LETTER

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OMB Reviewing Administration's Reauthorization Bill; NCI Special Authority Probably Will Remain

The Administration's bill reauthorizing biomedical research and renewing the National Cancer Act was still being reviewed by the Office of Management & Budget this week, and

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In Brief

Cox Leaving Columbia To Be Physician In Chief At M.D. Anderson; Will Continue To Head RTOG

JAMES COX, professor and chairman of the Dept. of Radiation Oncology at Columbia Univ. College of Physicians & Surgeons, has been named vice president for patient care and physician in chief of the Univ. of Texas System Cancer Center/M.D. Anderson Hospital & Tumor Institute. In that role, he will report directly to UTSCC President Charles LeMaistre. Cox is chairman of the Radiation Therapy Oncology Group and will retain that position when he moves to Texas, in July. Cox' wife, Ritsuko Komaki, associate professor of radiation oncology at P&S, will have a similar position at M.D. Anderson, with major responsibility for research in lung cancer. Cox will replace Joe Ainsworth, who is retiring. He has been VP for patient care since Fred Conrad was murdered in 1982. At Columbia, a search committee has been formed to find a successor to Cox. . . . **BRISTOL-MYERS'** new grants for pain research will be awarded to Kenneth Casey, Ann Arbor VA Medical Center; Richard Chapman, Univ. of Washington; Howard Fields, Univ. of California (San Francisco); Kathleen Foley, Memorial Sloan-Kettering Cancer Center; and William Willis, Univ. of Texas Medical School (Galveston). . . . **LARRY NATHANSON**, director of the Div. of Oncology-Hematology at Winthrop-University Hospital and professor of medicine at State Univ. of New York (Stony Brook), will give the 1988 Thordur Thordarson Memorial Lecture in Internal Medicine April 30 in Reykjavik. . . . **CHILDREN'S INN** at NIH, a lodging facility where families can live with their children while the children are treated at the NIH Clinical Center, will be constructed on a two acre site on the Bethesda campus. The estimated $2.5 million cost will be underwritten by Merck. NCI's Pediatric Branch, headed by Philip Pizzo, did all the basic planning for the Inn. . . . **FINAL** regional hearing conducted by the National Cancer Advisory Board to assess and expand public awareness of cancer prevention and screening will be held April 19 at the College of Physicians of Philadelphia.

Universities Press Hard For New Biomedical Research Construction

(Continued from page 1)
could be sent to Congress any day. It is expected to renew the existing authorities, including those special to NCI, with no significant changes, barring a last minute change of direction.

The White House may still be smarting from the thumping defeat it suffered when President Reagan's veto of the reauthorization bill was overwhelmingly overturned by Congress three years ago. The President's advisors are not anxious to take on the scientific community again.

However, the Administration is expected to oppose some of the features in the bill (S.2222) introduced two weeks ago by Sen. Edward Kennedy (**The Cancer Letter**, April 1). OMB has traditionally opposed federal funding for construction and renovation of research facilities. S.2222 would establish a new NIH wide grant program, authorizing $150 million in matching funds for the first year.

The Kennedy bill would not create any new institutes at NIH, but responding to pressures for new categorical institutes, it authorizes centers for research on deafness and other communication disorders, and a National Center for Medical Rehabilitation Research. The bill also would create centers for study of biomedical ethics and mandates an ethics advisory board and a study on fetal therapy; and would create centers in geriatric research and training.

The Administration would oppose creation of any new institutes, but its response to the new centers in the Kennedy bill remains to be seen.

Sen. Orrin Hatch (R.-UT), the top ranking Republican on the Labor & Human Resources Committee, is still the strong supporter of NIH that he was as chairman of the committee, when his party controlled the Senate from 1981-87.

"I am here today to lend support for the reauthorization of the National Institutes of Health," he said in his statement at the committee's hearing on the Kennedy bill. NIH "is clearly a bright star in the galaxy of medical research steering our efforts to find the cures and causes of disease around the world. NIH remains the crown jewel of the Public Health Service."

Hatch expressed concern about loss of NCI scientists to universities and the private sector, citing the move of Marc Lippman from NCI to Georgetown Univ. as director of the Vincent Lombardi Cancer Center, "at a significant increase in salary. I look forward to discussing the problem of retention and recruitment and how proposals to establish a Senior Biomedical Scientific Service (as the Kennedy bill does) would solve the problem."

