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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.
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NOTICE

SIGNATURE REQUIREMENTS FOR NIH GRANT APPLICATIONS

This notice is both a reminder and a restatement of the National Institutes of Health (NIH) policy published in the August 14, 1970 issue of the "NIH Guide for Grants and Contracts" concerning applicant signature requirements for all NIH grant applications.

To be valid and acceptable for review, an application must have been properly executed by: 1) the proposed Principal Investigator and Program Director and 2) by an individual authorized to act for the applicant organization and to assume the obligations imposed by the requirements and conditions for any grant, including the applicable Federal Regulations.

"Per" signatures are not acceptable. If the official designated to sign for the applicant organization is not available to sign, an official authorized to act in his or her behalf may sign as "acting for" such official.
NOTICE

REVIEW PROCEDURES—REMINDER TO APPLICANTS

Sending Additional Materials for Your Grant Application:

If you need to send additional materials or corrections before your application has been reviewed by a study section or an initial review group, send these materials directly to the Executive Secretary of the group that will be reviewing your application. If you do not know the identity of the Executive Secretary or study section, send the material to:

Referral Section  
Division of Research Grants  
National Institutes of Health  
Westwood Building - Room 248  
Bethesda, Maryland 20205

Contacting NIH Staff after your Application has been Reviewed:

After your application has been reviewed by a study section or an initial review group, contact the appropriate program staff member of the funding Bureau, Institute, or Division for any information about your application. That person—not the Executive Secretary of the study section—is the appropriate source of information after the first level of review has been completed.
NOTICE

NIH/FDA REGIONAL WORKSHOPS - PROTECTION OF HUMAN SUBJECTS

P.T. 42; K.W. 0701028

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>
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| September 13-14, 1984 | Stanford, CA    | Ms. Phyllis S. Hall  
Human Subjects Coordinator  
Stanford University  
Encina Hall  
Stanford, CA. 94305  
Telephone: (415) 497-3638 |
| October 22-23, 1984 | Washington, DC  | Mrs. Lucille Holland  
Office of The Institutional  
Review Board  
Room 214, Annex 2  
Freedman's Square  
Howard University  
Washington, DC 20059  
Telephone: (202) 636-7812 |
| January 17, 1985   | Los Angeles, CA | Dr. Harry Neustein  
Professor of Pathology  
Chairman of Institutional  
Review Board  
Children's Hospital of  
Los Angeles  
4650 Sunset Blvd.  
Los Angeles, CA 90054  
Telephone: (213)359-8111 |
A final list of dates and locations will be published at a later date. For further information regarding education programs contact:

Roberta H. Garfinkle  
Office for Protection from Research Risks  
National Institutes of Health  
Building 31-Room 4B09  
9000 Rockville Pike  
Bethesda, MD 20205
ANNOUNCEMENT

AVAILABILITY OF REQUEST FOR APPLICATIONS: RFA

84-AM-05

AUTO-IMMUNITY RELATED TO ENDOCRINE DISEASES

P.T. 34; K.W. 1200050, 1200440

NATIONAL INSTITUTE OF ARTHRITIS, DIABETES, AND DIGESTIVE AND KIDNEY DISEASES

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Application Receipt date: December 3, 1984
Letter of Intent Receipt date: November 15, 1984

The DEMD Division of the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK) in collaboration with the National Institute of Allergy and Infectious Diseases (NIAID) and the National Institute of Child Health and Human Development (NICHD) announces the availability of a Request for Application (RFA) on the above subject. Copies of the RFA are currently available from the staff of the NIADDK.

This program will support research directed towards understanding the role of autoimmune antibodies in the manifestations of various endocrine diseases and the genetic factors involved, such as the relationships to the HLA antigens. The endocrine diseases will include Hashimoto's disease or primary myxedema, Grave's disease, idiopathic Addison's disease, adrenocortical insufficiency (Schmidt's Syndrome), primary ovarian failure, autoimmune testicular failure, idiopathic hypoparathyroidism, renal tubular acidosis, and autoimmunity associated with sterility in both men and women.

It is hoped that this announcement will be of particular interest to investigators in endocrinology, immunology, cell biology, membrane biochemistry, clinical endocrinology, pathology, epidemiology and genetics.

This program is described in the Catalog of Federal Domestic Assistance No. 13.847, Diabetes, Endocrinology and Metabolism; 13.855, Immunology, Allergic and Immunologic Diseases Program; and 13.865, Center for Research for Mothers and Children. 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.
The date for receipt of the applications will be December 3, 1984.

Request for copies of the RFA should be addressed to:

    Robert A. Tolman, Ph.D.
    Endocrinology Research Program Director
    NIH, NIADDK, DEMD
    Westwood Building - Room 626
    5333 Westbard Avenue
    Bethesda, Maryland 20205
AVAILABILITY OF REQUEST FOR COOPERATIVE AGREEMENTS ANNOUNCEMENTS: RFA 84-CA-19

STUDIES ON BOVINE LEUKEMIA

P.T. 34; K.W. 1002014, 1002008, 1002004

NATIONAL CANCER INSTITUTE

Application Receipt Date: November 15, 1984

The Division of Cancer Etiology (DCE), National Cancer Institute (NCI), invites applications for cooperative agreements to support investigator-initiated research in bovine leukemia. Studies of interest include, but are not limited to: (1) research to determine the nature of the target cells that undergo neoplastic transformation in vivo in cattle and sheep; (2) investigations to search for and develop a sensitive lymphoid cell transformation assay in vitro and delineation of the cellular and molecular events that lead directly to the cell transformation event; (3) research to determine the nature of the different protein products of the viral genome, including those involved in cell transformation; (4) research to determine the nature of the transforming DNA sequences in BLV tumors and lymphocytes; (5) investigations on the BLV genome through nucleotide sequence analyses and comparison to the genomes of other retroviruses, including HTLV; (6) investigations to delineate the nature of the plasma blocking factor and its mode of regulation of the expression of BLV; and (7) investigations to determine the role of cellular immunity in infection and expression of disease.

Applicants funded under this RFA will be supported through the Cooperative Agreement mechanism. These are assistance relationships involving substantial involvement of NCI staff during the performance of the project. The nature of NCI staff participation is included in the RFA. The recipients will have primary responsibility for the development and conduct of research. NCI involvement will be in regard to coordinating and synthesizing the research effort in regard to approaches, methodologies, and exchange of information. The total project period for applications submitted in response to the present RFA should be three years. The intent is to fund approximately four to five projects with a total program cost for all Cooperative Agreements under this RFA equal to approximately $500,000 of FY85 funds for the first year. This funding level is dependent on the receipt of a sufficient number of applications of high merit. Although this program is included in the financial plans of the NCI, the awards pursuant to this RFA are contingent upon the availability of funds for this purpose. The issuance of this RFA does not represent a guarantee that any funds will be awarded. No funds are available for the purchase of large capital equipment.
Copies of complete Request for Applications (RFA) and additional information may be obtained from:

Padman S. Sarma, D.V.M., Ph.D.
Program Director, RNA Virus Studies I
Biological Carcinogenesis Branch
Division of Cancer Etiology
Landow Building, Room 9A22
National Cancer Institute
Bethesda, Maryland 20205

Telephone: 301/496-9734

To ensure their review, applications should be received by November 15, 1984.
ANNOUNCEMENT

AVAILABILITY OF REQUEST FOR COOPERATIVE AGREEMENT APPLICATION: RFA 84-CA-27

STUDIES ON HUMAN T CELL LEUKEMIA/LYMPHOMA VIRUS TYPES I & II (HTLV-I, HTLV-II)

P.T. 34; K.W. 1002045, 1201150, 1200650, 1201310

NATIONAL CANCER INSTITUTE

Application Receipt Date: November 15, 1984

The Division of Cancer Etiology (DCE), National Cancer Institute (NCI), invites applications for cooperative agreements to support investigator initiated research on HTLV type I and II. Studies of interest include, but are not limited to: 1) investigation of the viral genome of various substrains of HTLV including studies of the LTR, env and pX regions; 2) identification and characterization of viral genome protein products as a clue to determining if they are transforming proteins and to understand the functional activity of the resultant products; 3) investigations of virus integration sites in various systems and/or hosts to determine if the transforming function acts in the cis or trans mode; 4) investigations directed to characterizing the clinically relevant biological activities of the virus, especially its immunosuppressive and/or immunoregulatory effects on the host; 5) determination of the exact mode of horizontal transmission of the virus, including investigations of possible insect transmission; 6) studies in virus-host interactions; including geographical localization, determination of host-range, endemic areas other than the Caribbean and Japan (i.e. Africa and Far East) and localization and overlap of different types of HTLV virus; 7) characterization of HTLV-like viruses of non-human primates and determination if there is an evolutionary link to HTLV; and 8) investigation of the possible use of vaccines to prevent or suppress the horizontally transmitted HTLV associated diseases.

