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SENATE VOTE ON OVERRIDE OF NIH REAUTHORIZATION VETO DELAYED UNTIL AFTER US-USSR SUMMIT MEETING

Senate leaders have postponed a vote to override President Reagan's Nov. 8 veto of the Health Research Extension Act of 1985 until the President's summit meeting with Soviet leader Mikhail Gorbachev

(Continued to page 2)

In Brief

TRAVEL GRANTS AVAILABLE FOR 14TH INTERNATIONAL CONGRESS; NIH SEEKS NURSES FOR STUDY SECTIONS

TRAVEL GRANTS for active participants in the 14th International Cancer Conference Aug. 21-27 in Budapest will be available to U.S. investigators. Up to $1,400 per grant will be awarded on a competitive basis, with some invited speakers and panel chairmen qualifying automatically. A special fund will be set aside for young (under 35) investigators. Contact Dr. Edwin Mirand, U.S. liaison member of the Congress organizing committee, at Roswell Park Memorial Institute, 666 Elm St., Buffalo, N.Y., 14263, phone 716-845-2300 .... **ABSTRACT DEADLINE** for International Cancer Congress is Nov. 30. Phone Mirand for copies of abstract forms.... **NURSE SCIENTISTS** are being sought for study sections that review grant applications for research and training by NIH's Div. of Research Grants. Names and CV should be sent to Mischa Friedman, PhD, Chief, Referral and Review Branch, DRG, NIH, Bethesda, Md. 20892. . . .**NRSA ELIGIBILITY** for nurses will be emphasized by NIH. Graduate nurses may be eligible to apply for predoctoral or postdoctoral NRSA institutional training grants or for individual NRSA fellowships... **WISTAR INSTITUTE** and NCI scientists were included in team that found some multiple sclerosis patients may be infected with a virus related to the human T cell lymphotropic virus family. The findings were reported in the Nov. 14 issue of "Nature".... **THREE PIONEERS** in cancer research and treatment received awards this week at the M.D. Anderson 29th annual clinical conference. Felix Rutledge, international authority on gynecologic surgery, received the 20th annual Heath Memorial Award given for outstanding basic science contributions to improved care for cancer patients. Gordon Zubrod, director of the Univ. of Miami Comprehensive Cancer Center, received the 10th annual Jeffrey Gottlieb Memorial Award to recognize his contributions to therapeutic cancer research. Zubrod was director of what is now NCI's Div. of Cancer Treatment and headed initial development of chemotherapy in cancer treatment. William Christopherson, a pioneer in gynecologic cancer screening, received the ninth annual Joanne Vandenberge Hill Award, given to honor the contributions of pathology to improving cancer diagnosis.

HATCH VOWS TO OVERTURN NIH VETO; '86 ELECTIONS MAY AID SUPPORT

(Continued from page 1)

this week. Although Senate supporters of the NIH reauthorization measure have vowed to overturn the President's veto, they decided to delay action until after the summit. Senate Majority Leader Robert Dole (R-Kan.) met with Labor & Human Resources Committee Chairman Orrin Hatch (R-Utah), coauthor of the bill, on Nov. 13 to discuss Senate action to override Reagan's veto of the measure. Dole reportedly told Hatch that Republican votes to override the veto would be jeopardized if the vote were held before this week's summit, and urged the senator to delay a vote on the override, originally expected to go to the Senate floor last week.

The House of Representatives voted 380-32 to override Reagan's veto of the bill on Nov. 12 (**The Cancer Letter**, Nov. 15).

"We're going to do everything we can to overturn the veto" of the NIH bill, Hatch told a Nov. 13 hearing on nutrition and fitness. The committee's ranking minority member Edward Kennedy (D-Mass.) told the same hearing that he and Hatch will work together to override the veto.

In a statement released the previous day, Hatch charged that the Administration's "'concern about excessive congressional and political interference in the management of NIH' doesn't hold water.

"Quite frankly, I am dismayed by the President's action," he said. "This compromise legislation resulted from long arduous negotiations between the House, Senate, medical community and the Administration. We made a good faith effort to meet the President's concerns expressed in the 1984 memorandum of disapproval. I believe the President received bad advice on this and he underestimated its vast support on Capitol Hill. I will work to get an override."

