IN THIS ISSUE:

Notice
Change in Application Receipt Dates - Clarification ........................................ 1

Notice
Change in Receipt Date - RFA - Kidney and Urological Research Centers ..................... 1
National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases
Index - ARTHRITIS, DIABETES, AND DIGESTIVE AND KIDNEY DISEASES

Notice
NIH/FDA Regional Workshop - Protection of Human Subjects
"Mock IRB Meetings: ............................................ 2
Index - NATIONAL INSTITUTES OF HEALTH FOOD AND DRUG ADMINISTRATION

Notice
NIH/FDA Regional Workshop - Protection of Human Subjects .......................... 3
Index - NATIONAL INSTITUTES OF HEALTH FOOD AND DRUG ADMINISTRATION

Notice
NIH Regional Workshop on the Humane Care and Use of Laboratory Animals by Awardee Institutions ........................................ 4
Index - NATIONAL INSTITUTES OF HEALTH

Notice
Repository of Human DNA Probes and Libraries ........................................ 5
National Institute of Child Health and Human Development
Division of Research Resources
Index - CHILD HEALTH AND HUMAN DEVELOPMENT RESEARCH RESOURCES

The NIH Guide is published at irregular intervals to announce scientific initiatives and to provide policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in grants and contracts activities administered by the National Institutes of Health.

Two types of supplements are published by the respective awarding units. Those printed on yellow paper concern contracts: solicitations of sources and announcement of availability of requests for proposals. Those printed on blue paper concern invitations for grant applications in well-defined scientific areas to accomplish specific program purposes.

Have You Moved?
If you present address differs from that shown on the address label, please send your new address to: Grants and Contract Guide Distribution Center, National Institutes of Health, Room B3BN10, Building 31, Bethesda, Maryland 20205, and attach your address label to your letter. Prompt notice of your change of address will prevent your name from being removed from our mailing list.
Announcement
Availability of Request for Applications: 86-HL-16-P - Clinical Centers for Trials of Hypertension Prevention and 86-HL-18-P - Coordinating Center for Trials of Hypertension Prevention
National Heart, Lung, and Blood Institute
Index - HEART, LUNG, AND BLOOD

Announcement
Availability of Request for Applications: 86-HL-17-P - Clinical Centers for a Trial of Dietary Intervention in Children with Elevated Low Density Lipoprotein Levels to Assess Feasibility, Acceptability, Efficacy and Safety and 86-HL-19-P - Coordinating Centers for a Trial of Dietary Intervention, etc.
National Heart, Lung, and Blood Institute
Index - HEART, LUNG, AND BLOOD

Announcement
Availability of Request for Applications: 86-HL-10B - Prevalence and Consequences of Hepatitis Delta Infection in Hemophilia
National Heart, Lung, and Blood Institute
National Institute of Allergy and Infectious Diseases
Index - HEART, LUNG, AND BLOOD
ALLERGY AND INFECTIOUS DISEASES

Announcement
Availability of Request for Applications: 86-CA-08 - Studies on the Etiology of Neoplasia in Poikiloothermic, Aquatic Animals: Finfish and Shellfish
National Cancer Institute
National Institute of Environmental Health Sciences
Index - CANCER ENVIRONMENTAL HEALTH SCIENCES

Announcement
Availability of Request for Applications: 86-HD-02 - The Pathogenesis of Sudden Infant Death Syndrome
National Institute of Child Health and Human Development
Index - CHILD HEALTH AND HUMAN DEVELOPMENT

Announcement
Availability of Request for Applications: 86-AM-01 - Digestive Diseases Core Centers
National Institute of Diabetes and Digestive and Kidney Diseases
Index - DIABETES AND DIGESTIVE AND KIDNEY DISEASES
Announcement
Availability of Request for Applications: 86-CA-07 -
The Transformation Mechanisms of Human Polyomaviruses..............17
National Cancer Institute
Index - CANCER

Announcement
Biological Role of Exocyclic Nucleic Acid Derivatives in Carcinogenesis........................................19
National Cancer Institute
Index - CANCER

Announcement
Characterization of Multidrug Resistant Human and Other Mammalian Tumor Cell Lines
..................................................................................22
National Cancer Institute
Index - CANCER

Announcement
Mechanisms of Site Specific Metastasis in Prostate Cancer
..................................................................................24
National Cancer Institute
Index - CANCER

Announcement
Program Supplement for Research Grant Applications - Engineering Control Systems Research
..................................................................................27
National Institute for Occupational Safety and Health - Centers for Disease Control
Index - OCCUPATIONAL SAFETY AND HEALTH
NOTICE

CHANGE IN APPLICATION RECEIPT DATES—CLARIFICATION

P.T. 04, 22, 34, 44; K.W. 0710030, 0404000

The notice of new application receipt dates, published in the NIH Guide for Grants and Contracts on September 13 and November 8, 1985, did not include a date for supplemental applications for program project and center grants. Supplemental applications for such grants should be submitted for the February 1, June 1, and October 1 receipt dates.

Supplemental applications will be accepted for the March 1, 1986 receipt date in view of the ambiguity in the original notices. It would be helpful, however, if applicants who can do so would submit as early as possible.

NOTICE

CHANGE IN RECEIPT DATE - REQUEST FOR APPLICATIONS

KIDNEY AND UROLOGICAL RESEARCH CENTERS

P.T. 04; K.W. 0710030

NATIONAL INSTITUTE OF ARTHRITIS, DIABETES AND DIGESTIVE AND KIDNEY DISEASES

The National Institute of Arthritis, Diabetes and Digestive and Kidney Diseases (NIADDK) published a Request for Applications (RFA) for Kidney and Urological Research Centers on October 11, 1985 (RFA No. 86-AM-01). The receipt date for this RFA has been extended by four months. The new date is July 15, 1986.
NOTICE

NIH/FDA REGIONAL WORKSHOP - PROTECTION OF HUMAN SUBJECTS

P.T. 42; K.W. 0783005

The National Institutes of Health (NIH) and the Food and Drug Administration (FDA) are continuing to sponsor a series of workshops on responsibilities of researchers, Institutional Review Boards, (IRBs), and institutional officials for the protection of human subjects in biomedical and behavioral research. The workshop in Little Rock, at the University of Arkansas, will be an intensive one-day workshop in IRB functions and responsibilities. The workshop will focus on selected case studies, illustrating representative problems of interpreting and applying the human subjects regulations. Participants will serve as IRB members in "mock IRB" meetings and compare strategies and solutions to issues raised by the cases. Enrollment will be restricted to 35-40 participants. Written materials will be supplied in advance to participants.