Applicants funded under this RFA will be supported through the cooperative agreement mechanism. An assistance relationship will exist between NCI and the awardees to accomplish the purpose of the activity. The recipients will have primary responsibility for the development and conduct of research. NCI involvement will be in regard to coordinating and synthesizing the research effort in regard to approaches, methodologies and exchange of information.

The total project period for applications submitted in response to the present RFA should be three years. The intent is to fund approximately five to seven projects with a total program cost for all Cooperative Agreements under this RFA equal to approximately $750,000 of FY85 funds for the first year. This funding level is dependent on the receipt of a sufficient number of applications of high merit. Although this program is included in
the financial plans of the NCI, the awards pursuant to this RFA are contingent upon the availability of funds for this purpose. The issuance of this RFA does not represent a guarantee that any funds will be awarded. No funds are available for the purchase of large capital equipment.

Copies of complete Request for Applications and additional information may be obtained from:

Padman S. Sarma, D.V.M., Ph.D.
Program Director, RNA Virus Studies I
Biological Carcinogenesis Branch
Division of Cancer Etiology
Landow Building - Room 9A22
National Cancer Institute
Bethesda, Maryland 20205

Telephone: 301/496-9734

To ensure their review, applications should be received by November 15, 1984.
ANNOUNCEMENT

AVAILABILITY OF REQUEST FOR COOPERATIVE AGREEMENT APPLICATIONS: RFA 84-CA-17

THE PHYSIOCHEMICAL EFFECTS OF DIETARY FIBER IN HUMANS.

P.T. 34; K.W. 0202022, 1002014, 1002028, 1002034, 1200410

NATIONAL CANCER INSTITUTE

Letter of Intent Receipt Date: October 16, 1984
Application Receipt Date: December 11, 1984

The Division of Cancer Prevention and Control (DCPC), National Cancer Institute (NCI), invites applications for cooperative agreements to support research on the physical, chemical and biologic effects of dietary fibers and their possible protective role in carcinogenesis. Studies of potential interest to NCI include, but are not limited to, the effects of fiber on: (1) fecal mutagenic activity, (2) fecal content of bile acids, and (3) colon cell kinetics, morphology, and physiology. Investigators are encouraged to be creative and to explore novel physiochemical effects of various fiber fractions. While some of these studies can only be done in animal models, the intent is that results from these studies shall be directly related to human carcinogenesis.

Applicants funded under this RFA will be supported through the cooperative agreement mechanism. An assistance relationship will exist between NCI and the awardees to accomplish the purpose of the activity. As more completely described later in the RFA, the recipients will have primary responsibility for the development and conduct of the research with cooperation and assistance from NCI staff.

Copies of the complete Request for Applications and additional information may be obtained from:

Elaine Lanza, Ph.D.
Diet and Cancer Branch
Blair Building - Room 619
National Cancer Institute
Bethesda, Maryland 20205

Telephone: (301) 427-8753

To ensure their review, applications should be received by December 11, 1984.
ANNOUNCEMENT

AVAILABILITY OF REQUEST FOR COOPERATIVE AGREEMENT APPLICATIONS: RFA 84-CA-18

SELECTED CANCER PREVENTION CLINICAL TRIALS

P.T. 34; K.W. 1200180, 0202022, 0701042, 0411005

NATIONAL CANCER INSTITUTE

Application Receipt Date: December 10, 1984

The Division of Cancer Prevention and Control (DCPC), National Cancer Institute (NCI), invites applications for cooperative agreements to support risk reduction clinical trials which are directed toward examining the role of various preventive agents and/or diet in the prevention of cancer. Studies of populations at increased risk to colon, breast, bladder, and head and neck cancer are particularly appropriate at this time. Studies of occupational cohorts who have been exposed to known initiators and/or promoters are also encouraged. Situations where the dose response to the promoter can be estimated are particularly relevant. Another category of possible prophylactic trials involve studies of populations at risk to second malignancies. For example a number of studies have reported that Hodgkin's disease patients treated with alkylating agents have an increased incidence of leukemia. Several trials involving skin and lung cancer risk reductions with carotenoids and retinoid compounds have been implemented and additional studies at these sites with the agents indicated are not encouraged at this time.

Applicants funded under this RFA will be supported through the cooperative agreement mechanism. An assistance relationship will exist between NCI and the awardees to accomplish the purpose of the activity. As more completely described in the RFA, the recipients will have primary responsibility for the development and conduct of the research. Programmatic involvement by the Government will be in the form of: (1) NCI assistance with the FDA in securing INDs, if required, (2) safety toxicity review, (3) safety monitoring in cases when the NCI is the IND sponsor, (4) assistance from NCI staff relating to drug availability, and (5) review of clinical laboratory quality assurance activities in the assay of collected sera if necessary.

The terms of award of these cooperative agreements will detail the Government involvement and will specify the level of NCI program assistance and cooperation.

Copies of the complete Request for Applications and additional Information may be obtained from:

Mary Ann Sestili, Ph.D.
Chemoprevention Branch
Blair Building - Room 616
National Cancer Institute
Bethesda, Maryland 20205

Telephone: (301) 427-8643
ANNOUNCEMENT

AVAILABILITY OF REQUEST FOR APPLICATIONS: RFA

84-CA-24

P.T. 34; K.W. 1200250, 1200410, 1200130, 1200490, 1002023

USE OF ONCOGENE RELATED PRODUCTS FOR CANCER THERAPY

NATIONAL CANCER INSTITUTE

Application Receipt Date: December 14, 1984

The Division of Cancer Treatment (DCT) of the National Cancer Institute (NCI) invites grant applications from interested investigators for basic and applied studies to evaluate the therapeutic efficacy of oncogene-related products in animal tumor models.

I. BACKGROUND

Biological response modifiers refers to agents or approaches that alter the relationship between tumor and host by modifying the host's biological response to tumor cells, with a resultant therapeutic benefit. The application of these agents with a primary intent of therapy is the major focus of the Biological Response Modifiers Program.

The components of the BRM program include immunoaugmenting, immunomodulating and immunorestorative agents, interferons and interferon inducers, lymphokines, cytokines, antigrowth factors, thymic factors, tumor antigens and modifiers of tumor antigens on cell membranes, antitumor antibodies, antitumor cells, maturation, differentiation and tumor growth factors.

This RFA addresses use of oncogene and oncogene-related products for cancer therapy in animal models. A number of cellular genes collectively called "proto" oncogenes have been identified which are involved in the control of cellular proliferation and differentiation and have been shown to be direct mediators of cell transformation. Activation of these cellular genes as oncogenes appears to play an important role in both initiation and maintenance of oncogenesis. Several "proto" oncogenes have been identified in the human genome and a number of these have been found to be expressed in the activated form in various human tumors. In tissue culture, inhibition of oncogene activity appears to be associated, in several instances, with reversion of the transformed state. Where functional products of oncogenes have been described, they have been localized to the cell membrane, cytoskeletal elements, or the nucleus. These all represent areas where alterations might be expected to lead to the expression of a malignant phenotype, such as lack of contact inhibition and uncontrolled cell division. Expansion of knowledge of how biological response modifiers and oncogenes interact through investigator initiated research could provide useful information for the future understanding of how oncogenesis is initiated and maintained and how immunity may be enhanced towards specific oncogene induced malignancies.
II. OBJECTIVES AND SCOPE

This Request for Applications (RFA) is intended to stimulate research that will develop and utilize oncogene products or reagents made against these products for therapy in animal model systems. Development of oncogene or oncogene-related products for therapeutic evaluation may involve use of tumor associated membrane antigens for monoclonal antibody production and development of vaccines, use of monoclonal antibodies directed against growth factors or growth factor receptors controlled by or encoded by oncogenes or analysis of factors that inhibit the action of oncogene products that control cell division. Other reasonable approaches directed toward cancer therapy employing oncogene or oncogene-related products or related reagents with antitumor potential may be proposed. Studies may involve the isolation and characterization of these products for the purpose of evaluating their ability to modify or alter tumor initiation, growth and/or metastases as well as stimulating cytotoxicity in vivo or in vitro through activation of macrophages, cytotoxic T cells or natural killer cells. Additional proposals involving studies on how oncogene or oncogene-related products may interfere with specific immune functions will also be considered. Therapeutic potential may be evaluated in the treatment of transplanted, induced or spontaneous animal tumors or human tumor xenografts in nude athymic mice or rats.