Chase Peterson, president of the Univ. of Utah, was a member of the panel of experts convened by NIH to consider biomedical research facilities needs and to make recommendations on how those needs could be met. The panel's chief recommendation went somewhat farther than the provision in the Kennedy bill, asking for a total of $2.5 to $3 billion over eight years. The Kennedy authorization would be for only three years, the same as for the rest of his bill.

The panel's complete report has not yet been released, but Peterson discussed its recommendations and their justification at the hearing on the Kennedy bill.

"We advocate a program in which the colleges and universities can participate in partnership with the federal government in revitalizing research facilities," Peterson said, noting that he was speaking for his university, the Assn. of American Universities, the National Assn. of State Universities and Land Grant Colleges, and the Assn. of American Medical Colleges.

"I firmly believe that without such a program we cannot keep this nation's biomedical science at the cutting edge. Investment in improved facilities is essential to maintain our preeminance in biomedical research, one of only a few areas where this nation still holds a position of international superiority."

Referring to the NIH panel, Peterson said, "Not surprisingly, because of differing priorities among groups, there is some lack of consensus on issues related to infrastructure, such as the need for expanded vs. renovated facilities, or the best mechanism for support. One issue on which all parties do agree involves the need for development of a well coordinated, long range strategy for support at the federal level. All parties agree that research is hampered by aging and obsolete research facilities and instrumentation, and assert that the need to reduce the backlog of maintenance, renovation and expansion of these facilities is crucial."

Peterson quoted two of the panel's recommendations:

"For almost 20 years, federal support for the nation's effort in maintaining the physical infrastructure for biomedical research has been negligible. There is a need for strong and well defined federal leadership and a dependable and long term flow of funds for new construction, renovation and renewal and replacement of obsolescent equipment."

And, "NIH should be given an overall construction authority to address research facility construction needs. This authority should not supersede existing institute authorities, nor should in preclude the establishment of new authorities for other institutes."

Protecting NCI's separate authority, which it has via the National Cancer Act, was the vital concern of NCI representatives at the panel's meetings.

"While there is universal agreement that we suffer from a facilities deficit," Peterson said, "it is useful to understand better how these problems affect the conduct of research." He presented a memo issued by the dean of the Univ. of Michigan School of Medicine advising all researchers that the "inventory of research space is completely depleted" and that no grant applications may go forward absent a plan for space. "I also understand that the Univ. of California alone has a backlog of $4 billion in all facilities.

"At the Univ. of Utah, we are forced to spend nearly $300,000 annually to rent research space off campus. . . We rent this space because we have been unable to attract capital funds to construct appropriate facilities on campus. To do otherwise means that important research efforts in medicinal drugs and drug delivery, cancer research, and continued development of the totally implantable artificial heart would go undone. . . We believe a renewal of federal commitment is an essential factor in coordinating and motivating private sector commitment to refurbishing the research infrastructure."

Peterson noted that the AAMC has concluded that an annual investment of $301 million is needed to prevent deterioration of the current medical school research space devoted to NIH sponsored medical research.

"Many universities use a patchwork of funding mechanisms to finance their biomedical research facilities, including tax exempt borrowing, charitable giving, corporate support, return on operations, and private foundation money. Two of these funding mechanisms, tax exempt borrowing and charitable giving, were severely compromised by the 1986 changes in the tax code. The tax exempt bond market is now closed to numerous research universities because of the $150 million cap on private university borrowing.

". . . With regard to full reimbursement of indirect costs, there are some serious points to be made. If institutions must borrow, especially outside the tax exempt bond market, in support of the national mission and federally funded research, indirect cost recovery rules must recognize that fact and fully fund depreciation. It is also well known that the present policy of direct and indirect cost reimbursement does not fund the full cost of research experienced by a university."

Peterson mentioned concern with the "increasing number of earmarked appropriations of federal science budgets for specific university projects. Although our associations have expressed concern about the process of earmarking, many of our members have pursued such funds. These institutions have pointed to the hard reality that there have been no opportunities to compete for funds at the federal level in support of research facilities. Formal legislation which would remedy this problem and provide the necessary funds is certainly a better approach."