<table>
<thead>
<tr>
<th>Date</th>
<th>Location</th>
<th>Contact</th>
</tr>
</thead>
<tbody>
<tr>
<td>March 12, 1985</td>
<td>Little Rock, AR</td>
<td>Ms. Kathleen Masterson</td>
</tr>
<tr>
<td></td>
<td></td>
<td>University of Arkansas Med. Ctr.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4301 W. Markham</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mail Slot 636</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Little Rock, AR 77205</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(501) 661-5502</td>
</tr>
</tbody>
</table>

A final list of dates and locations will be published at a later date. For specific program and registration information, contact:

Roberta H. Garfinkle
Office for Protection from Research Risks
National Institutes of Health
Building 31 - Room 4B09
9000 Rockville Pike
Bethesda, Maryland 20892
NOTICE

NIH/FDA REGIONAL WORKSHOP - PROTECTION OF HUMAN SUBJECTS

P.T. 42; K.W. 0783005

The National Institutes of Health (NIH) and the Food and Drug Administration (FDA) are continuing to sponsor a series of workshops on responsibilities of researchers, Institutional Review Boards (IRBs), and institutional officials for the protection of human subjects in biomedical and behavioral research. The workshops are open to everyone with an interest in research. The meetings should be of special interest to those persons currently serving or about to begin serving as a member of an IRB. The current schedule includes:

<table>
<thead>
<tr>
<th>Date</th>
<th>Location</th>
<th>Contact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feb. 27-28, 1986</td>
<td>Sante Fe, NM</td>
<td>Pat Johnson or Ann Armijo&lt;br&gt;IRB/Sante Fe Conference&lt;br&gt;Lovelace Medical Foundation&lt;br&gt;Research Division&lt;br&gt;5400 Gibson Blvd., SE&lt;br&gt;Albuquerque, NM 87108&lt;br&gt;(505) 262-7415</td>
</tr>
<tr>
<td>Mar. 1, 1986</td>
<td></td>
<td></td>
</tr>
<tr>
<td>May 15-16, 1986</td>
<td>Seattle, WA</td>
<td>Susan Charrier&lt;br&gt;Fred Hutchinson Cancer Research Ctr.&lt;br&gt;1124 Columbia Street&lt;br&gt;Mail Stop 1725U&lt;br&gt;Seattle, WA 98104&lt;br&gt;(206) 467-4867</td>
</tr>
</tbody>
</table>

Additional workshops will be announced later. For further information regarding education programs contact:

Roberta H. Garfinkle<br>Education Program Coordinator<br>Office for Protection from Research Risks<br>National Institutes of Health<br>Building 31 - Room 4B09<br>9000 Rockville Pike<br>Bethesda, Maryland 20892
NOTICE

NIH REGIONAL WORKSHOP ON THE HUMANE CARE AND USE OF LABORATORY ANIMALS BY Awardee Institutions

P.T. 42; K.W. 0201011, 1014003

The National Institutes of Health (NIH), Office for Protection from Research Risks (OPRR)) is continuing to sponsor a series of workshops on implementing the revised "Public Health Service Policy on the Humane Care and Use of Laboratory Animals by Awardee Institutions" and the NIH Guide for the Care and Use of Laboratory Animals. The workshops are open to institutional administrators, and others who share in responsibility for sound management of humane animal research. The current schedule includes:

<table>
<thead>
<tr>
<th>Date</th>
<th>Place</th>
<th>Contact</th>
</tr>
</thead>
<tbody>
<tr>
<td>March 11, 1986</td>
<td>Little Rock, AR</td>
<td>Ms. Kathleen Masterson</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Univ. of Arkansas Medical Ctr.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mail Slot 636</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Little Rock, AR 77205</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(501) 661-5502</td>
</tr>
<tr>
<td>April 4, 1986</td>
<td>Boston, MA</td>
<td>Mrs. Virginia B. Werwath</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Harvard Medical School, NERPBC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>One Pine Hill Drive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Southborough, MA 01772</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(617)481-0400 Ext. 202</td>
</tr>
<tr>
<td>May 8, 1986</td>
<td>Atlanta, GA</td>
<td>Dr. M. S. Silberman</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Emory University</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Robert Woodruff Health Sciences Ctr.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P. O. Drawer KK</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Atlanta, GA 30322</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(404)321-0111 Ext. 4388 or 4389</td>
</tr>
</tbody>
</table>

Additional workshops will be announced later. For further information regarding education programs contact:

Roberta H. Garfinkle
Education Program Coordinator
Office for Protection from Research Risks
National Institutes of Health
Building 31 - Room 4B09
9000 Rockville Pike
Bethesda, Maryland 20892
REPOSITORY OF HUMAN DNA PROBES AND LIBRARIES

P.T. 36; K.W. 0780015

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
DIVISION OF RESEARCH RESOURCES

The National Institute of Child Health and Human Development (NICHD), with the participation of the Division of Research Resources (DRR), announces the award of a contract to the American Type Culture Collection (ATCC) of Rockville, MD, to establish a collection of cloned human genes, DNA probes, and human chromosome-specific libraries. The collection will serve as a major international resource center for distribution of the rapidly proliferating human DNA clones and libraries. The collection is expected to assume a vital role in supporting the recombinant DNA gene mapping technology that is revolutionizing human genetics.

Probes and cloned genes will be actively sought among the genetics and molecular biology research communities for addition to the repository. Initial preference will be given to clones of representative genes, and restriction fragment length polymorphisms (RFLPs) that have proven to be most useful in genetic linkage analysis. The clones will be expanded and verified, and multiple samples will be stored for distribution to interested investigators who request their use. Approximately 200 clones will be added to the repository each year during the five-year contract award.

Human chromosome-specific libraries will be deposited in the ATCC as they are available from a collaborative project supported by the Department of Energy at the Los Alamos and Lawrence Livermore National Laboratories. Thirty-four libraries representing 20 chromosomes will be available from ATCC early in 1986. Distribution of these libraries is supported by DRR. The general availability of these libraries should greatly increase the rate at which important probes are produced.

A computerized database holding complete listings as well as background information on the probes and chromosome-specific libraries will be established by the ATCC as a resource to investigators. Follow-up information on the results derived from use of the collection will be actively collected and stored. On-line access to this database will be developed early in the project.

For further information, investigators are encouraged to contact the following ATCC directors of the Repository or the participating NIH staff:

William C. Nierman, Ph.D., or
Leonard E. Benade, Ph.D.
American Type Culture Collection
12301 Parklawn Drive
Rockville, MD 20852

Telephone: (301) 881-2600
Delbert H. Dayton, M.D.
Genetics and Teratology Branch
National Institute of Child Health
    and Human Development
National Institutes of Health
Bethesda, Maryland  20892

Telephone: (301) 496-5541

W. Sue Badman, Ph.D.
Biological Models and Materials Resources
Division of Research Resources
National Institutes of Health
Bethesda, Maryland  20892

Telephone: (301) 496-5507
ANNOUNCEMENT

AVAILABILITY OF REQUEST FOR APPLICATIONS: (RFA)
86-HL-16-P - CLINICAL CENTERS FOR TRIALS OF HYPERTENSION PREVENTION and
86-HL-18-P-COORDINATING CENTER FOR TRIALS OF HYPERTENSION PREVENTION
P.T. 04; K.W. 0715115, 0745055, 0755015
DIVISION OF EPIDEMIOLOGY AND CLINICAL APPLICATIONS
NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: April 21, 1986

The Clinical Trials Branch of the Division of Epidemiology and Clinical Applications, National Heart, Lung, and Blood Institute (NHLBI) announces the availability of Request for Applications (RFA) on the above subject. Copies of the RFA will be available on or about January 31, 1986 from staff of the NHLBI. Interested institutions may request copies of either or both of the RFAs. Note that awards will be made to foreign institutions only for research of very unusual merit, need, and promise.