III. STAFF CONTACT

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

Dr. Cedric W. Long, Acting Chief
Biological Resources Branch
Biological Response Modifiers Program
Division of Cancer Treatment
National Cancer Institute
Frederick Cancer Research Facility
Building 426 - Room 1
Frederick, Maryland 21701

Telephone: (301) 695-1098
ANNOUNCEMENT

AVAILABILITY OF REQUEST FOR APPLICATIONS: RFA

84-CA-25

INNOVATIVE APPROACHES TO DEVELOPMENT OF CANCER CHEMOPREVENTIVE AGENTS

P.T. 34; K.W. 1002014, 1200250, 0701038, 1200420

NATIONAL CANCER INSTITUTE

Application Receipt Date: December 15, 1984

I. BACKGROUND

The Division of Cancer Etiology (DCE) of the National Cancer Institute (NCI) invites investigator-initiated research grant applications for basic studies emphasizing innovative approaches to the inhibition and/or suppression of carcinogenesis. These studies are especially needed since strategies for cancer prevention involving reduction or elimination of human exposure to environmental carcinogens may not always be possible, and since significant portions of the human cancer burden may be due to endogenous carcinogens, cocarcinogens, and promoters. Inhibition of the development of cancer by administration of chemical, biochemical, and biological compounds, which directly and/or indirectly inhibit the cancer-producing effects of neoplastic and promoting substances, is well known in animal systems and may offer an alternate approach to human cancer prevention. Especially important in these new approaches, regardless of preventive agent(s) employed, will be deep inquiries into the mechanisms of anticarcinogenesis which take full cognizance of the developing frontiers of molecular biology and carcinogenesis, cellular biology, mechanisms of carcinogenesis and genetic aspects of carcinogenesis such as genetic susceptibility and resistance in experimental animal systems (including known, well-defined systems of "spontaneous" tumorigenesis).

II. OBJECTIVES AND SCOPE

Research conducted under this RFA seeks innovative approaches that will expand basic knowledge and understanding of the role and mechanism(s) of action of chemopreventive agents in modulating the carcinogenic process. Specifically, this RFA seeks high quality, innovative approaches, with agents of the applicants' choosing, which will emphasize any of the following areas:

A. Thorough studies on mechanisms of action. Studies are needed from both in vitro and in vivo perspectives.
B. The pharmacokinetics of promising agents should be established for optimizing dose and delivery schedule in chemoprevention and for deriving basic understandings of the absorption, distribution, metabolism and excretion of these agents during the course of chemoprevention.

C. Structure activity relationships of promising compounds should be investigated.

D. Comparative studies on pathways of metabolism should be pursued in human vs animal systems in view of possible differences in biohandling and response.

E. Compounds showing particular promise in short-term assays require animal studies to investigate their efficacy as blocking and/or suppressing agents of the carcinogenic process. In these animal studies, dose and pharmacokinetics vs. response relationships should be derived for those compounds demonstrating anticarcinogenic effectiveness. Investigations should develop time/response relationships for efficacy as well.

F. Toxicologic investigations coupled with appropriate metabolic and pharmacokinetics studies should be pursued on these blocking and/or suppressive compounds.

III. MECHANISM OF SUPPORT

This RFA will use the traditional National Institutes of Health grant-in-aid. 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 four years. The intent is to fund multiple projects, with total costs amounting to approximately $1.0 million for the first year. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the National Cancer Institute, the award of grants pursuant to this RFA is also contingent upon the availability of funds for this purpose.

The present RFA announcement is for a single competition with a specified deadline of December 15, 1984, for receipt of applications.

IV. COPIES OF THE RFA MAY BE OBTAINED FROM:

Dr. Carl E. Smith
Program Director
Chemical and Physical Carcinogenesis Branch
Division of Cancer Etiology
National Cancer Institute
Landow Building - Room 9B06
Bethesda, Maryland 20205

Telephone: (301) 496-4141
ANNOUNCEMENT

AVAILABILITY OF REQUEST FOR APPLICATIONS: RFA

84-CA-26

MUTAGENS IN HUMAN FOODS

P.T. 34; K.W. 1002028, 0202022, 1002014

NATIONAL CANCER INSTITUTE

Application Receipt Date: December 15, 1984

The Division of Cancer Etiology (DCE) of the National Cancer Institute (NCI) invites grant applications from interested investigators for basic studies intended to provide insights and approaches to an understanding of the possible role of food mutagens in human cancer causation.

I. BACKGROUND

Concern over the presence of mutagens in human foods is part of a large and growing interest in the role of diet in human cancer causation and in the possible inhibition of cancer by dietary means. In this context, the relevance of dietary mutagens derives from their genotoxic effects which could lead to cancer induction. Concern over dietary mutagens gains further emphasis from the widespread occurrence of mutagens in human foods. Apart from the well-publicized association of mutagens with charcoal-broiled steak, mutagen formation has been reported to occur upon the boiling of beef stock, the broiling of hamburgers at a relatively modest surface temperature, the frying of potatoes, and the toasting of bread. Mutagens have also been found to be present in many vegetables, in alcoholic beverages, spices, coffee, and tea. Various contaminants may also constitute a source of mutagens present in human foods. According to one estimate, the foods and beverages ingested by an individual in the course of a single day might contain 1-2 grams of mutagens.

II. OBJECTIVES AND SCOPE

The purpose of this RFA is to accelerate the development of additional understanding relative to the possible role, fate, and cancer relevance of known dietary mutagens commonly present in human foods. Applications submitted in response to this RFA should be responsive to one or more of the items selected from any one or from a combination of the following categories:

A. In depth, basic studies on a small number of mutagens selected from among those which are known to occur naturally in human foods, those found in human feces, and those human dietary mutagens the formation of which is associated with the processing and preparation of food; compounds of particular interest include, but are not limited to, the following six classes: (1) heteroaromatic amines of the carboline and imidoquinoline types (2)
hydroxylated flavonoids (3) carbonyl compounds such as acrolein, malonaldehyde and methylglyoxal (4) fecapentaenes (5) endogenous N-nitroso compounds and (6) aromatic hydrocarbons.

B. Development of analytical procedures for the quantitation of the foregoing mutagens in foods and for the quantitation of them and their respective metabolic products present in blood, body fluids and tissues, and feces.

C. In vitro and in vivo studies relative to the absorption, metabolism, and possible carcinogenicity of selected compounds such as quercetin and the human fecapentaenes. However, full scale animal bioassays will not be supported through this announcement.

III. MECHANISM OF SUPPORT

This RFA will use the traditional National Institutes of Health research project grant and all policies and requirements which normally govern the grant programs of the PHS apply. 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 four years. The intent is to fund multiple individual research project grants with total costs amounting to approximately $750,000 for the first year.

The present RFA announcement is for a single competition with a specified deadline of December 15, 1984, for receipt of applications.

IV. INQUIRIES

Copies of the RFA may be obtained from:

Dr. David G. Longfellow
Acting Chief
Chemical and Physical Carcinogenesis Branch
Division of Cancer Etiology
National Cancer Institute
Landow Building - Room 9A02
Bethesda, Maryland 20205

Telephone: (301) 496-5471
ANNOUNCEMENT

AVAILABILITY FOR REQUEST FOR APPLICATIONS: RFA

84-HL-16H

NATIONAL RESEARCH AND DEMONSTRATION CENTERS ON ISCHEMIC HEART DISEASE

P.T. 04; K.W. 1200240, 1200230, 0403004

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: December 3, 1984

The National Heart, Lung, and Blood Institute (NHLBI) announces its intent to solicit grant applications from the current Specialized Centers of Research (SCORs) on Ischemic Heart Disease in a single competition for designation as National Research and Demonstration Centers (NRDCs). To apply for this program, current SCOR grantees will be asked to submit competing supplemental applications that detail plans for demonstration and education research activities that are thematically related to ischemic heart disease and for core activities that will serve to coordinate and integrate the various components of the NRDCs.