Hatch noted that 76 senators had joined him in sending a letter to Reagan urging the bill be signed into law prior to the veto. In order to overturn a presidential veto, the measure must be supported by two thirds of members present and voting in the House and Senate. Hatch appears confident that he can obtain the necessary support to override the veto of the NIH bill in the Republican controlled Senate.

During discussion on the override in the House last week, Minority Leader Robert Michel (R-Ill.) also expressed displeasure with the President's action. Although noting that his position as a party leader in the Democrat controlled House made it almost mandatory for him to vote to sustain the veto, Michel said, "my heart won't be in it. Of all those measures which have come down the pike that are candidates for veto, this is the least of them."

Political analysts have predicted an increased independence among Republican legislators in this Congress, with the crucial 1986 election looming on the horizon. The Republicans gained control of the Senate in 1980 for the first time since 1954. Twenty two Republican senators are up for reelection in 1986, which makes them more sensitive to pressures from constituents. That independence could also be fueled by resentment by some Republicans toward what was seen as insufficient support from the White House for Republican candidates during last year's Congressional election.

While Hatch said he appreciated the President's decision to create a new National Institute of Arthritis & Musculoskeletal & Skin Disease by executive order, he emphasized that "this was not the only significant item in the legislation. The Center for Nursing Research, restrictions for fetal research, guidelines for animal welfare and the other provisions included in the bill are vital if our nation is to maintain a standard of excellence in biomedical research necessary for effective health care delivery and disease prevention."

Hatch's statement cites the authorization of appropriations for NCI and the National Heart, Lung & Blood Institute as other highlights of the bill. The bill also includes the renewal of the National Cancer Act.

Other "significant" items cited by the senator include: provisions for HHS to require recipients of federal funds for the conduct or support of biomedical or behavioral research to establish an administrative process to review reports of scientific fraud; the establishment of a permanent Biomedical Ethics Advisory Board and Biomedical Ethics Advisory Committee in the legislative branch of government; and authorization for the National Institute of Aging to support centers of basic and clinical research into Alzheimer's disease.

Reagan insisted in his veto message that the action "in no way should be interpreted as lessening our commitment to the endeavors of the National Institutes of Health." The measure, he said, "would impose numerous administrative requirements which would interfere with carrying on research activities in the most cost effective manner. It would diminish administrative flexibility. It is overloaded with objectionable provisions that threaten NIH's capacity to manage itself."

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NCI DIET GUIDELINES AND PREVENTION EFFORTS OUTLINED AT SENATE HEARING

NCI's dietary recommendations for the prevention of cancer received the endorsement of a variety of panelists testifying at a Senate hearing on nutrition and fitness Nov. 13. Discussing NCI's Cancer Prevention Awareness Program, Div. of Cancer Prevention & Control Director Peter Greenwald outlined the formulation of the institute's dietary recommendations before the Senate's Labor & Human Resources Committee.

While Greenwald's testimony noted that "we do not know everything we need to know about diet and cancer," he emphasized that the institute's recommendations "are based on the findings of hundreds of laboratory, animal and human studies."

Both Greenwald and fellow witness Oliver Alabaster, an associate professor of cancer research at George Washington Univ. and author of a recent book, "What You Can Do To Prevent Cancer," told the committee that sufficient evidence exists to make dietary recommendations to the public on how to reduce the risk of certain kinds of cancer.

Noting that "it's becoming clear that diet affects everyone's cancer risk," Committee Chairman Orrin Hatch (R-Utah) repeatedly asked witnesses whether "we know enough to recommend" specific dietary practices to the public.

Asserting that "we do know enough," Alabaster emphasized that "any recommendation in '85 is obviously an interim recommendation" that will require updating in the future, but that such recommendations should be made. "We currently have diet anarchy," he said, adding that scientists have a responsibility to make the public aware of what is known about diet and cancer and to act upon that knowledge.