Peterson said AAMC has pointed out, "Simply maintaining the current inventory (of academic research facilities) is very costly. But maintaining the inventory is just the beginning. The survey of animal facility needs, conducted by the National Academy of Sciences Institute of Laboratory Animal Resources now almost a decade old, indicated the need for $500 million to bring animal facilities up to standard. Despite interim assistance from NIH for animal facilities, the revision of this estimate, now in progress, will not likely be smaller. In most of our institutions, research space is intensively used and the current inventory is not really even adequate for the programs currently housed in them. Expanded research activities cannot be mounted without new facilities."

Peterson urged the committee to enact legislation to meet the following goals:

1. NIH should be granted construction authority for biomedical research.

2. NIH funding authority should be centralized.

3. The award process should be governed by merit review with clear criteria for awards.

The criteria should take into account the need to broaden the base of biomedical research and thereby acknowledge the responsibility to institutions with emerging excellence in research. New construction authority could include provisions for emerging institutions, taking into account such factors as underrepresentation in health sciences careers; the health status deficit of a large segment of the population; or a regional deficit in health care technology or services that can adversely affect health status in the future.

"It is essential that none of these provisons override merit review," Peterson insisted. Rather, these factors should be considered in the process of establishing funding priorities."

4. Institutions should be required to match federal funding in some systematic way. In addition, consideration should be given to a flexible match with a greater federal portion allowable for projects in categories of national interest. These categories could include facility renovation to meet federally mandated requirements for animal care or health and safety; facilities at institutions of emerging excellence; or specialized research facilities for research on public health emergencies, such as AIDS. It should be recognized that previously available options for the generation of matching funds have been curtailed; it is critically important that Congress remove the $150 million cap on tax exempt financing for private universities. At the minimum, borrowing for research facilities should be permitted to exceed the cap.

5. Indirect cost recovery should fund facility depreciation fully. Of course, indirect cost recovery would continue to be disallowed for any portion of the cost of a facility directly funded by the government."

NIH Director James Wyngaarden talked about a façility need by NIH itself.

Wyngaarden revealed, in responding to a question from a member of Sen. Barbara Mikulski's staff, that NIH is developing plans for construction of a new building on the Bethesda campus. It would be financed through a lease purchase arrangement.

About 2,900 NIH employees work in rented space in Bethesda, Silver Spring and Rockville, Wyngaarden pointed out. "Some are scientists, but they are chiefly grants management people. It is a disadvantage to have them so far away from the campus. They are people with scientific backgrounds, for the most part. They must retain their expertise through participation in activities such as seminars, which are centered around the campus."

Wyngaarden said that space is available for the building, and that preliminary designs have been drawn up, which include underground parking.

"We've looked at relative costs of new construction vs. lease purchase vs. rental. Over 20 years, we could save $100 million with a lease purchase."

The building design can be completed within one to two years, and construction would require two to two and a half years, Wyngaarden said.

Other comments by Wyngaarden at the hearing included:

Research training. "Between 10,000 and 11,000 National Research Service Award positions are supported by NIH each year, with approximately equal numbers of pre and postdoctoral positions. Most predoctoral positions are PhD traineeships. More than half the postdoctoral traineeships support MDs. In FY 1988, NIH will award more than one half percent of NRSA funds for institutional training grants related to primary care research training.

"With the dynamic expansion and sophistication of biomedical research, there continues to be a need to provide adequately trained manpower to answer the important research questions. At the same time, with the number of graduates in total declining, commensurate falling enrollments in fields of study related to biomedical science and pressures to pursue lucrative nonresearch careers challenge us to assure a steady flow of manpower into biomedical research. The number of employed biomedical scientists has increased--412,000 life scientists were working in 1986, up from 353,000 in 1984 and 214,000 in 1976. Continued support of NRSA awards, as proposed in the President's FY 1989 budget, would add more biomedical researchers to this pool."

Biomedical research facilities. "Special requirements for protection of research workers and the public from biological and chemical hazards and increased security needs have placed greater demands on our existing facilities. There are continual needs for alteration and renovation of laboratory animal facilities, as well as an inevitable backlog of repairs and remodeling of aging and deteriorating facilities. Some facilities should not be repaired or renovated but completely replaced."