A Request for Applications (RFA) has been issued to the current SCOR grantees in Ischemic Heart Disease. The application receipt date is December 3, 1984; after initial technical merit review these competing applications will be reviewed by the National Heart, Lung, and Blood Advisory Council in May 1985. The award date for successful applicants will be June 1, 1985; the duration of these supplemental grants will be approximately 4-1/2 years.

Although the competition is limited to current Ischemic Heart Disease SCOR grantees, other interested parties may receive an informational copy of the RFA by writing to the following:

Dr. Michael C. Lowe
National Heart, Lung, and Blood Institute
National Institutes of Health
Federal Building - Room 3C06
Bethesda, Maryland 20205

Telephone: (301) 496-1081

The issuance of the RFA for NRDCs on Ischemic Heart Disease does not imply any intent to discontinue support for a separate and distinct Ischemic Heart Disease SCOR program. The NRDC and SCOR grant mechanisms of support, together with that of investigator-initiated research, training, and contract support, serve to promote the Institute's comprehensive research program; the support of each of these mechanisms will be continued.
ANNOUNCEMENT

GERIATRIC LEADERSHIP ACADEMIC AWARD (K07)

P.T. 34; K.W. 0404002, 0404000, 1200180, 0502000

NATIONAL INSTITUTE ON AGING

I. PURPOSE

The National Institute on Aging (NIA) invites academic health centers and other health professional schools to submit applications for the support of leadership activities in the development of research and research training programs in aging. (As used in this announcement, "aging" refers to all aspects of gerontology and geriatrics, i.e., biomedical, behavioral, and social aspects of aging and the special problems of older persons.) This Award is aimed at encouraging and assisting more health professional schools to increase their efforts in research and training in aging.

Priority is given to those academic centers or schools with limited activities in aging but which have a strong interest in, and commitment to, expanding their research and training efforts in aging. These awards offer opportunities for supporting start-up or expansion of such activities. Thus, this program is aimed at meeting needs which have not been met by other types of awards available from the NIA and other Federal agencies.

II. BACKGROUND

The Report on Education and Training in Geriatrics and Gerontology (submitted by the US Department of Health and Human Services (DHHS) to the Congress in February 1984) presents ten general principles identified by the DHHS Ad Hoc Committee on Enhancement of Training in Geriatrics and Gerontology and its expert consultants.

Among these principles are the following:

- All students preparing for careers in the health and other human services professions should receive education about the aging process and the strengths and problems of the aged.

- Health professional schools should have faculty with expertise in aging to conduct substantial and high-quality basic, graduate, and continuing education programs and to serve as role models.

- Faculty members should have opportunities to engage in research on aging and the aged in order to maintain their expertise and expand the available body of knowledge.

- Interdisciplinary experiences should be a regular and integral part of training programs in geriatrics and gerontology in light of the complex needs of many elderly persons.
Educational resources should be shared among schools at academic health centers and other university campuses to achieve maximum impact and avoid unnecessary duplication.

The Report also emphasizes the fact that information on the aging process and the elderly should be incorporated, as appropriate, throughout health profession curricula and clinical experiences; specialized courses should provide more intensive materials. The Report indicates that research on aging should be encouraged and enhanced in the many relevant disciplines and fields.

To achieve these objectives, there must be concentrated and coordinated efforts on the part of many faculty members and departments in various biomedical, behavioral, and social sciences and in numerous health professional schools. Experiences in other programs have demonstrated that these types of efforts can be assisted and strengthened when responsibilities for leadership are assigned to a designated faculty member who has the active support of the principal officials of the institution.

III. PROGRAM OBJECTIVES AND ELIGIBILITY CRITERIA

The objectives of this program are to help strengthen the capacities of health professional educational institutions to incorporate information and instruction on aging throughout their curricula and to encourage and enhance research and training activities related to aging.

A faculty leader is to be the focal point for developing and improving research and teaching in aging. The individual is to provide leadership and coordination, including such activities as encouraging and assisting other faculty members to integrate aging issues into their research and teaching, organizing and conducting studies and courses focused on aging, developing resources for aging research and teaching, and linking related activities among and within various health professional schools. The faculty leader should have the active and continuing support of the principal executive officials of the institution and should be at a level in the organization that indicates and encourages such interest and support (e.g., reporting to the Vice President for Health Affairs).

The faculty leader should have demonstrated competence and continuing interest in research and teaching on aging. A candidate with established research credentials but with limited background in geriatrics may qualify for appointment without the full range of skills provided a clearly described plan for acquiring them is incorporated in the application. The candidate should have sufficient stature, training, and experience so that no more than one year of intensive supplemental preparation is needed.

The institution's program may be based on one of a number of approaches in line with local circumstances. For example, one of the following approaches might be adopted:

A. An academic health center program including all of the health professional schools of the institution.

B. A program involving the medical school and one or more other health professional schools.
C. A program involving a single health professional school.

In all cases, the program should include a faculty committee with representation from the various participating schools and/or departments to work with the designated faculty leader in planning and developing research and training activities in aging.

Regardless of the type of overall approach selected, the following elements must be considered in each proposal:

The candidate must:

- Have an appropriate academic appointment at the institution at the time the award is activated.
- Have sufficient research experience and background in geriatrics and/or gerontology to be effective in developing and actively implementing a quality research and education program in geriatrics.
- Specify a program for enhancing personal skills as needed.
- Present a program for developing or improving geriatric research and education in the grantee institution and for evaluating the outcome of the effort.
- Commit a substantial portion of effort to the proposed programs.
- Agree to report annually on the status of the program.
- Agree to meet annually with other recipients of Geriatric Leadership Academic Awards to exchange ideas, methods and program evaluations.

The institution must:

- Name and sponsor a senior or mid-level faculty member with competence and a major career interest in geriatric research and related training programs. (The candidate must be a citizen, a noncitizen national of the U.S. or have been lawfully admitted to the U.S. for permanent residence.)
- Present plans to develop or improve geriatric research and educational programs.
- Identify and demonstrate availability of the resources (populations, patients, manpower, materials, equipment, laboratory facilities) necessary to implement the proposed program.
- Provide the candidate with time to acquire the skills necessary for personal development and for the development of the geriatric research and training program.
- Provide access to facilities for rigorous geriatric research.
o Provide evidence of commitment from the administration and from the sponsoring departmental chairmen to implement the proposed program so that the geriatrics program is coordinate with other relevant research and training programs.

o State the mechanisms for continued institutional support of the geriatric program.

IV. CONDITIONS OF THE AWARD

A. Awards for up to three years; after competitive review, may be extended for one additional three-year period.

B. A portion of the salary of the faculty leader and related fringe benefits, up to a maximum of $40,000.

C. Additional costs for the further preparation of the faculty leader in aging (not to exceed the equivalent of one year's training).

D. Domestic travel expenses of the faculty leader and a limited number of other faculty members to attend professional meetings and an annual meeting of awardees.

E. Limited secretarial support.

F. Teaching aids.

G. Indirect costs not to exceed 8 percent of the direct costs, exclusive of tuition fees and equipment expenditures

H. Allowable direct costs not to exceed $80,000 a year.

NOTE: These awards are not to replace current funding. In addition, investigators who have received the Geriatric Medicine Academic Award in the past are ineligible for this support.

V. REVIEW CRITERIA

The following characteristics will be considered:

A. Commitment of the institution to strengthening research and educational activities in aging.

B. Background and potential of the candidate as a leader in research and educational and clinical programs and as a teacher and research investigator.

C. Merit of the institutional plan to strengthen research and training activities in aging beyond to the current status of activities and capacities

D. Scope and nature of collaboration among participating schools and/or departments.
VI. REVIEW PROCESS AND METHOD OF APPLYING

Applications will receive technical review by an initial review committee appointed by the National Institute on Aging and secondary review by the National Advisory Council on Aging of the NIA.

