or phone inquiries concerning the objectives and scope of this PA should be directed to: NCI Referral Officer, Review Logistics Branch, Div. of Extramural Activities, NCI, Westwood Bldg. Rm 850, Bethesda, MD 20892, phone 301/496-7173; fax 301/402-0275.

Final Cancer Letter Of 1991, Next Issue Dated Jan. 3, 1992

This issue of **The Cancer Letter,** Number 48, Volume 17, is the final issue of 1991. The next issue, Volume 18, Number 1, will be dated Jan. 3, 1992.

The **Cancer Letter** office will be closed from Dec. 23 to Jan. 2. Staff members may be contacted by leaving messages on the phone answering machine during this time (202/543-7665). News items, subscription orders, and other important documents will be welcomed by our fax machine (202/543-6879) at any hour, every day.

Best wishes for the holiday season and New Year.