Hatch also asked Greenwald about chemoprevention trials underway, asking when results would be available in order to make recommendations on vitamin supplements. NCI expects preliminary results from the trials to be available between 1989 and 1992.

The senator also expressed interest in alternative therapies for cancer treatment. While Greenwald noted that most NCI investigations of such therapies have failed to support the therapeutic claims, John Fink, a member of a California based organization entitled "The Cancer Victors," testified about his visits to a number of "alternative treatment" centers in which "nontoxic primarily nutritional methods" are used exclusively or in conjunction with conventional treatments. One such facility visited was the Bristol Cancer Help Center, which opened in England in 1983. "The center's program emphasizes a change of life style, nutrition, and stress control which often are added to conventional treatments and enhance the patients immune response and powers of self healing," he said.

"There is now a wealth of scientific information establishing the link between nutrition and the cause of some major forms of cancer," he said. "Clinical practice is showing us that nutrition can be an important complementary therapy."

Commending Congress' role in the establishment of NCI's Diet, Nutrition & Cancer Program in the mid '70s and the creation of the Dietary Goals Report, Fink urged research into the use of nutrition in the treatment of cancer. "Congress can further the cause of improved health by calling for new research using nutrition in the treatment of cancer."

Hatch however, questioned how patients can distinguish between a cancer center carrying out "real research" into dietary treatment versus one "preying on the fears" of a cancer victim. Fink acknowledged that while all the centers he visited "have their testimonials, a gray area" existed in some. "It's too complex and difficult a question for me to answer," he said.

Greenwald stressed the importance of cancer patients having "the best in diagnosis and state of the art therapy." NCI's biggest concern is that cancer patients do not receive adequate diagnosis and therapy, and use an unproven therapy, he said.

Hatch also asked whether NCI educational programs are adequate to deal with high risk groups or if those groups need to be targeted. Greenwald acknowledged that more emphasis is needed in target populations, particularly in the area of applied research.

Hatch and Kennedy plan to introduce a bill to create a President's Council on Health Promotion and Disease Prevention. A similar measure will be introduced in the House by Reps. Don Ritter (R-Pa.) and Henry Waxman (D-Calif.).

Surgeon General C. Everett Koop told the committee that PHS will publish "a comprehensive analysis of the current state of our knowledge about the relationships of nutrition with diseases and conditions that continue to cause premature death and untold suffering and economic costs to Americans." To be published in 1986, the Surgeon General's report is being developed primarily by scientists within PHS and "is receiving careful peer review by nutrition scientists across the country," he said. "Our purpose in preparing and promulgating this report on nutrition and health is to provide a firm foundation for public health policy related to nutrition as we move forward to meet our 1990 objectives, and beyond that, as we formulate our national health goals and strategies for the next decade leading to the year 2000."

PB-8511 - 018797

NEW NIH APPLICATION RECEIPT DATES TO GO INTO EFFECT JAN. 1, 1986

NIH revised application receipt dates, review and award schedule will go into effect Jan. 1, 1986.

Jan. 10, May 10 and Sept. 10 are the new application receipt deadlines for:

* All individual NRSA applications.
* All new and competing continuation institutional NRSA Training grant applications.

Feb. 1, June 1, and Oct. 1 are the new application receipt dates for:

* All new research grant applications, unless specified differently in a program announcement or RFA.
* Career Development awards and Conference grant applications.
* New and competing continuation Program Project and Center applications.

March 1, July 1 and Nov. 1 are the new application receipt dates for:

*Competing continuation and supplemental research grant applications.

April 15, Aug. 15 and Dec. 15 are the new deadlines for:

*Small Business Innovation Research (SBIR) Program, both phases. (Phase 2 applicants must have completed a federally funded phase 1 project).

The initial review group dates for the first round of applications is May/June; for the second round, Oct./Nov., and Feb./March for the third round.

Applications from the first round will go to the National Advisory Council or Board in September/October; from the second round in January/February; and from the third round, in May/June.

The earliest possible beginning date for projects is Dec. 1 for the first round; April 1 for the second round; and July 1 for the third round. The start dates for individual NRSA applications are approximately four months earlier because NRSA applications are not reviewed by council.