Senior level recruitment and retention. "Recruitment and retention problems as well as limitations on the number of senior level

positions have resulted in critical vacancies and deferred recruitment. A great many highly motivated senior staff have elected to remain at NIH, but recruiters from academia and industry make highly attractive offers that at best are unsettling, and only too often are accepted. While the Senior Executive Service allows NIH to promote some of our most accomplished scientists and administrators into the senior ranks, we have had limited success in attracting top caliber candidates from outside the government. Academic institutions, industry, and independent research laboratories offer substantial salary increases. Compensation of physicians and other doctorates in academic institutions is considerably higher than that available at NIH. In the academic sector, on the average, the compensation of senior physicians is 62 percent higher than that received by NIH senior physicians, while the base pay of senior PhD staff is 23 percent higher than that received by NIH senior PhD staff.

"At the same time, NIH offers advantages that for many researchers offset the salary differentials. Among these are the intellectual stimulation and prestige of being a part of NIH, as well as the scientific freedom to choose their own research pursuits. Scientists at NIH have access to state of the art equipment, freedom from administrative and teaching responsibilities, and opportunity for rewarding associations with outstanding scientists from many disciplines. Also, there are opportunities for consulting, although these are subject to some limitations.

"Employment in the academic sector provides the prospect of superior salary supplements, fringe benefits such as tuition subsidies, and better opportunities to supplement income through private practice and consultation. In addition, the fact that there is no limit upon university salaries supported through NIH extramural mechanisms further fuels the pay competition from the academic sector.

"Recent advances in the biomedical sciences and biotechnology have opened many potentially valuable and lucrative commercial applications and have caused a dramatic increase in competition for top caliber researchers and science managers in the private and academic sectors. The emergence of the biotechnology industry has contributed to the competition between senior NIH staff and their counterparts in industry and universities.

"Recruitment and retention should be viewed in the context of training. As a training ground for post doctoral researchers, the intramural laboratories of NIH have helped staff the nation's research universities. Many junior scientists complete their training at NIH and continue their research careers in the universities. A high percentage of this country's leading researchers are NIH alumni.

"If NIH is to remain the international leader in the biomedical sciences, new approaches must be found to make our senior level personnel systems competitive with the private and academic sectors. We have asked the Institute of Medicine to study the structure and organization of NIH intramural research including recruitment and retention difficulties; their causes and effects on NIH research quality; and potential strategies to address them if warranted. We would like to study the IOM findings and recommendations before we make final recommendations on recruitment and retention issues."

Ada Sue Hinshaw made her initial appearance at a reauthorization hearing as director of the National Center for Nursing Research.

"The nursing research community is proud to be represented by the center as the newest part of the National Institutes of Health," Hinshaw said.

After complimenting Doris Merritt, who served as NCNR's acting director during the first few months of its existence for "diligent efforts" in organizing the center, Hinshaw described its "vigorous growth. Our staffing has increased to 28 and our budget has grown by 41 percent to a total of $23.3 million in fiscal year 1988. This year, we plan to award 128 research project grants and support 191 research trainees, compared to 100 grants and 165 trainees in FY 1986. We are programmatically and administratively sound and fully functional.

"The ultimate purpose of nursing research is to generate and test knowledge that will enable health care providers including nurses to give better care. The client and the family, as they respond to the promotion of health and the treatment of illness, are the foci of nursing research. To this end, the center supports basic and clinical research and research training in nursing science through research project grants, research training grants, and career development awards. Scientific program areas include acute and chronic illness, health promotion and disease prevention, and nursing systems.

"NCNR has undertaken a number of initiatives addressing society's and the profession's concern with the nursing shortage," Hinshaw continued. "In fiscal year 1987, a supplemental appropriation provided $1 million to NCNR for a joint endeavor with the Div. of Nursing of the Health Research Services Administration to address the shortage of nurses and to support hospital based clinical research projects. These funds, and other NCNR dollars, provided support for 25 research project grants, fellowships and career development awards related to nursing resources and patient care delivery. These include studies of nurse retention in intensive care units, and studies of drug use, stress and job performance among nurses."

David Satcher, president of Meharry Medical College, focused his remarks on research facility construction, representing the Assn. of Minority Health Professions Schools. Satcher also served on the NIH panel which reviewed research facility needs.