This program will support clinical or biostatistical investigators and supporting staff to collaboratively plan and execute randomized clinical trials of non-pharmacologic interventions aimed at preventing sustained increases of arterial blood pressure in healthy adults. The program will utilize the cooperative agreement mechanism, and will encompass a feasibility phase and a full-scale clinical trial phase.

Requests for copies of the RFA should be addressed to:

Jeffrey A. Cutler, M.D.
Division of Epidemiology and Clinical Applications
National Heart, Lung, and Blood Institute
Federal Building - Room 216
Bethesda, Maryland 20892
Telephone: (301) 496-3107

This program is described in the Catalog of Federal Domestic Assistance No. 13.837, Heart and Vascular Diseases. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.
ANNOUNCEMENT

AVAILABILITY OF REQUEST FOR APPLICATION: (RFA)

86-HL-17-P - CLINICAL CENTERS FOR A TRIAL OF DIETARY INTERVENTION IN CHILDREN WITH ELEVATED LOW DENSITY LIPOPROTEIN LEVELS TO ASSESS FEASIBILITY, ACCEPTABILITY, EFFICACY, AND SAFETY and

86-HL-19-P - COORDINATING CENTERS FOR A TRIAL OF DIETARY INTERVENTION IN CHILDREN WITH ELEVATED LOW DENSITY LIPOPROTEIN LEVELS TO ASSESS FEASIBILITY, ACCEPTABILITY, EFFICACY, AND SAFETY

P.T. 34; K.W. 0710095, 0755015, 1010013

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: April 21, 1986

The Prevention and Demonstration Research Branch of the Division of Epidemiology and Clinical Applications, National Heart, Lung, and Blood Institute (NHLBI) announces the availability of a Request for Applications (RFA) on the above subject. Copies of the RFA will be available January 31, 1986 from staff of the NHLBI. Note that awards will be made to foreign institutions only for research of very unusual merit, need, and promise.

This program will support biostatistical and clinical investigators and supporting staff to collaboratively plan and execute a randomized clinical trial of dietary intervention aimed at lowering elevated LDL cholesterol levels in children. The program will utilize the cooperative agreement mechanism and will encompass a feasibility phase and a full-scale clinical trial phase. Interested institutions may request copies of either the Coordinating Center or Clinic RFA or both.

Requests for copies of the RFA should be addressed to:

Sue Y.S. Kimm, M.D., M.P.H.
Division of Epidemiology and Clinical Applications
National Heart, Lung, and Blood Institute
Federal Building - Room 6A10
7550 Wisconsin Avenue
Bethesda, Maryland 20892

Telephone: (301) 496-3503

This program is described in the Catalog of Federal Domestic Assistance No. 13.837, Heart and Vascular Diseases. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.
ANNOUNCEMENT

AVAILABILITY OF REQUEST FOR APPLICATIONS: RFA

86-HL-10-B

PREVALENCE AND CONSEQUENCES OF HEPATITIS DELTA INFECTION IN HEMOPHILIA

P.T. 34; K.W. 0715125, 0750010

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
NATIONAL INSTITUTE OF ALLERGY AND INFECTION DISEASES

Application Receipt Date: May 1, 1986

The Blood Resources Branch of the Division of Blood Diseases and Resources, National Heart, Lung, and Blood Institute (NHLBI), and the Development and Applications Branch, National Institute of Allergy and Infectious Diseases (NIAID), announce the availability of a Request for Applications (RFA) 86-HL-10-B on the above subject on or about February 15, 1986. Copies of the RFA may be obtained from staff of the NHLBI or the NIAID.

This special grant program is for the support of research on the role of hepatitis delta virus (HDV) in the evolution of chronic liver disease among treated hemophiliacs.

With the recent recognition of outbreaks of HDV infections in the United States, and in view of the transmissibility of the disease through blood, the Division has begun research efforts to understand the role of delta infection in the development of chronic liver disease in patients who receive multiple transfusions. This project should provide important new information on the prevalence and consequences of HDV infection in persons with hemophilia. The focus on an affected subpopulation composed of persons with a genetic disorder who need blood products is clearly of primary importance to the NHLBI. However, since HDV is a newly identified infectious agent causing major liver disease, a study of this nature is also in the interest of the NIAID. Therefore, the two institutes have agreed to cosponsor and cofund this research program.

The programs of the Division of Blood Diseases and Resources, National Heart, Lung, and Blood Institute, are identified in the Catalog of Federal Domestic Assistance, number 13.839. The programs of the Development and Applications Branch, National Institute of Allergy and Infectious Diseases, are identified in the Catalog of Federal Domestic Assistance, number 13.856. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 291) and administered under PHS grant policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to intergovernmental review requirements of Executive Order 12372, or to Health Systems Agency review.
About one-half of the cases of chronic hepatitis in hemophiliacs can be attributed to hepatitis B virus (HBV) infection. There is accumulating evidence to suggest that superinfection of the HBV carrier with the delta agent may play an important role in the development of severe chronic hepatitis B and cirrhosis.

Studies to be supported by this RFA will focus on the prevalence of HBV and HDV serologic markers in individuals with hemophilia; the frequency and effect of superimposed acute HDV infection on the chronic HBV carrier and, comparative studies of chronic liver disease in patients with presumed chronic non-A, non-B hepatitis, chronic hepatitis B alone, and combined chronic HBV and HDV infections.

Requests for copies of the RFA should be addressed to:

Luiz H. Barbosa, D.V.M.
Division of Blood Diseases and Resources
National Heart, Lung, and Blood Institute
National Institutes of Health
Federal Building - Room 5C10
Bethesda, Maryland 20892

Telephone: (301) 496-1537

or

Leslye Johnson, Ph.D.
Development and Applications Branch
National Institute of Allergy and Infectious Diseases
Westwood Building - Room 750
Bethesda, Maryland 20892

Telephone: (301) 496-7051
ANNOUNCEMENT

AVAILABILITY OF REQUEST FOR APPLICATIONS: RFA
86-CA-08
STUDIES ON THE ETIOLOGY OF NEOPLASIA IN POIKILOTHERMIC, AQUATIC ANIMALS: FINFISH AND SHELLFISH
P.T. 34; K.W. 0715035, 0755030, 0710030
NATIONAL CANCER INSTITUTE
NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

Application Receipt Date: May 1, 1986

I. BACKGROUND

In the last 20 to 25 years there has been a remarkable growth of interest in the study of neoplasms of poikilothermic animals. On a world-wide basis, a comparatively small number of investigators have generated a large body of information. Studies which initially, in the 1960s, focused on the description of pathologic characteristics of numerous neoplasms and their species specificity have led today to a heightened interest in aquatic animals for bioassay testing, for detection of carcinogens in the environment, and even as comparative oncology models for human cancer.