Applications will be reviewed three times a year according to the following schedule:

<table>
<thead>
<tr>
<th>Applications Received by</th>
<th>Council Review</th>
<th>Earliest Starting Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>November 1</td>
<td>May</td>
<td>June 1*</td>
</tr>
<tr>
<td>February 1</td>
<td>Sept.</td>
<td>Oct. 1</td>
</tr>
<tr>
<td>June 1</td>
<td>Feb.</td>
<td>Mar. 1*</td>
</tr>
</tbody>
</table>

* of the year following receipt

Applicants are encouraged to discuss their plans and the evaluation criteria with, and direct any other inquiries to:

Associate Director
Biomedical Research and Clinical Medicine Program
National Institute on Aging
National Institutes of Health
Building 31 - Room 5C09
Bethesda, Maryland 20205

Telephone: (301) 496-4996

or

Associate Director
Behavioral Sciences Research Program
National Institute on Aging
National Institutes of Health
Building 31 - Room 4C32
Bethesda, Maryland 20205

Telephone: (301) 496-3136

Application kits may be secured from, and submitted to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205
ANNOUNCEMENT

COMPLEMENTARY TRAINING AWARDS FOR RESEARCH ON AGING (T32)

P.T. 44; K.W. 0404002, 0404000, 1200170

NATIONAL INSTITUTE ON AGING

I. INTRODUCTION AND PURPOSE

The National Institute on Aging (NIA) invites complementary applications from well-established research training programs to train investigators in the biomedical, behavioral, or social aspects of the established program that are related to research on aging. This initiative is intended to encourage and assist these established programs to increase their efforts to train investigators for careers in aging and thus to increase the number of investigators trained in the aging aspects of related disciplines. (Aging, as used in this Announcement, refers to all aspects of gerontology and geriatrics, i.e., biomedical, behavioral, and social aspects of aging and the special problems of older persons.)

This announcement is in addition to and does not replace the previous NIA announcement regarding training programs in aging and geriatrics. Institutions with established research programs in aging or geriatrics are encouraged to consider applying for training program support as described in the previous announcement (NIH Guide for Grants and Contracts, Vol. 12, No. 3, March 25, 1983).

II. BACKGROUND

Research in aging encompasses a wide range of issues and complexities. In order to address these subjects effectively, investigators who have preparation in both the field of aging and a related scientific field or discipline are often required.

The Report on Education and Training in Geriatrics and Gerontology (US Department of Health and Human Services submitted to Congress in February 1984) pointed out that an effective method of preparing individuals for research in aging is to build upon the strengths and capacities of established training programs in related fields. Examples of the wide variety of fields in which such activities might be undertaken are programs in the neurosciences, clinical pharmacology, cognitive psychology, cell biology, sociology, and various disease-oriented research areas.

This approach recognizes and takes advantage of the relevance and resources of established research training programs in various scientific fields. It offers a unique opportunity to prepare individuals for research careers focused on aging issues. Such efforts can also further understanding and collaboration between the aging field and other scientific fields.
III. PROGRAM OBJECTIVES AND SPECIFIC REQUIREMENTS

The objective of these complementary awards is to assist strong, well-established research training programs in various scientific fields relevant to aging to expand their efforts in the preparation of more individuals who are interested in careers in aging-related research and education through an additional training program supported by the NIA.

The following elements must be considered in each proposal:

A. Initiation by a strong, well-established research training program in a field relevant to aging.

B. Administration by a program director interested in, and committed to, expanding the current program to give more attention and emphasis to aging-related training.

C. Commitment of potential trainee(s) to careers with a major emphasis in aging-related research and training.

D. Arrangements for the trainee(s) to be associated on a continuing basis with others working in the aging field at the sponsoring institution (or, in special circumstances, through agreement with another nearby institution).

E. A career development plan indicating how the program director and trainee(s) will enhance research competencies in both aging and the specialized field of the sponsoring program during the training period, including active and ongoing participation in aging-related projects.

IV. APPLICANT ELIGIBILITY REQUIREMENTS:

Domestic nonprofit private or public institutions may apply for grants to support research training programs. The applicant institution must have, or be able to develop, the staff and facilities required for the proposed program.

Under certain conditions, the Secretary of Health and Human Services may extend the period for undertaking service or for repayment, permit breaks in service, or otherwise waive or suspend the payback obligation of an individual.

STIPENDS AND OTHER TRAINING COSTS: The current stipend level for predoctoral individuals at all levels of experience is $5,292 per annum.

For postdoctorals, the stipend for the first year of support is determined by the number of years of relevant postdoctoral experience at time of appointment. Relevant experience may include research experience (including industrial), teaching, internship, residency, or other time spent in full-time studies in a health-related field beyond that of the qualifying doctoral degree. The stipend for each additional year of NRSA support is the next level on the stipend structure. Current postdoctoral stipends are as follows:
<table>
<thead>
<tr>
<th>Years of Relevant Experience</th>
<th>Stipend</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>$14,040</td>
</tr>
<tr>
<td>1</td>
<td>14,736</td>
</tr>
<tr>
<td>2</td>
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<tr>
<td>5</td>
<td>17,892</td>
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<tr>
<td>6</td>
<td>18,780</td>
</tr>
<tr>
<td>7 or more</td>
<td>19,716</td>
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</tbody>
</table>

NRSA stipends may be supplemented by an institution from non-Federal funds. No Federal funds may be used for stipend supplementation unless specifically authorized under the terms of the program from which funds are derived. Under no circumstances may the conditions of stipend supplementation detract from or prolong the training.

Tuition, fees, and medical insurance are allowable trainee costs if such charges are required of all persons in a similar training status at the institution, without regard to their source of support. Tuition at the postdoctoral level is limited to that required for specific courses in support of the approved training program. Costs of trainee travel including attendance at scientific meetings which the institution determines to be necessary to the individual's training may be requested.

Institutional costs of up to $1,500 per year per predoctoral trainee and up to $2,500 per year per postdoctoral trainee may be requested to defray the costs of training-related expenses such as staff salaries, consultant costs, equipment, research supplies, staff travel, and other expenses. The availability of funds may modify the maximum levels of institutional costs awarded. An indirect cost allowance based on 8% of total allowable direct costs, or actual, whichever is less, may be requested. Applications from State and local government agencies may request full indirect cost reimbursement.

The training program director at the institution will be responsible for the selection and appointment of trainees to receive National Research Service Awards and for the overall direction of the program. The training program must provide opportunities for individuals to carry out supervised biomedical or behavioral research with the primary objective of extending their skills and knowledge. Special attention should be given to the appointment of minority students and women.

**TRAINEE ELIGIBILITY REQUIREMENTS:** The individual to be trained must be a citizen or a noncitizen national of the United States or have been lawfully admitted for permanent residence at the time of appointment. Individuals on temporary or student visas are not eligible.

Predoctoral trainees must have received a baccalaureate degree as of the beginning date of their NRSA appointment, and must be training at the postbaccalaureate level in a program leading to the award of doctor of philosophy or science or equivalent degree. Individuals who wish to interrupt their medical, veterinary, dental, or other professional school studies for a
year or more to engage in full-time research training before completing their professional degrees are also eligible. National Research Service Awards may not support study leading to the M.D., D.O., D.D.S., or other similar professional degrees, nor may these awards support residency training.

Postdoctoral individuals must have received, as of the beginning date of the NRSA appointment, a Ph.D., M.D., D.O., D.D.S., D.M.D., D.V.M., O.D., D.P.H., Sc.D., Eng.D., Dr.P.H., D.N.S., or equivalent degree from an accredited domestic or foreign institution. Certification by an authorized official of the degree granting institution that all degree requirements have been met is acceptable.

Trainees are required to pursue their research training on a full-time basis. Trainees in clinical areas are expected to confine clinical duties to those that are part of the research training.

PAYBACK PROVISIONS: Before individual trainees can be appointed to a training grant, they must sign an agreement that they will fulfill the NRSA payback requirements. Recipients agree to engage in biomedical or behavioral research and/or teaching for a period equal to the period of NRSA support in excess of 12 months. Once an individual has had 12 months of postbaccalaureate NRSA support, all subsequent NRSA support is subject to payback.

