THE CANCER LETTER

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NCI To Fund 160 P01s in FY91, About Same As Last Year; Considering New 'Interactive' R01

NCI intends to fund approximately 160 total program project (P01) grants this year, about the same number as last year, despite tight Congressional directives on grant funding that threatened to severely limit the number of P01s. However, due to the Congressional constraints, NCI is considering a new mechanism, called "interactive" R01s, which would act like program projects but would count more toward the

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In Brief

Niederhuber Moves To Stanford As Surgery Chief; Jerome Urban, Breast Specialist, Dead

JOHN NIEDERHUBER will be leaving Johns Hopkins Univ. to take the position of chief of surgery at Stanford Univ. He also will direct a new cancer center Stanford is planning. Niederhuber, who recently completed his term as chairman of the Div. of Cancer Treatment Board of Scientific Counselors, was praised by DCT Director **Bruce Chabner** for his role in promoting better relations between NCI and FDA, among other issues. "He has often expressed the sentiment that NIH is a great place to work, and I have personally appreciated his comments," Chabner said. Other BSC members whose terms expired were **Charles Balch, Frank Huennekens, James Cox,** and **Mark Groudine.** . . . **JEROME URBAN,** perhaps the most outspoken, and last, proponent of the extended radical mastectomy, died June 13 in New York following a stroke. He was 77. Urban retired several years ago from Memorial Sloan-Kettering Cancer Center. He was also a leader in development of breast reconstruction. Among the honors he received were the Lucy Wortham James Award (Clinical) and James Ewing Lecture from the Society of Surgical Oncology. . . . **LYNN COLQUITT,** management and financial advisor for a number of clinical oncology practices around the country, died June 6 in Tucson from a massive heart attack. He was 52. Colquitt founded JRB Associates and later was a partner in CDP Associates, firms which carried out a variety of support contracts for NCI. Colquitt was based in Orlando and was in Tucson to work with clients. . . . **PAYLINE FOR CCOPS** first annual recompetition has been set at 167, and NCI will fund the top five competitors, with no exceptions. **The Cancer Letter** has learned three of the top five are (in no particular order) **Spartanburg CCOP,** John McCulloch, PI; **San Joaquin Community Cancer Center,** Marshall Flam, PI; and **Cancer Institute of Brooklyn,** Sameer Rafla, PI. . . . **THOMAS GLYNN** was promoted to branch chief of the Prevention & Control Extramural Research Branch in DCPC's Cancer Control Science Program.

NCI To Fund 160 P01s; 40 Competing By Funding Some As Exceptions

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Institute's total grant target.

NCI was directed to fund a total of 840 new and competing grants for an average of four years in grant length and at an average cost of $250,000 per year, without across the board cuts in recommended funding levels. NCI officials have expressed alarm that these instructions discriminate against P01s, which cost six times the average R01 research project grant, and, though comprised of several projects, count as only one grant.

NCI has had a historical commitment to P01s because it is a mechanism ideally suited for lab-to-clinic research. PO1s constitute 25 percent of NCI's grant funding, and in the Div. of Cancer Treatment, they account for 50 percent of the division's grant funding.

The initial P01 payline was set at 130, but the NCI Executive Committee, following the third round of grant funding, decided to fund additional grants as exceptions, DCT Director Bruce Chabner said last week. "In effect, we will fund all [P01] grants with scores better than 140," he told his Board of Scientific Counselors. However, dollar amounts have been reduced from recommended levels, he said.

Of the total of 160, NCI will fund about 40 competing P01s in FY 91, one or two less than last year; about 20 of those come out of DCT. Altogether, P01s account for $180 million of NCI's research project grant funds.

Chabner said he was "disturbed" that, without the exceptions, fewer P01s would have been funded. "I view the P01 grant as a primary mechanism for pursuing integrated laboratory and clinical research," he said. "The list of P01 holders in this division includes the very best clinician-investigators in the field of cancer research. However, if the trend of setting tight constraints on grant numbers and average sizes of grants continues, we will be forced to consider alternatives for supporting this type of research."

One alternative the NCI Executive Committee is considering is the interactive R01, Chabner said. Under this mechanism, several R01 grants are submitted and reviewed as a package. Each is given a priority score, but NCI has the option of funding some of the grants in the package as exceptions if they do not receive fundable scores. Each of the components counts as a single grant.