Tumors have been identified in several species of finfish and shellfish at one or more of the following sites: skin, gill, mantle, oral region, pharynx, stomach, pancreas, liver, kidney, gonads, heart, thyroid gland, nervous system, soft tissues, skeleton, and lymphoreticular and hematopoietic tissues. There are, however, large gaps in our knowledge about how neoplasms in aquatic animals conform to what is known about neoplasms of mammals, their morphologic characteristics, biologic course, relation to host-regulating mechanism, and their transplantability and transmissibility.

This program is described in the Catalog of Federal Domestic Assistance No. 13.393, Cancer Cause and Prevention Research. Awards are under authorization of the Public Health Service Act, Section 301(c) and Section 402 (Public Law 78-410, as amended; 42 USC 241; 42 USC 282) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency Review.
I. RESEARCH GOALS AND SCOPE

The purpose of this RFA is to accelerate the development of additional understanding relative to studies on the possible etiology of neoplasia in poikilothermic, aquatic animals: finfish and shellfish. In order to encourage applications from a diverse spectrum of scientists, particularly those with requisite expertise but presently without access to feral or laboratory aquatic animals, we have compiled a list of laboratories that have established resources for aquatic animals and whom applicants may wish to contact regarding collaboration, provision of resources, and/or consortial arrangements as appropriate. This list, compiled by state, is not necessarily comprehensive and those listed have not given prior consent to be involved in this initiative. It is made available at this time so that interested investigators can begin to establish their own contacts. It is recognized that the expertise and logistics needed for the conduct of meaningful multidisciplinary research rarely resides in a single agency or institution and it will be a focus of this initiative to foster new relationships which seek to encompass the required expertise. Consistent with the title of this proposed RFA are a broad spectrum of studies that would greatly facilitate our understanding of the etiology of neoplasia in finfish and shellfish. For further information, interested investigators should request a copy of the complete RFA as noted below (IV. Inquiries).

III. MECHANISM OF SUPPORT

Awards will be made as research project grants and all policies and requirements which normally govern the grant programs of the PHS apply. It should be noted that both non-profit and for-profit institutions, domestic and foreign, may apply. The total project period for applications submitted in response to the present RFA should not exceed four years. Each application submitted in response to the RFA will be given dual institute assignment to NCI and NIEHS. The primary assignment will be determined by mutual agreement of the Program Directors from the supporting programs.

IV. INQUIRIES

A copy of the complete RFA describing the research goals and scope, the review criteria and the method of applying can be obtained by contacting:

Dr. David G. Longfellow
Chief, Chemical and Physical Carcinogenesis Branch
Division of Cancer Etiology
National Cancer Institute
Landow Building - Room 9B-01
Bethesda, Maryland 20892-4500

Telephone: (301) 496-5471

Written or telephone inquiries concerning this RFA are encouraged and should be directed to the Program Director above. The program staff of the Chemical and Physical Carcinogenesis Branch would appreciate the opportunity to clarify any issues or questions from potential applicants.
ANNOUNCEMENT

AVAILABILITY OF REQUEST FOR APPLICATIONS: RFA

86-HD-02

THE PATHOGENESIS OF SUDDEN INFANT DEATH SYNDROME

P. T. 34; K.W. 0715205, 0755030, 1002030, 0710085

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Application Receipt Date: May 23, 1986

I. BACKGROUND

The Pregnancy and Perinatology Branch of the National Institute of Child Health and Human Development (NICHD) invites investigator-initiated research grant applications for studies on the etiology and pathogenesis of sudden infant death syndrome (SIDS). SIDS accounts for about 7000 deaths a year, taking the lives of two infants per 1000 live births. The syndrome is defined as the sudden death of an infant that is unexpected by life history and where the death remains inexplicable after post-mortem examination. The NICHD Cooperative Epidemiological Study has identified some features found more frequently in SIDS victims than in age-matched control infants. The peak incidence of SIDS is between 2 and 4 months of age. It is more common in male infants, low birth-weight infants, black infants, infants of teenage mothers, and infants of mothers who smoked during pregnancy. SIDS infants also were likely to have received less postnatal pediatric care. Research also has revealed that SIDS victims, as a group, tend to have more serious neonatal and early infant medical problems of various kinds. Pathologic and physiologic studies suggest that some SIDS victims have had chronic problems of respiratory control which may make these infants vulnerable, especially in the event of mild upper respiratory infections.

Despite the fact that various aspects of developmental physiology of young infants have been studied extensively over the past fifteen years, no specific biological markers for SIDS have been discovered, and the cause or causes of the syndrome remain unknown. Currently, many believe that SIDS may be caused by a combination of deficiencies of certain functions in the infant, or by their failure to adapt to the changing environment that accompanies growth.

This program is described in the Catalog of Federal Domestic Assistance No. 13.865, Research for Mothers and Children. Awards will be made under the authority of the Public Health Service Act, III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.
II. RESEARCH GOALS AND SCOPE

At a special expert consultation on new research directions in SIDS, participants agreed that one new and reasonable hypothesis to consider is that SIDS may result from a failure not just of one organ system or another, but rather from a failure of the complex interplay of the regulatory systems required to maintain life. The developing brain with its specific centers is the area where the control of life-sustaining functions takes place. New concepts in neuroscience are highlighting the complex interactions of many regulatory systems which are, in turn, affected by oscillators (physiological events which run in cycles). This RFA addresses questions regarding the pathogenesis of SIDS in the context of the role of the brainstem and other CNS centers in the control of vital functions. Investigators are invited to propose studies on the neurobiology and neurobehavioral aspects of infants who are considered at risk for SIDS on the basis of the epidemiologic data. Studies should consider the availability of new, highly sophisticated technology, and should not be limited to neonates and infants less than 6 months of age, but be extended to include the developing fetus. Measurement of metabolic activity of cells and tissues using appropriate techniques should be considered which would permit the evaluation of brain function in normal and at-risk fetuses and infants. Studies examining the functional development of the blood-brain barrier (endothelium of cerebral vessels) with regard to both barrier and carrier functions, are also encouraged. The development of the autonomic nervous system and its role in the regulation of vital functions with evaluation of the synchronous development of reflex and central neural regulation is important and should be investigated. The potential role of circadian rhythms endogenously generated by a multiple oscillator system and the possible relationship to SIDS are possible areas of study. Interest also exists to determine whether structural abnormalities are present in the brainstem and other CNS areas of SIDS victims. Studies may be carried out with human babies and in appropriate experimental animals. Although the search for an experimental animal model for SIDS has not been successful so far, investigators are encouraged to examine the possibility of developing such a model.

III. STAFF CONTACT

For further information and a copy of the RFA, contact:

Charlotte Catz, M.D.
Chief, Pregnancy & Perinatology Branch
National Institutes of Child Health and Human Development
National Institutes of Health
Landow Building - Room 7C09
Bethesda, Maryland 20892

Telephone: (301) 496-5575
ANNOUNCEMENT

AVAILABILITY OF REQUEST FOR APPLICATIONS: RFA

86-AM-01

DIGESTIVE DISEASES CORE CENTERS

P.T. 04; K.W. 0715085, 0710030, 0780000

NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

Application Receipt Date: June 16, 1986

The National Institute of Arthritis Diabetes and Digestive and Kidney Diseases (NIADDK) invites applications for a Digestive Diseases Core Center grant to be awarded in Fiscal Year 1987. NIADDK anticipates the award of one Digestive Diseases Core Center Grant in Fiscal Year 1987.