Recipients must begin to undertake the obligated service on a continuous basis within 2 years after termination of NRSA support. For individuals who fail to fulfill their obligation through service, the United States is entitled to recover the total amount paid to the individual for the obligated period plus interest. Financial payment must be completed within 3 years.

PERIOD OF SUPPORT: Institutional grants may be made for competitive segments of up to five years and are renewable. No individual trainee may receive more than five years of aggregate NRSA support at the predoctoral level and three years of aggregate NRSA support at the postdoctoral level including any combination of support from institutional and individual awards. Any exception to this policy requires a waiver from NIH.

REVIEW PROCESS: Applications are evaluated for scientific merit by an NIA initial review group based on the following criteria: the proposed research training objectives and program design, the qualifications of participating faculty, the previous training record of the research program and its ability to attract high caliber trainees, the availability of research support, the extent of the institutional commitment, and the available facilities. Applications are also reviewed by the National Advisory Council on Aging. Final selection will be made by the NIA based on the review group's recommendations, the need for research personnel in specified program areas, and the availability of funds. The BID will notify the applicant of the final action shortly after the meeting of the National Advisory Council on Aging.
V. REVIEW SCHEDULE:

<table>
<thead>
<tr>
<th>Application Receipt Date</th>
<th>Initial Review Meeting</th>
<th>Council/Board Meeting</th>
<th>Earliest Start Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>February 1</td>
<td>June</td>
<td>September/October</td>
<td>December 1</td>
</tr>
<tr>
<td>June 1</td>
<td>October/November</td>
<td>January/February</td>
<td>April 1</td>
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<tr>
<td>October 1</td>
<td>February/March</td>
<td>May</td>
<td>July 1</td>
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</table>

VI. APPLICATION MATERIAL: Application must be made on Form PHS 6025-1. This form is usually available at institutional Offices of Sponsored Research, Grants and Contracts Offices or their equivalent. Applications are available also from the Office of Grants Inquiries, Division of Research Grants (DRG) NIH, Bethesda, Maryland 20205. A self-addressed mailing label will expedite handling.

Applicants are encouraged to discuss their plans and the evaluation criteria with, and direct any other inquiries to:

Associate Director  
Biomedical Research and Clinical Medicine Program  
National Institute on Aging  
National Institutes of Health  
Building 31 - Room 5C09  
Bethesda, Maryland 20205

Telephone: (301)496-4996

or

Associate Director  
Behavioral Sciences Research Program  
National Institute on Aging  
National Institutes of Health  
Building 31 - Room 4C32  
Bethesda, Maryland 20205

Telephone: (301)496-3136
EPIDERMOLYSIS BULLOSA AND THE BIOLOGY OF THE BASEMENT MEMBRANE ZONE

P.T. 34; K.W. 1200750, 1002004, 1002010, 1002023, 1003002, 1201000

NATIONAL INSTITUTE OF ARTHRITIS, DIABETES, AND DIGESTIVE AND KIDNEY DISEASES

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

NATIONAL INSTITUTE OF DENTAL RESEARCH

The Skin Diseases Program of the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK), in cooperation with the National Institute of Child Health and Human Development (NICHD) and the National Institute of Dental Research (NIDR), is encouraging the submission of applications for research grants in epidermolysis bullosa (EB) and in studies of the basic biology of the cutaneous basement membrane zone (BMZ).

Epidermolysis bullosa is a group of hereditary diseases in which skin and other epithelial surfaces, including the mucous membrane of the gastrointestinal and respiratory tracts, form blisters and become denuded after physical trauma of varying degree. In many cases, symptoms of the diseases resemble severe burns. As many as 20 possibly genetically distinct forms of EB have been described. In its mildest form, blisters of EB may be confined to hands and feet. The dystrophic forms of EB, however, may show widespread blistering and skin erosions which heal slowly, if at all; and may result in severe pain, scarring, deformities, and contractures; malnutrition and anemia; and gastro-intestinal problems, corneal erosions, and dental problems. Severe forms of the disease may manifest themselves in utero and can result in premature death, often in infancy or childhood.

The basic underlying cause for the sensitivity of epidermolysis bullosa patients to physical trauma is unknown; it may differ in various genetic forms of the disease. It is thought, however, that the basic cause may involve either a structural defect in proteins or other components that bind epidermis to the underlying dermis, or an abnormal enzyme that degrades one or more of those structural elements. As a result, the attachment between epidermis and dermis is weakened.

Since the initial pathologic changes of EB appear to occur in the basement membrane zone, the NIADDK and its collaborating Institutes, the NICHD and NIDR, seek studies

This program is described in the Catalog of Federal Domestic Assistance No. 13.846, Arthritis, Musculoskeletal and Skin Diseases, No. 13.865, Research for Mothers and Children, and No. 13.84., Periodontal 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.
aimed at achieving a better understanding of pathophysiologic mechanisms and/or structural abnormalities which contribute to the onset of EB, as well as studies to gain further insight into the basic biology of the basement membrane zone. In addition to its clear importance to EB, research investigation of the basement membrane zone is directly relevant to other important areas of biomedical research, including burns, wound healing, development of artificial skin, the structure-function relationship of collagen and collagenolysis and their genetic control, and the biochemical basis of genetic and congenital abnormalities of the BMZ in the adult and at prenatal and subsequent developmental stages. Such determinations should provide the information on the underlying cause and ontogeny of different forms of epidermolysis bullosa on which alleviation, prevention, and treatment of these diseases could be based. Research proposals are encouraged that utilize research advances in genetics, pathology, cell and developmental biology, biochemistry, and immunology as they relate to various types of EB and to the biology of the basement membrane zone.

I. METHOD AND CRITERIA OF REVIEW

A. Assignment of Applications

Applications will be received by the NIH's Division of Research Grants (DRG) referred to an appropriate initial review group for scientific review, and assigned to the NIADDK, NICHD, or NIDR for possible funding. These decisions will be governed by programmatic considerations as specified in the DRG Referral Guidelines.

B. Review Procedures

Applications in response to this announcement will be reviewed in accord with the National Institutes of Health peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants. Following initial review, the application will be evaluated for program relevance by the Advisory Council of the Institute to which the application is assigned. Review criteria customarily employed by the National Institutes of Health (NIH) for regular research grant applications will prevail. Approved applications will compete for available funds with other approved grant applications assigned to the NIADDK, NICHD, or NIDR.

C. Deadline

Applications will be accepted in accordance with the announced receipt dates for new applications (see receipt dates and review schedule in application kits).

D. Method of Applying

Applications for research grants should be submitted on form PHS 398, which is available in the business or grants and contracts office at most academic and research institutions. The phrase, "PREPARED IN RESPONSE TO RESEARCH GRANTS ANNOUNCEMENT IN THE AREA OF EPIDERMOLYSIS BULLOSA AND BASEMENT MEMBRANE ZONE BIOLOGY" should be typed across the top of the first page of the application.
The original and six copies of the application should be sent or delivered to:

Applications Receipt Office  
Division of Research Grants  
National Institutes of Health  
Westwood Building - Room 240  
Bethesda, Maryland 20205

For further information, investigators are encouraged to contact the following program directors:

Alan N. Moshell, M.D.  
Skin Diseases Program Director  
National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases  
National Institutes of Health  
Westwood Building - Room 405  
Baltimore, Maryland 20205  
Telephone: (301) 496-7326

Anne K. Krey  
Health Scientist Administrator  
Genetics and Teratology Section  
National Institute of Child Health and Human Development  
Landow Building - Room 7C09  
Bethesda, Maryland 20205  
Telephone: (301) 496-5575

Health Scientist Administrator  
Periodontal & Soft Tissue Diseases Branch, EP  
National Institute of Dental Research  
Westwood Building - Room 319  
Bethesda, Maryland 20205  
Telephone: (301) 496-7784
SEXUALLY TRANSMITTED DISEASES - RESEARCH ON CHLAMYDIAL INFECTIONS AND VAGINOSIS (VAGINITIS)

P.T. 34, 22; K.W. 1200670, 1201360, 1002023, 1201335

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

The National Institute of Allergy and Infectious Diseases (NIAID) invites applications for regular research grants for the purpose of conducting studies on the subjects of (a) chlamydial infections in males and females and (b) vaginosis (vaginitis). Applications for research in all areas of chlamydial infections and in vaginosis are encouraged through this announcement.