All applications must be received by the above dates. If the receipt date falls on a weekend, it will be extended to Monday; if the date falls on a holiday, it will be extended to the following workday. The receipt date will be waived only in extenuating circumstances.

To request a waiver, include an explanatory letter with the signed completed application. No waiver will be granted prior to receipt of the application. NIH advises, "It is in an applicant's best interest to submit early and avoid the otherwise unavoidable rush associated with announced receipt dates."

PB-8511 - 018798

AIDS BIOLOGICAL SPECIMENS AVAILABLE TO RESEARCHERS FROM NIH REPOSITORY

Biological specimens for AIDS related research are available from NCI and the National Institute of Allergy & Infectious Diseases.

NCI and NIAID have developed a repository of biological specimens from homosexual men, The specimens were collected through contracts with five major U.S. universities for studies of the natural history of acquired immune deficiency syndrome (AIDS). Information about applying for collaborative use of the specimens and pertinent epidemiological data is available from Project Officer, AIDS Repository, Epidemiology & Biometry Section, NIAID, Westwood Bldg.- Rm. 739, NIH, Bethesda, Md. 20892.

PB-8511 - 018799

NTP BOARD OKAYS $4 MILLION CONCEPT TO STUDY MOUSE STRAIN VARIATIONS

The National Toxicology Program Board of Scientific Counselors has approved the concept of a four year, $1 million a year contract supported study of mouse strain differences in hepatocarcinogenesis. Approval was not unanimous, with Board member Henry Pitot objecting strenuously, and was conditioned on Board participation in redesigning the protocol recommended by staff and possibly reducing the cost.

Objective of the study is to evaluate possible strain differences in hepatocarcinogenesis in genetically defined mice, particularly those closely related to the standard NTP mouse strain, B6C3F1. This would be done, NTP staff proposed, by comparing the carcinogenic activity of two established inducers of liver tumors, 1,1,2,2-tetrachlorethane and 2,6-dichloro-p-phenylenediamine, in B6C3F1, reciprocal cross C3B6F1, hybrid B6D2F1, parental C57B1/6N, C3H and DBA/2N, and unrelated Balb/c mice. Selection of doses for chronic testing will depend on prior establishment of maximum tolerated doses for these chemicals by means of 90 day subchronic toxicity testing.

The staff proposal noted that most reliable toxicologic data is obtained from tests carried out in animals of several unrelated reproducible genotypes (i.e., inbred strains) rather than using a single inbred strain as is commonly done. Given the utilization by NTP of the B6C3F1 mouse as the standard murine host for toxicologic testing, the proposed study is designed to provide preliminary data as to the relative susceptibility of B6C3F1 and related inbred mice to hepatocarcinogens.

"It should be noted that of the 86 chemicals tested by NTP which have recently been reviewed

by Haseman et al," the proposal stated, "31 were positive in mice and 21 of these induced liver tumors. Of these 21 chemicals, 13 also induced tumors at other sites. Thus, only eight of the 86 chemicals have been positive for the mouse liver only. In light of the concerns which have been expressed with respect to the high spontaneous incidence of liver tumors in (male) B6C3F1 mice, it is important to determine whether carcinogenesis limited to the B6C3F1 mouse liver accurately reflects hepatocarcinogenicity of a given chemical or rather is particular to this mouse hybrid. It is, therefore, important to conduct a comparative evaluation of selected chemicals for heaptocarcinogenicity in mouse strains which will allow an analysis of the genetic influence of the C3H parental strain (which is responsible for introducing the high spontaneous liver tumor incidence that characterizes the B6C3F1 mouse) at the same time that the chemical effects are compared. A closely related proposal, utilizing short term prechronic studies and directed primarily at a determination of the mechanisms responsible for any differences which may be revealed, will be submitted if the prechronic studies indicate substantial strain differences in toxic response."