The objectives of the Core Center are to bring together, on a cooperative basis, clinical and basic science investigators in a manner which will enhance and extend the effectiveness of research being conducted in the field of digestive diseases. Within the research activities of the Center should be research that is relevant to the underlying cause, mechanism, diagnosis, early detection, prevention, control and treatment of digestive diseases and related physiological, pathophysiological, congenital or metabolic disorders resulting from such diseases. The focus can be on a disease such as pancreatitis, functional bowel disease, chronic hepatitis; an organ such as liver, esophagus, large bowel; a process such as absorption, secretion, motility or an appropriate combination thereof which may also involve areas of relevant technology.

The Core Center Grant is a mechanism designed to enhance and extend the effectiveness of a group of related projects and investigators that are already funded through other mechanisms such as Research Project Grants or Research Program Projects. In this respect the Core Center mechanism builds upon an established base of research excellence. The Core Center Grant may provide funds for (1) core resources such as tissue culture, immunoassay or biostatistics units which must be utilized by two or more center participants, (2) pilot/feasibility projects to encourage new investigators or investigators from other fields to pursue new and innovative ideas to a point where they can compete for independent support; in addition, temporary salary support for one named new investigator in a specified area of research and with a defined pilot/feasibility project may be requested for up to 24 months, with subsequent individuals to be named and reviewed by the Center's Advisory Board and the NIDDK, and (3) program enrichment funds to provide for small conferences or symposia, advisory board expenses and special consultants.

This program is described in the Catalog of Federal Domestic Assistance No. 13.848, Digestive Diseases and Nutrition. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and CFR Part 74. This program is not to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.
Institutions that have the necessary foundation of multidisciplinary digestive diseases-related research are encouraged to apply for the Digestive Diseases Core Center Grant. Each applicant must show that at least fifty percent of the fiscal support for the ongoing research projects in areas relevant to digestive diseases are from the NIADDK and that the remainder of the research projects to be included in the center research base are relevant to the overall goals of the Core Center Grant. Foreign institutions are not eligible to apply.

NIADDK expects to award one Digestive Diseases Core Center Grant in Fiscal Year 1987 on a competitive basis. The receipt of one competitive continuation application is anticipated and it will be in competition for an award together with other applications received in response to this announcement. An average Center may include about 5 to 7 pilot/feasibility projects and 6 to 8 core units with a direct cost of up to approximately $500,000. However, the actual cost of the Center will vary depending on the needs of the Center. The anticipated award will be for five years and is contingent upon the availability of appropriated funds. The general description of a Core Center, copies of Core Center Guidelines, and consultation may be obtained from:

Dr. Ralph L. Bain  
Digestive Diseases and Nutrition  
Centers Program  
National Institute of Arthritis, Diabetes and Digestive and Kidney Diseases  
Bethesda, Maryland 20892  
Telephone: (301) 496-9717

Potential applicants are urged to submit a letter of intent regarding their application. The letter of intent is non-binding and is not a precondition for an award. The letter of intent should include: a concise statement of the objectives of the proposed center, a brief outline of the projects in the research base and the proposed pilot/feasibility projects for the center, names of research investigators and the intended Principal Investigator, the nature of the core facilities, and any unique features of the proposed center.

Applications for the grant for the Digestive Diseases Core Center will be evaluated in national competition by the NIH grant peer review process. Applications will be reviewed initially by a special review committee convened by the NIADDK, and subsequently by the National Arthritis, Diabetes and Digestive and Kidney Diseases Advisory Council. The special single receipt date for submissions in response to this announcement is June 16, 1986, with earliest funding June 1987.
ANNOUNCEMENT

AVAILABILITY OF REQUEST FOR APPLICATIONS: RFA

86-CA-07

THE TRANSFORMATION MECHANISMS OF HUMAN POLYOMAVIRUSES

P.T. 34; K.W. 1002045, 0755030, 0715035

NATIONAL CANCER INSTITUTE

Application Receipt Date: July 15, 1986

I. INTRODUCTION

The Biological Carcinogenesis Branch, Division of Cancer Etiology, National Cancer Institute is inviting grant applications from interested investigators to elucidate the molecular mechanisms by which human polyomaviruses, e.g. JC virus and BK virus, transform human and animal cells in vitro and in vivo. The present RFA announcement is for a single competition with a deadline of July 15, 1986 for receipt of applications. Applications should be prepared and submitted in accordance with the aims and requirements which are described in the complete RFA document and summarized in the following sections.

II. RESEARCH GOALS AND SCOPE

The major emphasis of research to be funded under this RFA will be in two areas: basic studies on the mechanisms of transformation of human polyomaviruses and their possible role in the etiology of human cancer. Applications may be submitted in either or both of these areas. The scope of this RFA includes both known human polyomaviruses, BK and JC viruses. Applications may propose studies focused on one or both of these viruses. In addition the scope of these studies may be expanded, where appropriate, to include new human polyomaviruses which may be isolated.

Examples of pertinent studies (which are not all encompassing) are: 1) characterization of the viral enhancer/origin sequences and the proteins and genes with which they interact. Determination of the significance for transformation of the hypervariability of these sequences and other regions found in natural variants of these viruses. 2) characterization of the viral tumor antigen proteins, particularly with regard to defining functionally and immunologically distinct domains within the proteins. 3) development and utilization of modified human cell lines which can

This program is described in the Catalog of Federal Domestic Assistance No. 13.393, Cancer Etiology Research. Awards are under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended; 42 USC 282) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.
be efficiently transformed by these polyomaviruses or can support high titer lytic growth. Development of such cell lines could also help delineate the co-factors needed to produce transformation in vivo. 4) studies of the incidence, integration state, and sequence structure of polyomavirus DNA in normal human tissues and human tumors, particularly tumors which are histologically similar to tumors induced by these viruses in animals. 5) functional analysis of polyomavirus DNA from human tumors with regard to the presence of gene products, transformation activity in transfection assays and the maintenance of viral sequences upon serial passage of tumor cells in culture. 6) studies of the mechanism of persistent polyomaviral infections in man and the identification of the transformed target cells involved in this interaction. As a subsidiary to these studies (particularly #4 and #5 above) the isolation and characterization of new human polyomaviruses with oncogenic potential is encouraged. In this regard, the putative B-lymphotropic virus described in the scientific literature is a candidate for isolation and characterization.

III. MECHANISM OF SUPPORT

The mechanism of support for this RFA will be the traditional National Institutes of Health (NIH) research project grant. Responsibility for the planning, direction and execution of the proposed research will be solely that of the applicant. The total project period for applications submitted in response to the present RFA should not exceed five years. Approximately $600,000 will be set aside to specifically fund applications which are submitted in response to this RFA. The earliest feasible start date for the initial awards will be March 1987. Although this program is provided for in the financial plans of the National Cancer Institute (NCI), the award of grants pursuant to this RFA is also contingent upon the availability of funds for this purpose. Non-profit and for-profit institutions are eligible to apply. Foreign as well as domestic institutions are eligible. All applications submitted in response to this announcement will be classified as new grants (Type 1). PHS grant policies governing regular research project grants, including cost sharing, apply to applications received in response to this request.