"The NCI review division is now determining whether the interactive R01 can be used as an alternative to the traditional P01 and whether core support can be built into a lead R01," Chabner said. "If the answers are affirmative, we will encourage grantees to consider this mechanism as an alternative to the standard P01."

Meanwhile, NCI will bring the difficulty with P01 funding to the attention of NIH and the Congressional appropriations committees, but, Chabner said, "We are not optimistic that we can effect a change in Congressional language in next year's budget."

The National Cancer Advisory Board at its recent meeting passed a resolution asking NIH to allow NCI flexibility in meeting its grant target in order to fund P01s (**The Cancer Letter,** May 31).

DCT Board Chairman John Niederhuber said P01s are valuable. "The sum of the work is usually greater than the parts. That never comes out until you sit there in an institution and peer review it."

THE CANCER LETTER

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Breast Component Planned For WHI, Even As Accruals Cut Due To Funds

NCI's Div. of Cancer Treatment will participate in the planning of a breast cancer treatment component of the NIH Women's Health Initiative, even though accruals to current breast cancer trials are being curtailed due to deficits in cooperative group funding.

The emphasis of the WHI is on prevention, early diagnosis and community intervention for cancer, heart disease and osteoporosis; however, a breast cancer treatment component will be planned, DCT Director Bruce Chabner told the DCT Board of Scientific Counselors last week. The WHI is a multimillion, 10 year study of the major diseases that affect older women; it was announced by NIH

Director Bernadine Healy soon after she took office.

The WHI might result in additional funding for clinical trials in breast cancer, but that is not certain.

"There is no lack of enthusiasm and willingness to participate in such trials, but we currently lack the funds to keep up with accrual to ongoing trials," Chabner told the board. "The cooperative groups are accruing new breast cancer patients at a rate that is creating a seven figure deficit. We are literally having to curtail accrual to trials for lack of group funding.

"In addition, at the level of phase 1 and 2 activity there are three compounds--taxol, anthrapyrazole, and amonifide--that have shown definite activity in early studies and deserve broad, expedited phase 2 testing. Expanded support for breast cancer studies may allow these projects to proceed at maximum speed.

"The funding situation for breast cancer research has been no worse than, and for the most part better than, the funding for other malignancies, but the rising incidence of breast cancer and the considerable opportunities to prevent, diagnose, and treat the disease certainly justify the additional investment of research dollars at this time," Chabner concluded.

In another development regarding women's health, DCT is taking steps to encourage training and research in gynecologic oncology. Chabner recently met with representatives from the Society for Gynecologic Oncology.

"We have discussed the possibility of establishing an intramural gynecologic oncology research unit in the Surgery Branch, and securing representation from this group on various divisional advisory boards," Chabner said.

Rod Mortel, professor of obstetrics and gynecology at Pennsylvania State Univ., will join the DCT board in October. The Cancer Therapy Evaluation Program has hired Ted Trimble, a gynecologist who recently completed oncology training at Memorial Sloan-Kettering Cancer Center.

"Thus we have made some progress in establishing better links to this subspecialty, and we intend to do more," Chabner said.

Antoines To Leave NCI For Jobs At Loma Linda Univ. Health Center

John Antoine, who directed the Radiation Research Program in NCI's Div. of Cancer Treatment for five years before leaving that position at the end of last year, has accepted a position at the Loma Linda Univ. Health Sciences Center. He will leave NCI July 1.

Antoine will be a professor of radiation medicine in the Dept. of Radiation Medicine, and associate director for clinical research, as well as senior investigator on Loma Linda's proton beam facility. His wife, Florence Antoine, a senior science writer in the Office of Cancer Communications, also will leave NCI to work at the Loma Linda center in science writing and communications. Both will be involved in the university's development of a new comprehensive cancer center.

Antoine said he believes that proton beam technology is "gaining a lot of momentum" at the national and international levels, and that his new job will be "consistent with what I've tried to develop in the Radiation Research Program over the last five years, a balanced approach to research and treatment."

He said he is "very pleased" with Loma Linda's proton beam, which is now strong enough to deliver dose quickly.