J.J. Collins of the NTP staff presented the concept and said that "NTP has taken seriously the recommendations of the Doull Committee (which presented a series of suggestions for improving carcinogenesis testing after conducting a series of meetings with investigators and consultants; the committee was chaired by John Doull of the Univ. of Kansas—the report appeared in **The Cancer Letter** Sept. 7, 1984)." Collins said one of the recommendations was to "take two well defined liver carcinogens and test them in parallel conditions in the B6C3F1 mouse and ask the question, do results with known carcinogens reflect the mouse strain in general or this particular one?"

Pitot's objections were based primarily on the issue of whether or not differences in results among the strains could be attributed to differences in diets. "The Doull Committee also suggested that dietary factors are important in testing," Pitot said. "Variations in strains could have a lot to do with diets. On the genetic influence analysis, I don't see how that can be done with this study."

Collins agreed on that last point. The proposed study will only "give us preliminary conclusions on the impact on the genotype," he said.

"I don't think it will even do that," Pitot said. "But shouldn't you know whether variations in diet are responsible for variations in results before you do this? Since you are trying to follow the recommendations of the Doull Committee, I think you should start rationally, not just here, there, anywhere. This is $4 million that you might not have to spend."

"I think this is the rational place to start," Collins insisted.

Board Chairman James Swenberg interjected that all animals get the same diet, but Pitot pointed out that the diet varies from month to month. "But they all get the same variations," Swenberg argued. Switching to another point, he asked Collins, "What scenario would cause you to change anything from what is being done now?"

"If it is strongly positive in the B6C3F1 only, which is highly unlikely," Collins answered, "we should consider changing to another strain. If we are to continue with this mouse, we have to have this data."

"If we were faced with cutting the cost of this study in half, what would you do?" Swenberg asked.

"The cost of getting the liver data only would be $2.5 million," Collins said. "But it would be more cost effective to spend the additional money and do the additional pathology." He added that participants at a recent meeting in which the issue was discussed "said we should spend $15 million and get even more information."

"What would they have said if we said, 'Okay, that money will come out of the NIH branch that funds their grants.'?" Swenberg responded.

"What I want to hear from the Board," NTP Acting Deputy Director Eugene McConnell said, "is, does the concept look okay? Are the chemicals we selected appropriate?"

"I strongly support the concept," Board member Norman Breslow said. "The information would be valuable, and I think we should do all the pathology. I'm not sure about the two test chemicals."

"I would go along," Board member Michael Gallo added. "The concept is good and overdue. The compounds are good and unique, but I would consider using compounds that we have more data on."

"A study of this magnitude ought to use compounds of societal importance," Swenberg said. "Both of these are highly important, and are involved in contaminating ground water supplies."

"What bothers me about this... is that to take this and go to the endpoint with only two chemicals seems not to be the best approach," Board member Mortimer Mendelsohn said. "This just addresses the narrow issue of variability for those two chemicals."

Swenberg suggested that the Board approve the concept with the provision that staff and a Board committee redesign the proposal before it goes out as an RFP. Gallo suggested that the cost also be reconsidered. The vote was 6-2, with Jeanne Manson joining Pitot in voting against it.

PROGRAM ANNOUNCEMENT
Title: The NCI outstanding investigator grant
Application receipt date: May 15

NCI will continue to accept applications for the outstanding investigator grant (OIG), the purpose of which is to provide long term support to experienced investigators with outstanding records of research productivity. OIG is intended to encourage investigators to embark on projects of unusual potential in cancer research. Emphasis will be placed on evidence of recent substantive contributions, i.e., seminal ideas and innovative approaches to resistant problems.

Applications may be made by domestic institutions on behalf of investigators who have recently demonstrated outstanding research productivity for at least five years. There are no age restrictions. Only United States citizens, nationals or permanent residents may be presented as candidates for this grant.

OIG is nontransferable and is awarded for a maximum period of seven years. The grant is not a lifetime award but is renewable. Application for competitive renewal should be submitted at the end of the fifth year according to the guidelines for the initial award.

The actual dollar award will reflect specifically the investigator's current and projected research needs evaluated by the initial reviewers, and reviewed by the NCI Executive Committee. The award will provide that fraction of the investigator's salary that approximates the total proportion of salary awarded through current grants, but not to exceed 75%. This limit may be waived under exceptional conditions such as evidence of institutional provision of unusual levels of support of other types.