I. CHLAMYDIAL INFECTIONS

A. BACKGROUND

Infections with Chlamydia trachomatis are now among the major sexually transmitted diseases in the U.S. and most other industrialized nations. Although firm data are lacking in the U.S., these infections probably supersede even gonorrhea as an overriding public health problem; estimates are that chlamydial infections in both males and females total over 3,000,000 cases annually. In males, the disease usually occurs as a mild urethritis. It is estimated, however, that epididymitis occurs in about one-half of the 500,000 cases of chlamydial infections in males. Epididymitis is a painful and serious sequela that can result in sterility. In females infected with chlamydial organisms, mucopurulent cervicitis, considered as a counterpart to urethritis in infected males, is being seen with increased frequency in STD clinics.

Chlamydial infections in females are even more important as a public health problem because of the increasing role of this agent in pelvic inflammatory disease (PID) and infertility. Estimates are that chlamydia are responsible for at least 20% of all PID cases in the U.S. In the absence of firm data, it is estimated that more than 200,000 women are hospitalized annually and another 1,000,000 are treated as out-patients. The costs to the health care system for this disease burden are enormous. Additionally, because of chlamydial infection, perhaps 11,000 women of child-bearing age are rendered involuntarily sterile owing to tubal damage, and another 3,600 will suffer ectopic pregnancies (with their associated risk of maternal death).

This program is described in the Catalog of Federal Domestic Assistance No. 13.856, Microbiology and Infectious Diseases Research. 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.
Of the more than 150,000 infants born to chlamydia-infected women each year, perhaps 75,000 may develop conjunctivitis and 30,000 may develop pneumonia. In fact, this may be the most frequent cause of pneumonia in infants.

B. Research Needs and Opportunities

Some suggested areas of research are outlined here. These are not to be considered as excluding other areas where needs and opportunities also exist.

1. Rapid and specific diagnostic tests should be considered as an area of interest. A newly licensed rapid diagnostic test (the Microtrak system - SYVA Corporation) may be of great value in diagnosing patients with asymptomatic infections. Other tests, however, should be developed.

2. Expansion of knowledge on the basic biology and immunology of chlamydia is an urgent need, to increase understanding of the pathogenesis of chlamydial infections. This will include studies on: surface structures and functions; antigen characterization and isolation; host immune responses. The problem of persistent or chronic infections should form part of the research thrust.

3. Animal model systems are also an area of much needed research, to provide better understanding of the pathogenesis of genital infections and of PID in humans.

4. The role of chlamydia in perinatal disease and in complications of pregnancy needs further definition.

II. VAGINOSIS (VAGINITIS)

A. BACKGROUND

This syndrome, characterized by pruritis, pain, inflammation and discharge is considered to have a multiple etiology. The majority of these cases are caused by the protozoan trichomonas, by yeasts (candida species) and by a variety of other microorganisms, many of them uncharacterized. Surveys have ranked the vaginosis syndrome as among the ten most frequently encountered female disorders; these infections result in a significant proportion of visits by women to primary and specialty health care providers. In STD clinics, about one-third of the visits by women are owing to infectious vaginosis. Early estimates are that $36 million is spent annually on treatment in STD clinics alone - this figure is very much higher if treatment by private physicians is included. The total impact in terms of cost of therapy, lost time from work, and personal suffering is indeed large. Knowledge and understanding of this syndrome lags far behind that of other sexually transmitted diseases.

It is only recently that a small number of investigators have begun to apply modern methods of microbiology, immunology and biochemistry to study this problem. Far greater efforts are required, however, to obtain the knowledge necessary to have a significant impact in controlling this complex syndrome.
Suggested areas of research needs and opportunities are briefly outlined below. These are provided primarily as guidelines, and are not to be considered as excluding other appropriate research areas.

B. Research Needs and Opportunities

1. Increasing understanding of the vaginal ecosystem. Multiple microbial species are involved and interact with one another and with the local environment, causing subtle changes associated with menstrual cycle phases, contraception, and possibly sexual activity. Study of the host immune responses and of the fundamental microbiology and biochemistry of the causal organisms provide wide opportunities for research.

2. Increased knowledge of trichomoniasis and development of newer methods of therapy are needed. The current treatment of choice is potentially toxic and drug resistant strains have also been reported. Alternative chemotherapies, virulence factors and host defenses are areas of research need.

3. Increased understanding of non-specific vaginitis is needed. The roles of Gardnerella vaginalis, other anaerobic bacteria, yeasts, and mycoplasmas need further clarification. Microbial synergism is not well understood in this milieu, particularly as related to etiology and pathogenesis.

4. The existence of recurrent or chronic disease, the nature of host immune responses, and the interaction of complex vaginal factors need clarification.

III. MECHANISMS OF SUPPORT

Research applications considered appropriate responses to this announcement include the traditional project grant (R01), the New Investigator Research Award (R23), and career development and research training applications. These can include the Career Development Award (K04), the Physician Scientist Award (K11), the Clinical Investigator Award (K08), and the Individual Post-doctoral Fellowship Award (F32). The specific application forms required are available from the Division of Research Grants (DRG) NIH.

Applications will receive competitive review by appropriate study sections of the Division of Research Grants and will be considered for funding by the Institute in competition with all other applications, based on scientific merit and the availability of funds. This is not a one-time announcement, but is a statement of continuing interest in these selected disease areas.

IV. METHOD OF APPLYING

Applicants are encouraged to advise the Institute of their intent to submit an application and to seek advice regarding the type of application and the nature of their intended research.

Application receipt dates, advisory council reviews, and dates of possible awards
are as presented in the information found in the application kits. These kits are available at most institutional business offices, or may be obtained from:

Office of Grant Inquiries
Division of Research Grants
National Institutes of Health
Westwood Building - Room 448
Bethesda, Maryland 20205
Telephone: (301) 496-7441

On page one, item 2, of the application form, the word "Yes" and the title of this program announcement "Research on Chlamydia Infections and Vaginosis" should be typed.

The completed original and six (6) copies should be sent to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
5333 Westbard Avenue
Westwood Building - Room 240
Bethesda, Maryland 20205

VI. STAFF CONTACT

Request for information or advice should be directed to:

Milton Puziss, Ph.D.
Chief
Bacteriology and Virology Branch
Microbiology and Infectious Diseases Program
National Institute of Allergy and Infectious Diseases
5333 Westbard Avenue
Westwood Building - Room 748
Bethesda, Maryland 20205

Telephone: (301) 496-7728
ANNOUNCEMENT

STUDIES OF DIABETES MELLITUS AND RELATED PROBLEMS

P.T. 34; K.W. 1200350, 1200770, 1200460, 1200240, 1201070, 1200190, 0701013

NATIONAL INSTITUTE OF ARTHRITIS, DIABETES, AND DIGESTIVE AND KIDNEY DISEASES
NATIONAL INSTITUTE ON AGING
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
NATIONAL INSTITUTE OF DENTAL RESEARCH
NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES
NATIONAL EYE INSTITUTE
NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE

The above-named Institutes of the National Institutes of Health (NIH) invite applications for research grants in the general area of diabetes mellitus and related problems. Investigators working in other areas of research are particularly encouraged to develop diabetes-related projects either independently or, where appropriate, in collaboration with individuals currently engaged in diabetes research.

I. PROGRAM SPECIFICATIONS

A. Program Objectives

Diabetes mellitus and its complications are major public health problems in the United States today. The NIH and other organizations have attempted to stimulate research into the cause, cure and prevention of diabetes and its related endocrinologic and metabolic disorders during the past several years. The National Diabetes Advisory Board with financial support from various corporations, foundations, voluntary health agencies and the NIH, (including NEI, NIADDK, NICHD, NHLBI, and NINCDS) recently sponsored a meeting, the Second National Diabetes Research Conference, to review the state-of-the-art in various areas of diabetes research, to identify and summarize progress which has been made since the last such meeting (1979), to identify current opportunities and needs and to make some priority recommendations for the next five years.

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, most specifically at 42 CFR Part 52 and CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency Review.
The purpose of this solicitation is to make the summary report from this meeting available to interested investigators in order to stimulate investigator-initiated applications in the perceived areas of need.