Eli Glatstein, chief of the intramural Radiation Oncology Branch, will become acting director of the RRP until a permanent director is appointed. Michael Friedman, director of the Cancer Therapy Evaluation Program, has been acting director of RRP for about six months.

DCT Director Bruce Chabner is recruiting for a permanent director, and says he has been "encouraged" by the response; however, he expects that it will be difficult to recruit a well qualified radiotherapist. "Probably our best chance is the pool of PhD radiobiologists," he said. He still intends to create a separate diagnostic imaging program and recruit a director for that unit.

DCPC Advisors Develop Priorities For Investigator Initiated Research

Advisors to NCI's Div. of Cancer Prevention & Control have begun a process to help the division develop priorities for areas in which it hopes to stimulate and improve investigator initiated prevention research.

DCPC's Board of Scientific Counselors formed three committees that met last month to hear overviews of ongoing NCI programs and to suggest future initiatives.

"The field of cancer prevention and control now is taking hold across the country," DCPC Director Peter Greenwald said. "We have a number of well qualified investigators who should be in a position to seek investigator initiated grants. It will be healthy for NCI to foster a much broader and stronger body of research in prevention and control that is driven by

investigators themselves."

DCPC's effort also is part of NCI's overall emphasis on using the research project grant pool to its fullest extent. This funding pool (R01s, P01s) continues to increase each year, while growth in other mechanisms has been flat or decreasing in real dollars. Over the past decade, prevention and control funding and clinical research funding both fell by a third in real dollars, while the R01 pool rose by 25 percent.

"Since the R01 pool is open to all types of investigator initiated research, it certainly would seem prudent to take advantage of these fiscal trends," Greenwald told the board.

Synchronized Approach

A related issue is the review of grant applications by study sections. Greenwald said he and other NCI executives are considering implementing a "synchronized approach" to the grant application submission process. NCI would ask investigators to submit related research applications at a specific time; NCI would work with the NIH Div. of Research Grants to ensure that the applications receive appropriate review.

For example, Greenwald said, if NCI could show DRG that it expected to receive 20 applications for prevention and control research on a certain date, it would provide the clout necessary to increase or change membership on study sections.

"Steady growth in investigator initiated prevention and control proposals should logically lead to appropriate change in the composition of scientific fields represented in study sections, for example, Epidemiology and Disease Control 2 or Behavioral Medicine," Greenwald said. "The ball is in the hands of the investigators. We can't expect creation of a study section on a promise; it will be in response to applications."

Board members said they supported NCI's and DCPC's effort, but were concerned about the propriety of asking investigators to spend time writing grant proposals that may not get funded.

"The whole issue is, who wants to be the sacrificial lamb, to create these applications that will bet turned down," said board member Shirley Lansky. "No one wants to fire the opening salvo. . . . It takes many thousands of dollars to prepare an application."

Board Chairman Edward Bresnick noted that, "Many experienced investigators go two, three, or four rounds before getting funded. The only people making money out of this process are Xerox."

At least 60 applications in one cycle would be needed to effect change in the study sections, though not all would have to be in cancer prevention; heart disease intervention could be included, Greenwald said. "Even if we had 20, it could be the basis for an ad hoc group," he said.

"There is so much skepticism, and the feeling that it is not worth the effort to write the application," said board member Carol D'Onofrio.

"The problem is, the first time through has to work and be credible," Greenwald acknowledged. "DRG is not willing to commit to a new study section until they begin to see applications. If we got 20 letters of intent, then we'd be in a strong position."

"There may have to be some sacrificial lambs. That may be the only route to take," Bresnick said.

Ideas For Future Initiatives

Greenwald asked the board's committees to suggest areas in which the division should attract more research, probably through program announcements. Following their first meetings, the committees submitted their initial suggestions, and the board members agreed to continue to refine these ideas. Following are excerpts from the committees' draft reports:

Nutrition, Nutritional Surveillance, Chemoprevention Studies: Chairman Elaine Feldman. The committee identified five targets;

1. Metabolic effectors of dietary origin of significance to cancer prevention and control. Solicit studies to be done to identify protective factors and elucidate mechanisms. Includes factors that modulate signal transduction, DNA repair, antioxidants, immunomodulators and other roles. Factors may be essential nutrients, other food constituents and xenobiotics of dietary origin that might be or lead to modulators as well as carcinogens. We recognize the need to attract multidisciplinary research including molecular genetics, cell biology, immunology and biochemistry in addition to nutritional scientists.