"The problem of facilities for the schools in our association is not unlike many of the other challenges we face in our year to year operation," Satcher said. "The collective missions of our institutions is train disadvantaged individuals to serve in underserved areas is a challenge to institutional financial stability. Because of that mission our institutions fall behind in the entire realm of rsearch infrastructure, from our research faculty, to instrumentation, to facilities. However, based on our past accomplishments with meager resources, we feel confident that we could make a significant contribution if these facilities and other support were provided. Particularly in terms of studying diseases and health conditions that disproportionately affect Blacks and other minorities, our schools and the health care facilities associated with our schools are in the most appropriate settings to have a great impact.

"The Assn. of Minority Health Professions Schools recognize the importance of a federal facility construction system that utilizes peer review based on institutional capabilities, track record, and scientific merit. We also recognize and urge that some federal resources be awarded to institutions based on the health status needs of our nation, and the needs and capabilities of the institutions that can have the greatest impact on addressing these needs. The historically Black health professions schools have an emerging excellence and capability to train faculty, and study diseases that disporportionately affect minorities and we believe that when considering federal facility renovation and construction resources, criteria should be developed that recognize these important unique capabilities.

"Funding of construction for research facilities to eligible institutions that demonstrate emerging excellence in biomedical and behavioral research could be considered under the following criteria:

"A. An institution that carries out research and training programs that have a special relevance to a problem, concern or unmet need of the United States.

"B. An institution that has already demonstrated a commitment to enhancing and expanding its research productivity.

"C. An institution that has been productive in research or research training in the face of significant challenges such as a disproportionate role in impacting the underrepresentation of minorities in health science careers or the health status disparity of a large segment of the population.

"D. An institution that has a plan for research advancement, and the ability to carry out such a plan."

Jako Asks For IOM Review Of Cancer Program, Delay Of Reauthorization

Geza Jako has wrapped up his six year term on the National Cancer Advisory Board by calling for a review of the National Cancer Program by the National Academy of Science Institute of Medicine before renewal of the National Cancer Act.

In letters to Sen. Orrin Hatch, the ranking Republican on the Labor & Human Resources Committee, and Congressman Edward Madigan, ranking Republican on the House Health & Environment Subcommittee, Jako expressed opposition to the NCAB's request for a five year reauthorization of biomedical research, including the National Cancer Act. Renewal should be placed on hold for a year while IOM conducts its review, Jako suggested.

"My main concern is that in recent years if the so well publicized NCI effort to decrease cancer mortality by 50 percent is not on target, then an unfilled promise to the American people by the Cancer Institute could backfire and then NCI could put the blame on Congress and the Administration and embarrass them by stating that the 'superfunding' that was requested in the bypass budgets was not

provided," Jako wrote. "In my opinion, there is not a direct linear relationship between funding, research success in treatment and decrease in mortality.

"It is my observation that while in the areas of cancer biology and etiology the NCI programs are excellent, in the area of cancer treatment and cancer prevention and control it does not have a well balanced program to achieve in the short term the year 2000 goal."

Jako appended a six page collection of "observations and questions" some of which "are adversarial in nature," he said, which he suggested as points for IOM to consider if it undertakes the review.

His "observations" included attacks on the bypass budget and suggestions it is used to build a "larger government bureaucratic empire" and to "increase the glut of medical oncologists-chemotherapists;" inferences that NCI has failed in communication and cooperation with other organizations; failure to place more emphasis on lung cancer treatment research; short changing surgery research; questioning whether diagnostic imaging research, which was moved into NCI's Radiation Research Program from elsewhere in NCI and other NIH institutes, should remain there.

Jako also criticized NCI's decision (approved overwhelmingly by the NCAB) to phase out the external Organ Systems Coordinating Center and move it into NCI. And he referred to NCI Director Vincent DeVita's criticism of practicing physicians for their alleged failures to make optimal use of proven drug regimens. "The NCI director, a pioneer in chemotherapy, frequently criticizes the medical oncology community for providing inadequate chemotherapy treatment," Jako wrote. "He also repeatedly declared publicly that this inferior treatment costs several thousands of cancer patients lives per year. If experts will confirm the NCI director's charges, should Congress take immediate remedial actions to save thousands of U.S. cancer patients lives per year?" He did not suggest what kind of remedial action Congress might take.