IV. INQUIRIES

A copy of the complete RFA describing the research goals and scope, the review criteria and the method of applying can be obtained by contacting:

Dr. Alan A. Schreier
Program Director, DNA Virus Studies II
Biological Carcinogenesis Branch
Division of Cancer Etiology
National Cancer Institute
Landow Building - Room 9A-22
Bethesda, Maryland 20892

Telephone: (301) 496-1953

Inquiries concerning this announcement are encouraged and should be directed to Dr. Alan A. Schreier of the above address and phone number. The program would appreciate the opportunity to clarify any issues or questions.
ANNOUNCEMENT

BIOLOGICAL ROLE OF EXOCYCLIC NUCLEIC ACID DERIVATIVES IN CARCINOGENESIS

P.T. 34; K.T. 0715035, 0790010, 1007009, 1002028, 0760045

NATIONAL CANCER INSTITUTE

Application Receipt Dates: June 1, October 1, February 1

The Division of Cancer Etiology (DCE) of the National Cancer Institute (NCI) invites grant applications from interested investigators for basic studies that are focused on providing insights and approaches to an understanding of the biological role of exocyclic nucleic acid derivatives in carcinogenesis.

I. BACKGROUND:

The current status of research on the types of adducts produced by exposure to vinyl halides, alkyl carbamates, mono and bifunctional aldehydes, epoxides, halonitrosoureas and related compounds and their role in carcinogenesis was discussed at a workshop entitled "Cyclic Nucleic Acid Adducts in Carcinogenesis" which was held at the International Agency for Research on Cancer in Lyon, France on September 17-79, 1984. A report of this meeting has been published (see Cancer Research 45: 5205-5209, 1985). A number of chemicals of the above types which include known or suspected human carcinogens (vinyl chloride, acrylonitrile, cyclophosphamide), several of which can be found in food and beverages (ethyl, carbamate, methylglyoxal, glycidaldehyde, malonaldehyde, N-nitrosopyrrolidine), chemotherapeutic agents (haloethylnitrosoureas) and others which humans are exposed to as environmental pollutants (acrolein, also detected in cigarette smoke) or through occupational exposure (acrylonitrile, vinyl chloride) have been shown to form a large variety of adducts with guanosine, and cytosine in nucleic acids. In addition, many of the compounds can also form interstrand crosslinks. From discussions on the mutagenicity and carcinogenicity of compounds such as vinyl chloride, acrylonitrile, methylglyoxal, ethyl carbamate and malonaldehyde, it was concluded that cyclic nucleic acid adducts could play a major role in the biological activity of these compounds. However, more work is needed since adducts of this type have not been identified in vivo for many compounds. The identification of adducts in DNA was determined to be a problem due to the lack of sensitive methods for the quantitation and identification of the adducts formed. It was also apparent that little is known about the repair of known exocyclic derivatives in mammalian cells.

This program is described in the Catalog of Federal Domestic Assistance No. 13.393, Cancer Cause and Prevention Research. Awards are under authorization of the Public Health Service Act, Section 301(c) and Section 402 (Public Law 78-410, as amended; 42 USC 241; 42 USC 282) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.
II. OBJECTIVES AND SCOPE:

It is the intent of this program announcement to encourage basic mechanistic studies focused on determining the formation, repair and relevance to mutagenesis and carcinogenesis of exocyclic nucleic acid derivatives. It is not intended to make or imply any delimitation to the research supported by the Chemical and Physical Carcinogenesis Program of the Division of Cancer Etiology. The compounds of interest which are known or are likely to form exocyclic nucleic acid derivatives include: vinyl halides (vinyl chloride, vinyl bromide), alkyl carbamates (ethyl and vinyl carbamate), halonitrosoureas (BCNU, CCNU), monofunctional unsaturated aldehydes (acrolein, crotonaldehyde), bifunctional aldehyes (glyoxal, malonaldehyde, glyceraldehyde), beta-propiolactone, acrylonitrile, N-nitrosopyrrolidine and related cyclic nitrosamines, and some halogenated ethers and aldehydes (chloro- and bromoacetaldehyde). Examples of important areas of research emphasis include the following: 1) the identification and quantitation of adducts which may be responsible for the carcinogenicity of the test compound in animals, the transformation of cells in culture, or the mutagenicity of the compound in cells in culture or in other test systems; 2) the formation and repair of exocyclic adducts in animals, cells in culture, or test organisms relevant to carcinogenicity, transformation of mutagenicity studies; and 3) the mechanism of mutagenesis or carcinogenesis by exocyclic nucleic acid adducts, other adducts of biological interest or crosslinks which may be formed by the above mentioned compounds. It is also recognized that there will be a need to develop more sensitive methods to analyze and quantitate the many possible adducts and to detect them in DNA from cells exposed to the chosen compounds. A desired sensitive method, not widely available, is an immunoassay using monoclonal antibodies to the chosen exocyclic adduct or other relevant adduct.

III. METHOD OF APPLYING

Any non-profit and for-profit institution, domestic and foreign, may apply. All PHS and NIH grants policies governing regular research project grants, including cost sharing, will apply to applications received in response to this announcement. Applications should be submitted on form PHS 398, Grant Application Kit, which is available in the grants and contracts business office at most academic and research institutions. Copies may also be requested by writing to:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Westwood Building - Room 449
5333 Westbard Avenue
Bethesda, Maryland 20892

Please type "Exocyclic Nucleic Acid Derivatives in Carcinogenesis" in item 2 on the face page of the application.

Additionally, a brief covering letter should accompany the application indicating it is being submitted in response to this program announcement. The original and six copies of the application should be sent or delivered to:
IV. DEADLINE

Applications will be accepted in accordance with the usual National Institutes of Health (NIH) receipt dates for new applications. Deadline dates are: June 1, October 1, February 1. Earliest possible start dates would be: April 1, July 1, December 1, respectively.

V. REVIEW PROCEDURES AND CRITERIA

Applications in response to this announcement will be reviewed in accordance with the usual NIH peer review procedures. They will first be reviewed for scientific and technical merit by an appropriate review group composed mostly of non-Federal scientific consultants. Following this initial review, the application will be evaluated by an appropriate National Advisory Board or Council. The review criteria customarily employed by the NIH for regular research grant applications will prevail.