2. Interactions of diet with drugs, hormones, and metabolites. Although these studies have existed in the past they tend to emphasize negative effects. We're particularly interest in promoting studies in which diet may be synergistic, perhaps as with chemoprevention studies. These studies would include small scale trials as well as animal research.

3. Nutrition as one component of healthy lifestyle modification. Other modifications would include exercise, smoking, stress management. This target includes studies of fundamental relationships between diet and cancer and behavioral change affiliated with modification.

4. Improve reliability of data on diet composition and food intake. This includes nutrition surveillance methodology development, testing, and validation. That is, beyond interviews and diaries--markers of compliance (stable isotopes, urinary metabolites such as hydroxy proline peptides of animal collagen origin, etc.)

5. Chemoprevention. The subcommittee endorses strongly support of R01 studies to strengthen the scientific rationale while addressing the regulatory process in the framework of applied drug development in chemoprevention. Chemoprevention studies suffer in particular from ad hoc review and funding problems, at renewal particularly. For example, of about 40 applications, only two or three were funded last year.

For each of these targets, one individual on the committee has

been assigned to rewrite appropriate language to be forwarded to staff.

Prevention and Control Research. Cochairmen Carol D'Onofrio and Maryann Roper. Areas for investigator assisted research:

1. Organization and operation of medical care delivery systems.
2. Coalitions/leadership networks. How they are formed, work, why and how long they survive, costs, benefits, advocacy, confirmatory research.
3. Extent to which local interventions are organized/sustained in response to national/state initiatives.
4. Family interventions for cancer prevention.
5. Policy related research--how policies affect cancer prevention and control, effectiveness of alternative policies, policy process.
6. Children. Follow a carefully selected cohort of children through life time of exposure. Nutrition and cancer risk in children. Adolescent smoking cessation. Reducing exposure to passive smoke at home.
7. Cancer and older Americans.
8. Cancer and women.
9. Cancer and people of color.
10. Cancer prevention in low income communities. Develop low literacy cancer prevention materials.
11. Prevention of skin cancer.
12. Prevention of oral cancer.
13. Alcohol.

Biomarkers, Training, Surveillance, Biometry, Early Detection, Health Services, Clinical Trials, Rehabilitation. Chairman Edward Bresnick.

1. Research should be encouraged to identify biomarkers that provide explanations for the major population group (e.g. international) variations in the rates of prominent cancers (e.g. breast, prostate, colorectal, stomach).
2. All large scale prevention/intervention trials should be required to include a stored blood specimen resource (along with other specimens where appropriate) and a plan for actively managing the ongoing use of such a resource. As an alternative for individual groups maintaining such a facility, a centralized resource could be located at Frederick under the aegis of DCPC. The availability of this and other resources must be periodically announced to the scientific community in cancer epidemiology, biomarkers and prevention.
3. Stimulate the submission of investigator initiated proposals to develop the necessary methods for quantification of well characterized intermediate markers in normal appearing target organs. These submissions should include the necessary validations of the methods.
4. Stimulate the submission of investigator initiated proposals for the development of a service oriented quality control/quality assurance program related to the validation of biomarker procedures and methods at research laboratories at individual institutions.
5. Encourage the development of a system for on line access to a computer bank of molecular and cytogenetic changes in neoplasia. A model is the existing gene bank and protein bank.
6. Develop a system for encouraging the dialogue between basic scientists who are developing early detection studies and the health care scientists who are involved in prevention implementation.
7. Consideration by the physicians who are utilizing biomarkers, doing early detection, etc., should be given to the realities of health service delivery. Special attention needs to be given to the effects of managed care programs, cost barriers, and existing practice patterns.
8. Companion studies of subject participation should be required in screening and early detection trials and in prevention studies.

At its next meeting, the DCPC board is scheduled to consider an RFA concept for an NCI version of California's "Five a Day" program, designed to promote consumption of fruits and vegetables. The proposal, "Eat Five a Day for Better Health," would cost about $5 million a year for five years to fund approximately 10 state health departments in the 10 largest media markets in the U.S. The goal of the project would be to launch a nationwide media campaign and state and community activities to increase awareness of the link between fiber consumption and lower cancer risk.