Jako sent his letters on NCAB stationery, which reportedly outraged other members who felt that this indicated his views were shared by them. He further endeared himself to his colleagues by inferring that many of them could not be "independent and objective" because they received NIH grant support.

NCI's intramural scientists did not escape Jako's attention. "NCI intramural research results seems to get more public attention, sometimes even prematurely, compared to other NIH institutes or NCI extramural programs," he wrote. "If this is true, could it be creating false hopes for people and misleading the American public?"

DeVita declined to comment on Jako's statements or his request for an IOM review. David Korn, NCAB chairman, told **The Cancer Letter** by phone from Palo Alto, where he is dean of the Stanford Univ. School of Medicine, that Jako's statements "are so full of inaccuracies and so inane that I don't want to waste any time commenting on them."

Jako's term on the Board expired after the February meeting, along with five other Board members. The White House is in the process making the new appointments, which are expected to be announced prior to the Board's next meeting, May 9-11.

RFAs Available

RFA 88-CA-05
Title: Identification of genetic alterations involved in bladder carcinogenesis
Application receipt date: July 7

The Organ Systems Program, through NCI's Div. of Cancer Prevention & Control, invites grant applications for development of multidisciplinary research programs involving specialists in molelcular biology, chemical carcinogenesis and organic chemistry. The major goal of this initiative is to increase understanding of the genetic alterations underlying multistage chemical carcinogenesis in the urinary bladder. A renewed experimental approach to this goal is made possible by recent successes in developing molecular, cellular and in vivo systems for the exploration of urinary bladder carcinogenesis. There is a unique opportunity to integrate these areas of research in efforts to achieve the following specific objectives:

1. Determine which alterations (mutations, translocations, amplifications) in known cellular proto-oncogenes are important in multistage bladder carcinogenesis in experimental systems.
2. Identify genes which might be involved in the pathogenesis of bladder cancers.
3. Use cytogenetic studies to provide clues to the molecular alterations in bladder cancer cells.
4. Determine the mechanisms by which carcinogens activate proto-oncogenes in bladder tumorigenesis.
5. Determine the roles and timing of genetic changes during the multistage development of bladder neoplasia.

This RFA is intended to initiate studies of the bladder in organizations which are already contributing significantly to research in molecular biology. An organization with a molelcular biology laboratory, which can establish associations with research efforts in chemical carcinogenesis and bladder cancer, is encouraged to respond to this RFA. At the time of submission, core support for molecular biology, qualified investigators, technical expertise and facilities should exist in the organizations which respond to this RFA.

The purpose of this initiative is to stimulate research on molecular genetic and cytogenetic mechanisms of bladder carcinogenesis. Several model systems already exist for studying chemical carcinogenesis in the mammalian urinary bladder. Responses to this RFA might incorporate such systems, e.g., make use of models for

multistage transformation. Other systems might be developed which could facilitate experimental approaches to understanding how genetic alterations are involved in the genesis and development of bladder tumors. Either animal or cell culture models (human or rodent) could be used, as long as the system studied has well defined biologic endpoints.

Highest priority should be placed on approaches which are likely to provide detailed molecular information pertinent to bladder tumor induction. Attempts might be made to elicit biologic responses with metabolites of carcinogens which are subject to metabolic activation in urinary bladder cells, as for example N-hydroxyarylamine derivatives. This would avoid the possibility that the target bladder cells could respond because of inadequate levels of N-oxidation potential. It is envisioned that it should be possible to employ DNA vectors which carry the potential for eliciting cellular transformation, e.g., proto-oncogenes, when modified by carcinogens. This approach should permit the direct exploration of biologic responses to carcinogens introduced into the DNA at single, specific sites, following transfection into mammalian cells.

Transformed cells should be analyzed for alterations in cellular genes thought to be important in the neoplastic process. This would involve analysis of isolated DNA and the use of in situ hybridization techniques. The technology employed should be able to detect base substitutions, frameshifts, translocations, amplifications and loss of genes (or ther reduction to homozygosity). The altered expression of specific genes, in the apparent absence of direct genetic alteration of the genes, might provide avenues of investigation into alternative control sequences.