VI. STAFF CONTACT

For further information, investigators are encouraged to contact:

Dr. Paul Okano
Chemical and Physical Carcinogenesis Branch
Division of Cancer Etiology
National Cancer Institute
Landow Building - Room 9C18
7910 Woodmont Avenue
Bethesda, Maryland 20892

Telephone: (301) 496-4141

In order to alert the Division of Cancer Etiology to the submission of proposals with primary thrust directed to chemical and physical carcinogenesis research, a copy of the covering letter should be sent under separate cover to Dr. Okano.
ANNOUNCEMENT

CHARACTERIZATION OF MULTIDRUG RESISTANT HUMAN AND OTHER MAMMALIAN TUMOR CELL LINES

P.T. 34; K.W. 0710045, 0745005, 0780015

DIVISION OF CANCER TREATMENT

NATIONAL CANCER INSTITUTE

Application Receipt Dates: June 1, October 1, February 1

The National Cancer Institute (NCI) is seeking grant applications for support of research projects to identify and characterize multidrug resistant tumor cells. The development of drug resistance in tumor cell populations treated with chemotherapeutic agents has been recognized as a major problem in cancer treatment. The Division of Cancer Treatment (DCT) desires to support research in this area in order to increase understanding of drug resistance phenomena and develop therapeutic strategies to overcome or circumvent the problem.

This announcement is specifically targeted to stimulate research in the area of multidrug resistance (MDR). Detailed studies in Chinese hamster and murine cell systems have shown that under some selective conditions, e.g. Colchicine, Vincristine, or Adriamycin treatment, cell populations demonstrating a multi-drug resistant phenotype emerge. In many of these cells, broad spectrum resistance to multiple agents of different modes of action is associated with reduced intracellular accumulation of drug and the appearance of a membrane glycoprotein marker. Recently, laboratory evidence has been presented that multidrug resistant cells also occur in human tumor cell populations. This latter evidence is consistent with clinical experience, particularly with previously treated patients, wherein resistance to multiple agents of different modes of action is observed.

While some potentially important collateral sensitivities to established anti-tumor drugs have been observed among mammalian cell types showing the multi-drug resistant phenotype, it seems likely that new agents specifically useful in treating these resistant cells will be needed. Development of such agents will require additional insight into the mechanism(s) of MDR and an adequate number of well characterized multidrug resistant cell lines in which new agents can be studied. This announcement is intended to stimulate applications for grants which propose to develop and characterize multidrug resistant human or mammalian tumor cell lines which have potential for this purpose. The primary emphasis in applications submitted in response to this Program Announcement should be elucidating the mechanism of resistance in multidrug resistant cell populations.

This program is described in the Catalog of Federal Domestic Assistance No. 13.395, Cancer Treatment Research. Awards will be made under the authority of Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.
Multidrug resistant cells may be selected in vitro or derived directly from patients or animals bearing tumors which have been shown to be resistant to chemotherapy. While the specific approaches and methods for development and characterization of the resistant cells will be left to the applicant, it is suggested that the following areas be addressed in the application:

A. Mechanism(s) of multidrug resistance.
B. Stability of the drug resistant phenotype.
C. Extent of cross resistance.
D. Tumorigenicity of the drug resistant cells.
E. Verification of the origin of the cells.

Applications in response to this announcement will be reviewed in accordance with the usual National Institutes of Health (NIH) peer review procedures. They will first be reviewed for scientific and technical merit by a review group (Study Section) composed mostly of non-government scientific consultants. Following this initial review, the application will be evaluated for program relevance by the appropriate National Advisory Council/Board. The review criteria customarily employed by the NIH for regular research grant applications will be utilized. All Public Health Service (PHS) grants policies, including cost-sharing, apply to applications received in response to this Program Announcement.

I. DEADLINE

Applications will be accepted in accordance with the usual NIH receipt dates for new applications. Deadline dates are June 1, October 1, and February 1.

II. METHOD OF APPLYING

Applications should be submitted on form PHS 398, which is available in the grants and contracts business office at most academic and research institutions or from the Division of Research Grants (DRG), NIH. In space #2 on the first page of this form, indicate the title of this Program Announcement. Additionally, a brief covering letter should accompany the application indicating that it is being submitted in response to this Program Announcement. The original and six copies of the application should be submitted to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20892

For further information, contact:

Dr. Mary K. Wolpert
Developmental Therapeutics Program
Division of Cancer Treatment
National Cancer Institute
Landow Building - Room 5C03B
Bethesda, Maryland 20892

Telephone: 301-496-8752
PROGRAM ANNOUNCEMENT

MECHANISMS OF SITE SPECIFIC METASTASIS IN PROSTATE CANCER

P.T. 34, K.W. 0715035, 0785140, 0765035

DIVISION OF CANCER PREVENTION AND CONTROL
NATIONAL CANCER INSTITUTE

Application Receipt Dates: June 1, October 1, February 1

The Organ Systems Program of the Division of Cancer Prevention and Control (DCPC), National Cancer Institute (NCI) seeks applications for studies to develop and evaluate new techniques to predict the metastatic potential of prostate cancer, and to identify steps in the metastatic cascade and characterize the host factors and cellular and molecular properties of prostate cancer cells which determine the incidence and organ distribution patterns of prostate cancer metastasis.

I. BACKGROUND

Prostate cancers have an extraordinary diversity of metastatic pathological examination which in most cases will not become clinically manifest. About 10% of men in the age range of 50-59 years and about 50% at 70-79 years have these latent prostate cancers. Only a few of these will manifest themselves as clinical prostatic cancer reaching a maximum incidence of 800 to 1,000/100,000 in the 7th and 8th decade. The few latent cancers that progress still provide a high enough mortality rate to make prostate cancer the second leading cause of cancer deaths in males. The high mortality rate may be related to the fact that about 80% of prostatic cancer patients first present with evidence of metastasis. A special effort is needed to investigate these peculiar properties of prostate cancer about which, in comparison with other forms of cancer, there is sparse information on the tumor biology of metastasis. In addition, there is a dramatic increase in the incidence of prostate cancer with advancing age. Aging of the male population will accentuate this problem within the foreseeable future.

This program is described in the Catalog of Federal Domestic Assistance No. 13.393, Cancer Prevention Research. Awards will be made under authorization of the Public Health Service Act, Title III, Section 301(c) and Section 402 (Public Law 78-410, as amended; 42 USC 241; 42 USC 282) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.
II. RESEARCH GOALS AND SCOPE

There is little information on the cellular and molecular events associated with prostate cancer metastasis. New techniques and models are now available to address specific biological questions in a quantitative manner that should provide specific new insight that might impact on the control of this disease.

Recent reports indicate that quantitative pathological techniques may be useful in assessing the aggressive nature of prostatic cancer in man and animal models. These techniques include quantitative pathology, flow cytometry, nuclear morphology, and biochemical indicators. There is a need to mount a systematic study to evaluate these procedures and to determine the biological factors associated with the different tumor types, and to determine the metastatic potential of specific cell types within the heterogeneous cells of a prostate cancer.

Studies on the relationship of cell biology events to metastatic potential are encouraged, e.g., cell motility, lytic enzymes and their inhibitors, cell-cell interactions, and interactions between prostate cancer cells and the extracellular components including the basement membrane and stromal elements.

There is a need to compare paths of metastatic dissemination using both the lymphatic route and the hematogenous route, in order to determine the relative importance of either route in the generation of pulmonary metastases as well as the importance of hematogenous dissemination to the liver. Studies are needed to characterize the factors which determine the organ patterns of metastases, including the tertiary spread of prostate cancer. These studies could include cancer cell delivery, numbers of cells delivered and their survival in different organs as well as comparison of metastatic properties of androgen sensitive and insensitive cell lines. Attention might also be directed towards factors responsible for the generation of skeletal lesions which present a particular problem since reports indicate that 55-70% of patients with prostate cancer develop bone metastases. These studies would necessitate the development of new experimental approaches since overt spontaneous skeletal metastases appear to be uncommon in existing animal tumor systems.