Project officer Jerianne Heimendinger of the Prevention & Control Extramural Research Branch, said 40 produce firms have formed a foundation and raised $350,000 for the project; NCI hopes the foundation will contribute $1 million for the RFA.

There would be an estimated 25 percent decrease in cancer incidence if Americans would increase consumption of fruits and vegetables to four servings a day, double the current national average, Heimendinger said. The DCPC Board is scheduled to consider the concept at its October meeting.

Proposed RFA on cancer risk reduction in high risk youth, unanimously approved by the DCPC board in January (**The Cancer Letter,** Feb. 8) with a set aside of $5 million, will be released as a program announcement instead, with no set aside funding.

The NCI Executive Committee said the RFA would have to be funded through the prevention and control budget line, and DCPC "could not do it at this point," DCPC Director Peter Greenwald told the board.

The decision raised the ire of board member James Holland. "This sounds to me like a game called Marching to Jerusalem. You send the troops out and hope they get lost." He noted that the idea for the concept came from DCPC staff, but that the division now thinks the concept is not a priority. "If you bring things forward it should be because they constitute an integral part of the division's effort."

"It is important for us to bring forward everything we think is important," Greenwald responded. "We don't know what our budget will be 18 months from now, when the money is awarded." The division needs to have concepts in place in case it receives the full bypass budget amount, he said.

Holland proposed a study of a cohort of young children following them through a lifetime of exposures. "We should do as much to save as much

life as possible, not as many. So we should begin with the beginning of life," he said.

NCI staff have told **The Cancer Letter** that the high risk youth concept generated a significant amount of interest among investigators. One concern has been whether the applications would do well in peer review. If enough applicants apply for the PA, an ad hoc review committee could be formed, said an NCI source.

New Grant Programs In Radiation, Clinical Correlation Ok'd In Concept

Advisors to NCI's Div. of Cancer Treatment gave concept approval to two new grant programs in radiation therapy and a new grant program to promote collaborations between basic researchers and clinical investigators.

The DCT Board of Scientific Counselors committed $3.75 million in first year funding for the three year grant programs.

Following are the concept statements:

National Collaborative Radiation Therapy Trials: 3-D Dose Escalation Study for Prostate Cancer. Concept for a new RFA, proposed first year award $750,000; 3 years.

Studies on patterns of failure after curative local-regional therapy for carcinoma of the prostate (i.e., surgery and/or radiotherapy) show that the incidence of metastatic disease significantly increases as a result of failure to control the primary tumor.

The rapid technological advances in three dimensional external photon beam radiation therapy have significantly improved tumor target coverage, while at the same time sparing surrounding normal anatomy. With the new 3-D technology, it is now possible to plan and deliver radiation therapy to higher doses than was ever before possible. The 3-D approach uses nontraditional beam directions and achieves precision treatments that are shaped to conform to the tumor target. Application of the 3-D technology requires not only sophisticated 3-D computerized treatment planning systems, but also high precision treatment delivery (patient immobilization and position verification). Several institutions have implemented prototypes of 3-D treatment planning and treatment delivery systems and pilot studies at Memorial Sloan Kettering and Univ. of Michigan using nonconventional 3-D conformal techniques have shown that doses in excess of 7000 cGy to the prostate are well tolerated. Normally, doses at this level result in an unacceptable rate of major complications to the bowel, rectum, bladder, or urethra. A clinical evaluation is needed to determine whether improved 3-D techniques are sufficient to achieve optimal local control.

The purpose of the project is to provide funding for an operations control and statistical center to coordinate a dose escalation clinical trial among a number of institutions that will compare treatment-associated morbidity of escalated dose using 3-D conformal radiation therapy techniques. This study would be accomplished by a Phase 1/Phase 2 trial, randomized between conventional dose schedules and an escalated dose, that would establish a new maximum-tolerated dose based on acute and acute-delayed (6 months) normal tissue tolerance.