Funds will be provided for the support of technical staff, research staff and graduate students, but not for other academic faculty or institute equivalents. Salaries of other principal investigators may not be included. Other expenses, as would be included in individual project grants, are legitimate costs. It is required that the OIG principal investigator will commit at least 75% of her/his time and effort to the research supported by this instrument.

Candidates for this award may concurrently apply for additional NIH research grant or research contract support for the balance of his/her time and effort, provided the requirement that the candidate institution provide 25% salary support has been waived. Renegotiation of all concurrent NIH funds upon acceptance of this grant is required.

Candidates for this award may apply concurrently for training grants, construction grants and capital equipment grants.

Applications submitted in response to this announcement will be assigned to an appropriate subset of a nationwide panel of recognized cancer investigators for review. The summary statements from this initial review group will be submitted to the executive secretary, Div. of Extramural Activities, NCI, to thje NCI Executive Committee to prepare its funding recommendations to the National Cancer Advisory Board. The NCAB will recommend awards to the NCI director for final action.

Reviewers will consider the following factors in evaluating the scientific merit of each response to this program announcement:

1. What has been the impact of the applicant's work on the field of biomedical research? Is her/his research cited often and as incentives for others' research efforts? Has the applicant developed new experimental approaches crucial to the progress of his/her area of research? Has she/he contributed to the collection of important reliable data? In what way is the applicant's work seminal in nature? Has the applicant productively exploited his/her own breakthroughs and/or those of others? Has the applicant demonstrated imagination, energy, and sensitivity to the potential of serendipitous findings?

2. What will be the significance of the investigator's continued work in the field described above? Does the proposed work break new ground or continue previous work? Are the questions posed of significant interest and importance to cancer research? Will this work provide impetus for others working in related areas?

3. Is there a strong likelihood that the investigator will continue at the frontiers of research?

In the evaluation, reviewers will be asked to comment on the way in which the applicant has achieved her/his present stature in the field, both to individual accomplishments and collaborative interactions. Has the applicant made significant contributions in the areas of teaching and research training and/or clinical research? Communicative, pedagogic and organization skills will be considered.

Will the applicant have adequate administrative support as indicated by institutional commitment of facilities and other resources, as appropriate?

Letters of intent are no longer required for this program. The applicant investigator and sponsoring institution must present a workable plan for phase out of the applicant's current research support and conversion of staff and facilities to support by OIG. Applications should be submitted on form PHS 398 (Rev. 5/82) and submitted in six copies to the Div. of Research Grants, NIH, Bethesda, Md. 20892.

For further details on application development, contact Mrs. Barbara Bynum, Div. of Extramural Activities, NCI, Bldg 31 Rm 10A03, Bethesda, Md. 20892, phone 301-496-5147.

RFA 85-CA-20
Title: Basic studies on the development and assessment of retroviral vaccines
Application receipt date: Dec. 13 (extension available on request due to delay in releasing this announcement)

The Div. of Cancer Etiology of NCI and the National Institute of Allergy & Infectious Diseases invite applications to conduct grant supported investigator initiated research on the development

and assessment of vaccines against retroviruses.

Recent research conducted with diverse viruses such as hepatitis B virus, herpes simplex viruses and foot and mouth disease virus demonstrates that modern approaches in vaccine technology such as packaging of genes coding for immunogenic protective proteins into appropriate expression vectors (such as vaccinia virus) and other recombinant DNA methods can be exploited to produce safe and effective vaccine preparations against the respective viruses. Similar modern approaches need to be explored for the prevention of equally important and devastating diseases caused by retroviruses.

The objective of this RFA is to encourage investigator initiated research on retroviral vaccines in various laboratories and to emphasize and address those aspects of research presently in need of research stimulation through grant support. Basic studies in the following specific areas, but not necessarily limited to these areas, are needed:

1. Development of naturally retrovirus animal models to systematically evaluate strategies for immunogen preparation, vaccination schedules, use of suitable adjuvants, determination of host target cells, induction of a protective immune response, and development of an appropriate measure for in vivo protection against challenge.