The proposed studies should represent a multidisciplinary effort, possibly involving collaboration among pathologists, molecular biologists, tumor biologists, cytogeneticists, organic chemists and experts in chemical carcinogenesis.

Applicants are encouraged but not required to submit letters of intent and to consult with NCI staff before submitting. The letter of intent is requested by May 6.

It is anticipated that five awards will be made at an overall annual total cost of about $650,000.

For copies of the complete RFA and further information, contact William Straile, PhD, Cancer Centers Branch, DCPC, NCI, Blair Bldg Rm 727, Bethesda, MD 20892, phone 301/427-8818.

RFA 88-CA-10

Title: Investigation of tissue composition and function by MRI using paramagnetic and/or superparamagnetic contrast agents

Application receipt Date: July 7

NCI's Div. of Cancer Treatment, through the Diagnostic Imaging Research Branch of the Radiation Research Program, seeks applications for studies to improve and demonstrate the ability to visualize selected tissues and to characterize their composition and functional states by the employment of paramagnetic and/or superparamagnetic resonance imaging (MRI) contrast agents.

The primary objective of this RFA is to promote studies employing paramagnetic and superparamagentic substances in the investigation of localization of tumors, tissue composition, tissue function, and quantitative measurement of normal and pathological processes, especially as these pertain to cancer. Although the principal focus of this RFA is predominantly on detection and diagnosis, diagnostic monitoring of treatment response is also an acceptable area of investigation. The employment of combined magnetic resonance imaging and spectroscopy in conjunction with contrast agents would also fall within the scope of this study. A variety of paramagnetic and superparamagnetic contrast agents have been developed and can be used in research and clinical applications as molelcular probes for the identification of specific tissues and as agents to monitor pharmacokinetic behavior in the assessment of physiologic function and pathology.

The mechanism of support for this award is the NIH grant in aid for a duration of three years. The estimated total budget for the first year of this program is $400,000. It is anticipated that approximately three scientifically meritorious applications can funded.

For copies of the complete RFA and further information, contact Roger Powell, Program Director, Diagnostic Imaging Research Branch, RRP, DCT, NCI, Executive Plaza North, Suite 800, Bethesda, MD 20892, phone 301/496-9531.

Program Announcement

Title: Basic studies in bone marrow transplantation

Application receipt dates: Feb. 1, June 1, Oct. 1

The Immunology, Allergic & Immunologic Diseases Program (IAIDP) of the National Institute of Allergy & Infectious Diseases invites grant applications for support of basic, preclinical studies in the area of bone marrow transplantation.

Bone marrow transplantation is becoming an increasingly important therapeutic procedure for the treatment of a wide variety of diseases, including aplastic anemia, leukemia, congenital immunodeficiencies, and most recently, AIDS. However, even though BMT is unparalleled in its effectiveness in curing many fatal diseases, this technique suffers from several serious side effects, including graft vs. host disease and prolonged immune deficiency following transplantation. To overcome the problem of GvHD, T cells have been removed from the donor inoculum prior to transplantation. This maneuver virtually eliminates GvHD, but results in two new complications, graft failure (i.e. graft rejection) and an increased rate of leukemic relapse. Further, even in the absence of GvHD, many BMT patients are susceptible to infections for as long as one year following transplantation, presumably due to impaired immune cell reconstitution.

NIAID is soliciting investigator initiated research grant applications that would lead to characterization of the mechanisms underlying the induction of GvHD, BM engraftment, marrow rejection and/or the graft vs. leukemia response. The proposed research may consist of in vitro studies, studies in animal models, or both, but must be preclinical in nature. Innovative approaches are sought and may address any aspect of bone marrow pretreatment, rejection, graft vs. host reaction, immune cell reconstitution, the role of lymphokines or growth factors in marrow reconstitution and rejection, the role of cell surface structures in this process, and the influence of the thymus gland on engraftment.

The mechanism of support will be the individual research project grant (RO1), and the first independent research support and transition (FIRST) award (R29). The standard NIH grant application (PHS 398) should be used and sent to the Div. of Research Grants.

For additional information, contact Dr. Jane Schultz or Dr. William Duncan, Genetics & Transplantation, Biology Branch, IAIDP, NIAID, Westwood Bldg Rm 754, Bethesda, MD 20892, phone 301/496-5598.

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