Normal tissue toxicity evaluation will require assessment of normal tissue physiology and functionality appropriate for the organs in the radiation field. An essential part of the proposed study will be the collection of precise and carefully quantified data that document the volume of normal tissue and normal organs that are irradiated, the spatial distribution of dose within the normal tissues, and where possible, pretreatment and posttreatment organ functionality tests to quantitate the degree and time course of radiation damage. Such data will form the basis for the development of dose-response models for the organs in the radiation fields.

The project will involve a consortium of institutions capable of calculating, displaying, and delivering 3-D radiation therapy treatments. The institutions will form a working group within a clinical trials group to develop the dose escalation studies for treatment of carcinoma of the prostate as the first tumor site. Dose escalation will be carried out in a prescribed way based on expected complication rates to the organs at risk to provide a broad range of normal tissue doses in a wide variety of clinical situations.

The objectives of this study are to fund six to eight clinical institutions and a statistical center to carry out a Phase I/Phase 2 trial that will: (1) establish a new maximum tolerated dose in the treatment of prostate cancer using 3-D conformal radiation therapy; (2) proceed quickly to Phase 3 trials; and (3) begin acquisition of a 3-D database of normal tissue tolerance for the prediction of complication probabilities for a limited number of organs in the pelvis.

Sandra Zinc, the DCT project officer for the concept, described three ongoing pilot studies of 3-D dose delivery, at Univ. of Michigan, Memorial Sloan-Kettering Cancer Center, and Fox Chase Cancer Center. No severe complications have been noted with doses as high as 76 Gy. "We know a number of institutions are capable of doing this. We think it's really ripe at this point for trials," she said.

Under a new system the board has instituted for review of concept statements, the reviewers were board members James Cox and Ralph Weichselbaum. Both spoke in support of the concept. "We're all very impressed with the technique, but what is this grant about?" board member Ronald Levy asked. Acting Radiation Research Program Director Michael Friedman said the grants funded would try to answer the question of whether the 3-D method "represents a real advance, or is it computer games?" Patients would be randomized between the conventional standard dose or the higher dose made possible by 3-D.

The board voted 14-1 in favor of the concept, with Levy opposed.

Gene Regulation of Radiation Resistance. Concept for a new RFA, proposed annual amount $1 million (4 awards anticipated); 3 years.

Failure of radiation therapy to effect cures or local control has been attributed to the resistance of the tumor cells to radiation. Compared with the numerous studies investigating the mechanisms responsible for drug resistance, very little is currently being done to identify the mechanisms of radiation resistance.

Research in this area needs to be stimulated.

The purpose of this award is the identification and characterization of the genetic mechanisms responsible for increased levels (inherent and/or acquired) of radioresistance that are frequently observed in some solid human tumors. Studies should be directed toward understanding whether the regulation of genes and their products have relevance to clinical radiotherapy problems. These studies could include, but not be limited to, the role of second messenger pathways, growth, molecular and chemical factors, and signal transduction pathways in radiation resistance.

The aim of this initiative is to better understand the mechanisms underlying unusually high levels of radiation resistance, exceeding that of normal cells, encountered in radiotherapy of solid tumors. This understanding should help optimize the activity of radiation therapy as a cancer treatment by modulating those mechanisms identified as playing significant roles in inherent and/or acquired radiation resistance. Additionally, important molecular and cellular prognostic factors for survival or recurrence of malignancy in patients treated with radiotherapy may be identified from the proposed award.

Primary reviewer Ralph Weichselbaum said the RFA concept represents "a piddling amount to give to what I think is an important area and an underfunded area." Secondary reviewer Mark Groudine quipped, "And it is an important mechanism for funding research in Ralph's lab." Groudine added, more seriously, that this type of research has "a lot of problems going through the conventional funding methods," and thus he supported the RFA.

Levy countered that the area is "ripe for regular review and if there are good ideas, they would be flushed out." JoAnne Stubbe agreed. Board Chairman John Niederhuber said the applications would receive more meaningful scientific review in a separate study section.

The board voted 9-4 in favor of the concept.

Clinical Correlative Studies in Solid Tumors. Concept for a new cooperative agreement (RFA). Proposed first year award $2 million; 3 years.