2. Basic studies to determine how retroviruses interact with and/or escape from the host immune surveillance system, such as by genetic recombination/antigenic shifts/drifts involving env gene alterations.

3. Characterization of retroviral components presumed to be immunosuppressive.

4. Identification and characterization of antigenic determinants of retroviruses that are most associated with eliciting group and interspecies specific protective immunity and studies on methodologies to enhance their presentation and immunogencity.

5. Utilization of newer methodologies to produce and evaluate retroviral vaccines such as (a) recombinant/subunit vaccines prepared in yeast, bacteria, and/or mammalian cells; (b) DNA sequence derived synthetic peptides; (c) modified live recombinant DNA retroviral vaccines; (d) retroviral gene segment expression vectors such as vaccinia and adenovirus; and (e) anti-idiotype antibodies against retroviral components employed as immunizing antigens.

6. Investigations to develop quantitative serological procedures to assess the in vivo immune status against retrovirus infections.

The total project period for applications submitted in response to this RFA should not exceed five years. Approximately $2 million ($1.25 million from NCI and $750,000 from NIAID) will be set aside to specifically fund applications which are submitted in response to this RFA. It is anticipated that 12-15 applications will be funded. Both nonprofit and for profit institutions may apply.

Inquiries and requests for a copy of the RFA may be directed to Padman Sarma, DVM, PhD, Biological Carcinogenesis Branch, NCI, Landow Bldg Rm 9A22, Bethesda, Md. 20892, phone 301-496-9734.

RFA 85-CA-21

Title: Studies on novel human exogenous and endogenous retroviruses

Application receipt date: Dec. 13 (extensions are available on request)

The Div. of Cancer Etiology of NCI invites grant applications to perform investigator initiated basic research to uncover the existence of and/or characterize novel exogenous and endogenous human retroviruses.

Recent evidence based on morphologic, molecular biologic and immunologic studies suggests the existence of hitherto uncharacterized retrovirus particles and endogenous retroviral sequences in human cells. Virus particles with type C morphology have been found in human placenta and in certain cell lines derived from human testicular tumors such as embryonal carcinoma and teratocarcinoma. The endogenous retroviruses present in proviral form in human cells are expressed at both messenger RNA and protein levels in certain human tissues. The true nature of these retroviral entities and their role in human cancer need to be determined.

The objective of this RFA is to encourage investigator initiated basic research to characterize the multiple type C virus particles and endogenous human retroviruses and determine their significance in human cancer. This RFA emphasizing basic studies on such novel exogenous and endogenous human retroviruses is intended to generate applications for grant supported studies in the following specific areas, but not necessarily limited to these areas:

1. Molecularly clone the genome(s) of type C virions found in human placenta and tumor tissues (e.g., germ cell tumors) and determine the molecular and antigenic relatedness between these entities and endogenous retroviral sequences found in human cells.

2. Identify and characterize protein and nucleic acid components of uncharacterized type C virions by modern technology, and perform studies on viral origin, distribution, and expression in different types of human or other species tissues. The cells of interest, for example, are germ cells, cells representing different types of germ cell tumors, and differentiating populations of embryonal carcinoma cells.

3. Insert cloned human proviral DNA into appropriate expression vectors to study various viral proteins, to determine antigenic composition and relatedness to other retroviruses.

4. Search human tumor tissues for viral RNA and protein expression using molecular and immunologic probes derived from novel human retroviral sequences (LTR, and structural regions) and from well conserved regions of known mammalian retroviruses.

5. Develop tissue culture methodologies suitable for cultivation of difficult to grow human tumor cells that may have an infectious etiology such as Hodgkin's disease, breast cancer and B cell lymphomas, using growth factors, special nutrients, and newer specialized cell growth technologies.

6. Isolate and characterize new retroviruses from nonhuman primates with tumors, other diseases, or no disease at all, with a view to using these newer isolates as probes to search for human counterparts.