Studies are encouraged to determine the biological or pharmacological factors which might regulate the degree or site of metastasis in animal characterized that have different growth properties, routes of metastasis and hormone sensitivity. In addition, human prostatic cancer cells are becoming increasingly available by the acceptability of needle aspiration that is associated with a low morbidity.

III. MECHANISM OF SUPPORT

Support for this program will be through the traditional research grant. Policies that govern research grant programs of the National Institutes of Health will prevail.
IV. APPLICATION AND REVIEW PROCEDURES

Applications in response to this announcement will be reviewed in accordance with the usual Public Health Service Peer Review (Study Section) procedures for research grants. Review criteria include the significance and originality of the research goals and approaches; feasibility of the research and adequacy of the experimental design; adequacy of available facilities; and appropriateness of the requested budget relative to the work proposed. Following Study Section review, the application will be evaluated for program relevance by the Organ Systems Program, DCPC, NCI. Funding decisions will be based on Initial Review Group and National Cancer Advisory Board recommendations, program relevance, and availability of funds.

Applications should be submitted on form PHS-398, available in the business or grants office at most academic or research institutions, or from the Division of Research Grants, National Institutes of Health. Applications will be accepted in accordance with the dates for the new applications on an indefinite basis:

February 1  June 1  October 1

The phrase "MECHANISMS OF SITE SPECIFIC METASTASIS IN PROSTATE CANCER" should be typed on line 2 of the face page of the application. The original and six copies should be sent or delivered to:

Grant Applications Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20892-4500

In addition, a copy of the face page and summary page of the application should be sent under separate cover to:

Dr. Andrew Chiarodo
Organ Systems Section
Cancer Centers Branch
DCPC, National Cancer Institute
Blair Building - Room 717
Bethesda, Maryland 20892-4200

Telephone (301) 427-8818
ANNOUNCEMENT

PROGRAM SUPPLEMENT FOR RESEARCH GRANT APPLICATIONS

ENGINEERING CONTROL SYSTEMS RESEARCH

P.T. 34; K.W. 0725020

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

CENTERS FOR DISEASE CONTROL

Application Receipt Dates: New applications - February 1, June 1, October 1; Exceptions: Career Development, Small Grants, and Competing renewal applications - March 1, July 1, November 1.

I. PURPOSE AND BACKGROUND

The National Institute for Occupational Safety and Health (NIOSH) invites grant applications for research and demonstrations in the area of engineering control systems (ECS) for the prevention of occupational injuries, illnesses, and deaths. This invitation supplements the existing NIOSH program announcement (Vol. 13, No. 13, December 7, 1984 of the NIH Guide for Grants and Contracts) by elaborating on item 11 (control technology research) in that announcement. The primary purposes are:

- To conduct high-quality, innovative engineering research and demonstrations on priority problems of long-term interest to NIOSH.
- To conduct engineering research and demonstrations which will raise the level of academic engineering competency in the health and safety field and result in the development of improved engineering curricula in this field.

Research and demonstrations of engineering control systems are integral parts of NIOSH's systematic approach to supporting research at the basic level and then advancing these developments to the ultimate goal of preventing occupational injuries, illnesses, and deaths for the Nation.

Many workplace injuries, illnesses, and deaths are preventable by proper workplace design. The logical sequel to the recognition and evaluation of occupational hazards is control. Effective control of occupational hazards usually requires a systematic application of various measures to provide adequate protection under any foreseeable conditions. Engineering controls and work practices are the essential mainstays of an effective control system, but in the absence of engineering control, personal protection is used. Workplace environment monitoring provides feedback on the effectiveness and state of control systems, allowing appropriate corrections to be made.
Control strategies can be expressed as a hierarchy of elements. These elements, in order of preference, are:

1. Prevent or contain hazardous workplace emissions at their source (e.g., engineering, substitution).

2. Remove emissions from the pathway between the source and the worker (e.g., engineering, work practices).

3. Control exposure with barriers between the worker and the hazardous work environment (e.g., engineering, personal protection).

Desirable characteristics of an engineering control system are:

- It must provide adequate and reliable protection for workers when functioning as designed.

- Potential modes of failure should be anticipated and backup control measures should be available to provide continued worker protection in the event that failures occur.

- The dependence on human intervention as a first step in control should be minimized. Where possible, mechanical or electronic pacing or warning devices should be used to supplement human intervention steps.

- The effectiveness of protection for each individual worker must be determinable.

- Provision for regular or continuous monitoring of critical process, hazard, exposure, and control parameters should be included.

- The control system must encompass all routes of entry into workers' bodies and should not exacerbate existing health or safety problems or create any additional ones.

- Engineering control systems can be used on a retrofit basis to solve existing occupational safety and health problems. However, engineering control systems are most efficiently used when incorporated into the initial design and construction of process equipment, facilities, and systems.

II. SCOPE OF RESEARCH INTERESTS

Research and demonstration projects are needed to address the hierarchy of elements listed above. Major areas of interest include chemical processing technology, nonferrous metals production, manufacturing processes such as tire building and spray painting, service industries such as dry cleaning, and control techniques such as air recirculation and push-pull local exhaust ventilation. In each of these situations, behavioral, motivational, and ergonomic considerations may be important factors in successful control of worker exposure to hazardous situations.

Engineering control research projects are important in developing and evaluating continuous monitoring techniques, protocols and control criteria which can be used in the development, implementation, and maintenance of control systems. Part of
this effort is to investigate the applicability of innovative control methods which are not currently in general use and demonstrate the effectiveness of existing workplace controls.

Control monitoring instruments and techniques would provide information on the operational status of control systems, provide warnings to plant personnel and provide corrective actions in the case of control failure. Monitoring systems can be an integral part of the control system and, in many cases, can be used to obtain estimates of long-term worker exposure data.

III. MECHANISM OF SUPPORT

The support mechanism for this program will be the research and demonstration project grant. All policies and requirements which govern the PHS grants programs apply, including the requirement for a minimum cost sharing of five percent. The specific amount to be awarded will depend on the merit and scope of the applications received and the availability of funds. The duration of the grant projects is not to exceed five years. Renewal of the grant support may be sought through the regular NIH grant review process.

Eligible applicants include non-profit and for-profit organizations. Thus, universities, colleges, research institutions and other public and private organizations including State and local governments and small, minority and/or women-owned businesses are eligible for these research and demonstration grants. For-profit organizations will be required to submit a certification as to their status as part of their application.

IV. INSTITUTE CONTACT

A copy of the complete program supplement describing specific research interests, review process, application procedures, and reporting requirements can be obtained from:

Roy M. Fleming, Sc.D.
Associate Director for Grants
National Institute for Occupational Safety and Health
Centers for Disease Control
1600 Clifton Road, N.E.
building 1 - Room 3051
Atlanta, George 30333

Telephone: (404) 329-3343