This RFA concept is designed to promote collaborations and interactions between basic researchers and clinical investigators to advance research on clinical correlations that can improve therapeutic approaches. NCI is seeking to encourage correlative laboratory studies linked to large scale clinical trials. In many instances the laboratory investigators are already recipients of R01 or P01 support for their basic research. Likewise, many clinical investigators are supported through the Clinical Trials Cooperative Group mechanism (U10) for clinical research.

This initiative proposes to link these peer approved activities and, for a relatively small additional investment, provides a mechanism to obtain definitive data on the relationship of biological features and the clinical behavior of the tumors. Objectives and approaches will be investigator-initiated, with participants funded via cooperative agreements-assistance mechanisms that retain the decision-making prerogatives of the principal investigator and his/her colleagues, but at the same time permit NCI coordination of activities among the participating laboratories. The Cancer Diagnosis Branch, Div. of Cancer Biology, Diagnosis, and Centers has been working closely with CTEP, under the aegis of the NCI Diagnosis Decision and Implementation Committee (DDIC), to assure that promising new approaches will be moved more rapidly into clinical practice. The charge to DDIC, created in 1989, is to identify assays ready for evaluation and to set priorities for large scale clinical evaluations. The role of DDIC in the proposed cooperative agreements will be to assist in coordination of studies and to provide information regarding NCI priorities. In addition, NCI staff from CTEP and the Cancer Diagnosis Branch will interact with grantees providing information on related ongoing research efforts elsewhere in the scientific community, as well as coordinating the activities of the basic and clinical research groups and facilitating exchange of information.

CTEP and the Cancer Diagnosis Branch are seeking applications for research grants (U01) concerned with clinical correlative studies relevant to cancer treatment or clinical outcome in patients with solid tumors. Solid tumors that account for significant cancer incidence, morbidity and mortality, e.g., breast, prostate, lung, colon-rectum, upper aerodigestive, ovary, bladder, pancreas, melanoma, stomach, kidney, as well as rarer tumors such as pediatric and adult brain and sarcoma, are relevant to this RFA. The therapeutic correlates must have a potential clinical application such as development of new treatment strategies or identification of patient subsets for specific treatment approaches. The laboratory assays must utilize tumor specimens from patients receiving defined treatments in Phase 3 clinical trials. These assays must have already been demonstrated to be applicable to tissue samples and/or body fluids. In order to obtain statistically valid data, applications are limited to investigators who have access to large numbers of tumor specimens. All investigators are encouraged to work with multicenter organizations in order to access large numbers of patients and adequate clinical information.

Some examples of therapeutic laboratory correlates may include but are not limited to: (1) phenotypic of genotypic alterations that appear to correlate with the development of therapy resistance; (2) loss or inactivation of tumor suppressor genes related to prognosis; (3) analysis of basal membrane factors related to tumor invasion and metastases; (4) studies of chromosomal rearrangements or deletions that may be used as prognostic indicators; (5) correlation of tumor growth factors or oncogenes with response to therapies; (6) characterization of tumor associated antigens that may lead to new immunotherapies; (7) evaluation of use of serum or tumor markers that correlate with tumor progression.

The objectives of this RFA are to foster collaborations and interactions between basic researchers and clinical investigators to advance therapeutic clinical research and conduct correlative studies in solid tumors on new prognostic factors that may influence cancer treatment and clinical outcome.

CTEP Director Michael Friedman said NCI staff gave this RFA concept "a great deal of thought" before bringing it before the board, which at its last meeting turned down one RFA concept and forced Friedman to withdraw another (**The Cancer Letter,** March 8). He noted that staff felt that the cooperative agreement was the key to this program, necessitating the use of the RFA set-aside funding. The program is not aimed solely at the cooperative groups, but does require access to large numbers of patients, he said.

Primary reviewer Donald Kufe said the concept does

represent an important priority and the area is underfunded. Weichselbaum said he objected to the restriction to phase 3 studies. "It would seem to restrict this to the cooperative groups," he said.

"It means cooperative groups will be applicants, but it is not restricted to them," Friedman said.

Paul Carbone also wondered whether the emphasis should be on developing new markers rather than testing currently known markers. "For a number of markers, we already have pilot data and urgently need them to be tested in large numbers of patients," Friedman said. "We're trying to make the most impact now."

The board approved the concept unanimously, with the amendment offered by Carbone that the RFA include some flexibility in allowing phase 2 studies.