B. Research Scope

The emphasis of this solicitation is upon the research needs outlined in the Summary Report from the Second National Diabetes Research Conference.

The following list includes the areas of research recommended by the twelve conference workgroups:

- Etiology and pathogenesis of IDDM
- Etiology and pathogenesis of NIDDM
- Cardiovascular Complications
- Eye Complications
- Neurological Complications
- Kidney Complications
- Insulin Biosynthesis and Gene Studies
- Pregnancy
- Insulin Secretion
- Hormone Action
- Transplantation
- Insulin Delivery Systems
- Dental Complications
- Epidemiology

These recommendations are not necessarily all-inclusive and any new ideas with creditable hypotheses that would appropriately fall within the scope of diabetes-related research could be the basis for an application.

Copies of the Conference Report can be obtained upon request from:

The Diabetes Research Program
Westwood Building – Room 605
National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases
National Institutes of Health
Bethesda, Maryland 20205

C. Mechanism of Support

The mechanism of support for this program will be the grant-in-aid (regular research grants - R01). The regulations (Code of Federal Regulations, Title 42, Part 52 and, as applicable to the state and local governments, Title 45, Part 74) and policies which govern the research grant programs of the NIH will prevail. The award of grants pursuant to this Program Announcement is contingent upon receipt of appropriated funds for this purpose.
II. METHOD AND CRITERIA OF REVIEW

A. Assignment of Applications

Applications will be received by the NIH Division of Research Grants (DRG) referred to an appropriate Study Section for scientific merit review, and assigned to individual Institutes (see page 1) for possible funding. Referral decisions will be governed by normal programmatic considerations as specified in the Referral Guidelines of the NIH DRG.

B. Review Procedures

Applications in response to this solicitation will be reviewed on a nation-wide basis in competition with other research grant applications, and in accord with the usual NIH peer review procedures. Applications will first be reviewed for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants (Study Section), and then by the National Advisory Council of the appropriate Institute(s). The review criteria customarily employed by the NIH for regular research grant applications will prevail.

C. Deadline

Applications will be accepted in accordance with the usual NIH receipt dates for new applications as follows:

<table>
<thead>
<tr>
<th>APPLICATION RECEIPT</th>
<th>INITIAL REVIEW</th>
<th>COUNCIL REVIEW</th>
<th>EARLIEST START DATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>March 1</td>
<td>June</td>
<td>Sept./Oct.</td>
<td>December 1</td>
</tr>
<tr>
<td>July 1</td>
<td>Oct./Nov.</td>
<td>Jan./Feb.*</td>
<td>April 1*</td>
</tr>
<tr>
<td>November 1</td>
<td>Feb./March*</td>
<td>May*</td>
<td>July 1</td>
</tr>
</tbody>
</table>

*of the year following application receipt.

III. METHOD OF APPLYING

Applications should be submitted on form PHS 398, which is available in the business or grants and contracts office at most academic and research institutions. On the face page of form PHS 398, indicate that the application was prepared in response to the Program Announcement entitled "Studies of Diabetes Mellitus and Related Problems". The original and six copies of the application should be sent or delivered to:

Application Receipt
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205
For further information, investigators are encouraged to contact one or more of the following individuals:

**National Institute of Arthritis, Diabetes, and Kidney and Digestive Diseases**

Diabetes Research Program Director  
NIADDK-DEMD-DPB  
Westwood Building - Room 605  
Bethesda, Maryland 20205

Telephone: (301) 496-7731

**National Institute on Aging**

Chief, Geriatrics Branch  
Extramural and Collaborative Research Program  
NIA  
Building 31 - Room 5C21  
Bethesda, Maryland 20205

Telephone: (301) 496-1033

**National Institute of Allergy and Infectious Diseases**

Medical Officer, Clinical and Epidemiology Studies Branch  
NIAID  
Building 31 - Room 749  
Bethesda, Maryland 20205

Telephone: (301) 496-5893

**National Institute of Child Health and Human Development**

Chief, Clinical Nutrition and Early Development  
NICHD  
Landow Building - Room 7C17  
Bethesda, Maryland 20205

Telephone: (301) 496-5575

**National Institute of Dental Research**

Deputy Associate Director  
NIDR Extramural Programs  
Westwood Building - Room 504  
Bethesda, Maryland 20205

Telephone: (301) 496-7748
National Institute of Environmental Health Sciences

Associate Director for Extramural Program
NIEHS
Building 31 - Room 2B55
Bethesda, Maryland 20205

Telephone: (301) 496-3511

National Eye Institute

Chief, Retinal and Choroidal Diseases Branch
NEI
Building 31 - Room 6A52
Bethesda, Maryland 20205
Telephone: (301) 496-5983

Further information on research opportunities in the NEI may be obtained by requesting the Institute's Research Plan entitled "Vision Research: National Plan 1983-84" from:

Office of Program Planning and Evaluation
NEI
Building 31 - Room 6A25,
Bethesda, Maryland 20205.

National Heart, Lung and Blood Institute

Associate Director
Arteriosclerosis, Hypertension
and Lipid Metabolism Program
Division of Heart and Vascular Diseases
NHLBI
Federal Building - Room 412C
Bethesda, Maryland 20205

Telephone: (301) 496-1613

National Institute of Neurological and Communicative Disorders and Stroke

Director, Convulsive, Developmental,
and Neuromuscular Disorders Program
Federal Building - Room 812
Bethesda, Maryland 20205

Telephone: (301) 496-6541
ANNOUNCEMENT

PHASE I/II CLINICAL EVALUATION OF VIRAL ONCOLYSATES PREPARED AGAINST HUMAN TUMORS - BIOLOGICAL RESPONSE MODIFIERS RESEARCH

P.T. 34; K.W. 1200280, 1200130, 1002023, 1002045

NATIONAL CANCER INSTITUTE

Application Receipt Dates: November 1, March 1, July 1

The National Cancer Institute's (NCI) Division of Cancer Treatment (DCT) desires to expand its support of clinical treatment research. The program is seeking applications for research grants concerned with the Phase I/II Evaluation of Viral Oncolysates Prepared Against Human Tumors. In making this program announcement it is not the intent of the NCI to make or imply any delimitation related to biological response modifiers research, but rather to stimulate investigator initiated research in biological response modifiers related to cancer therapy.

Inoculation of normal animals with lysates formed by infection of syngeneic tumor cells with certain viruses can provide a high degree of resistance against subsequent engraftment of uninfected tumor cells. Viral oncolysates can be formed either in the animal or in tissue culture. Uninfected tumor cell homogenates, viral particles, or mixtures of the two were not protective; it appears that active viral infection of the tumor cell is necessary to provide subsequent tumor resistance. Several animal tumor model systems have been described using a variety of viruses as well as tumors. Recently, a few preliminary clinical trials have been reported showing some evidence of tumor control. The BRMP wishes to verify and extend these observations to determine the therapeutic value of this approach for cancer treatment.

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 composed mostly of non-Federal scientific consultants. Following this initial review, the application will be evaluated for program relevance by the National Cancer Advisory Board. The review criteria customarily employed by the NIH for regular research grant applications will prevail. All PHS and NIH grant policies governing regular research project grants, including cost sharing, apply to applications received in response to this program announcement.

This program is described in the Catalog of Federal Domestic Assistance No. 13.395, Cancer Treatment Research. Awards are 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.
DEADLINE

Applications will be accepted in accordance with the usual NIH receipt dates for new applications. Deadline dates are: November 1, March 1, July 1.

METHOD OF APPLYING

Non-profit organizations and institutions, governments and their agencies, for profit organizations, and individuals are eligible to apply. 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 Office of Grants Inquiries, Division of Research Grants (DRG), NIH. In space #12 on the first page of this form, indicate the title of the Program Announcement.

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:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

For further information, investigators are encouraged to contact:

Dr. Cedric W. Long, Acting Chief
Biological Resources Branch
Biological Response Modifiers Program
Division of Cancer Treatment
National Cancer Institute
Frederick Cancer Research Facility
Building 426 - Room 1
Frederick, Maryland 21701

Telephone: (301) 695-1098

In order to alert the DCT to the submission of applications with primary thrust directed to biological response modifiers research, a copy of the covering letter should be sent under separate cover to Dr. Long.