The total project period for applications submitted in response to this RFA should not exceed five years. Approximately $750,000 will be set aside to specifically fund applications which are submitted in response to this RFA. Nonprofit and for profit institutions may apply. Copies of the complete RFA and further information may be obtained from Padman Sarma, address and phone number as shown with the previous RFA listed above.

PROGRAM ANNOUNCEMENT
Title: Studies on feline retroviruses
Application receipt date: Feb. 1, June 1, Oct. 1

The Div. of Cancer Etiology of NCI invites grant applications to perform investigator initiated research on the biology and/or molecular biology of the retroviruses of the cat. The award will enable successful candidates to investigate a defined research problem in this area of programmatic interest to NCI for three to five years.

Among the retroviruses, the leukemia inducing viruses of the cat (feline leukemia viruses, FeLV) are unique in many respects. First, they are responsible not only for malignant diseases such as leukemia, lymphosarcoma and other neoplastic conditions, but they also cause other serious diseases such as anemia, immunosuppression and reproductive failure. More cats die of complications arising from the immunosuppression caused by FeLV than through tumor induction. In this respect, a parallel exists between FeLV and the human retrovirus, human T cell lelukemia/lymphoma virus (HTLV), especially HTLV 3. The fact that FeLV has the potential to induce diverse disorders in the cat poses the question of whether differences in the induced diseases are a result of differences in the nature of the virus isolates. Differences between viral strains responsible for differences in the induced diseases in cats have not been elucidated and much research remains to be done in this area. Second, an examination of oncogene sequences in feline sarcoma viruses has revealed an abundance and diversity of oncogenes acquired through recombination with the cat genome, thus suggesting that the cat may be a reservoir of many different cellular oncogenes. Since oncogenes of different species appear to be similar and to be well conserved, the cat cellular oncogenes may have important implications for cancer in other species, including man. A third feature of the feline retroviruses, just beginning to be recognized, is the unexpected finding that certain leukemia inducing FeLV strains acquire, retain and transduce the oncogene myc in a manner reminiscent of the avian myelocytomastosis virus, MC-29. This finding, previously unknown for a mammalian retrovirus, remains to be fully studied for its relevance in the etiology of the malignancies and the other diverse diseases attributed to FeLV.

Examples of important areas of research emphasis (which are not all encompassing) are:

1. Elucidate the mechanisms of feline retroviral cell transformation/oncogenesis, with attention to the new knowledge of oncogene chromosomal translocations and other interactions.

2. Explore the origin and signifiance of virus subgroups in feline leukemia virus induced disease and immunity.

3. Elucidate the pathogenesis of the disease(s), define feline hemopoietic and lymphoid cell populations in order to identify the target cells in malignant and immunosuppressive disorders.

Additional studies that might be addressed are:

1. Define the significance of subgrwoup C FeLV envelope component and the apparently protective antibodies against feline leukemia that it induces.

2. Characterize myc containing feline leukemia viruses and determine their role in feline leukemia.

3. Determine the etiology of virus negative cat tumors which generally appear under natural conditions in cats raised in an FeLV infected environment.

Applications should be submitted on form PHS 398 following the usual procedures for RO1 grants. They will compete for support from NCI's RO1 pool. Submit applications to the NIH Div. of Research Grants, Bethesda, Md. 20892.

NCI is encouraging inquiries concerning this announcement. No letter of intent is necessary. Inquiries may be directed to Padman Sarma, DVM, PhD, at the address or phone number listed previously for him with RFAs above.

NCI CONTRACT AWARDS

Title: Nutrition education techniques for monitoring fat and fiber intakes
Contractor: The KBL Group Inc.
Title: Data Management system for monitoring preclinical progress of studies, agents, supplies and materials
Contractor: Data Management Services Inc., $48,519
Title: Information resource activities to identify, characterize and evaluate reports and scientific literature in the area of chemoprevention
Contractor: The KBL Group Inc., $50,000
Title: Information resource activities to identify, characterize and evaluate reports and scientific literature in the area of chemoprevention
Contractor: Information Management Consultants, $28,153
Title: Laser treatment control devices development
Contractor: Tacan Corp., $50,000

The Cancer Letter _Editor Jerry D. Boyd Associate Editor Patricia Williams
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