RFPs Available

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

RFP NCI-CP-15689-66

Title: Synthesis of selected chemical carcinogens and chemopreventive agents

Deadline: Approximately Sept. 3

The Chemical and Physical Carcinogenesis Branch of NCI's Div. of Cancer Etiology has a continuing requirement for the synthesis, purification, and characterization of a number of different research compounds of interest to the carcinogenesis research community.

The compounds are to be prepared in exploratory syntheses on a small scale and then prepared in a production run to yield one to several grams of sufficiently pure material (generally 99+ percent). Compounds are to be characterized by a meaningful combination of appropriate techniques including specific activity; melting points; boiling points; ultraviolet, visible and infrared spectroscopy; and NMR or mass spectroscopy.

Major responsibilities are: 1) resynthesis of polycyclic aromatic hydrocarbon PAH derivatives by established procedures for the restocking of NCI's Chemical Carcinogen Reference Standards Repository as necessary, and 2) development of synthesis or purification procedures for the preparation of a wide spectrum of selected chemical carcinogens, chemopreventive agents and certain of their metabolites or derivatives. Distribution to the research community will be handled by the repository contractor for all unlabeled compounds. Labeled compounds will be subdivided and shipped to designated recipients in the research community by the synthesis contractors. The contractors shall be required to provide analytical, handling, and storage data with all shipments. A high degree of cooperation with NCI, the repository contractor, and other synthesis program contractors is necessary. This is a recompetition of two existing contracts for similar work. Contracts will be awarded for a five year period.

Contract specialist: Donald Holt
RCB Executive Plaza South Rm 620
301/496-8611

Nominations Accepted For Columbus Discovery Awards Until June 30

The Christopher Columbus Medical Sciences Committee of the National Institutes of Health and the CCMSC/Genoa, under the auspices of the Quincentenary Jubilee Commission, will award eight to 10 prizes for scientific discoveries that have contributed significantly to the alleviation of disease and disability.

The prizes will be a one-time award offer in conjunction with two scientific meetings that are being held as part of the international activities celebrating the 500th anniversary of the Old World discovery of the New World. The CCMSC/NIH activities are being co-sponsored with donations from private sources.

The Awards Subcommittee of the CCMSC/NIH hereby invites and encourages nominations of outstanding scientists, of any nationality, from all areas of science that have an impact on health, for this award.

The closing date for nominations is June 30, 1991. For information regarding the nomination process and selection criteria, please contact: Dr. James Hill, Deputy Director, National Institute of Allergy and Infectious Diseases, Chairman Awards Subcommittee, NIH Bldg 31, Rm 7A03, 9000 Rockville Pike, Bethesda, MD 20892, phone 301/496-9118.

Active NCI Program Announcements

In addition to unsolicited grant applications and grant applications in response to other Program Announcements, NCI is currently accepting applications in response to the following Program Announcements (which have appeared in previous issues of **The Cancer Letter**, and the "NIH Guide to Grants and Contracts"). Also refer to the publication, "NIH Extramural Programs," available from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892.

--Individual Postdoctoral National Service Award Fellowships in Radiological Sciences Related to Cancer.

--Clinical Cancer Therapy Research.

--The NCI Outstanding Investigator Grant.

--Surgical Oncology.

--Multidisciplinary Research on Solid Tumors.

--Obesity, Endocrine and Fat Metabolism and Cancer Risk.

--Domestic Animal Models of Retroviral Associated Malignancies.

--Epidemiologic Studies of Cancer and Human Retroviruses.

--Underlying Molecular, Cellular and Immunological Factors in Age-Related Cancers.

--NCI/MARC Summer Training Supplement.

--Studies on Cancer Etiology in Finfish and Shellfish.

--Specific Cancer Cell Targeting Using Molecular Genetic Technology.

--Regulation of Prostatic Involution as Related to Prostatic Cancer.

--Small Grants Program for Epidemiology.

--The Role of Growth Regulatory Factors in Normal and Neoplastic Prostate.

Copies and information related to the Program Announcements are available by contacting: Vincent Oliverio, Associate Director, Div. of Extramural Activities, NCI, NIH Bldg 31, Rm 10A05, Bethesda, MD 20892, phone 301/496-9138, FAX: 301/402-0062.