

# NIH GUIDE

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**For Grants  
and  
Contracts**

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Vol. 15, No. 9  
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NOTICES

REVISED COMPETING INDIVIDUAL NATIONAL RESEARCH SERVICE AWARD APPLICATION KIT

P.T. 22, 44; K.W. 0710030

NATIONAL INSTITUTES OF HEALTH

A new competing Individual National Research Service Award Application, PHS 416-1, revised 6/85, is now available. This revision should be used for the September 10, 1986, and subsequent deadlines. The receipt dates (effective January 1, 1986) for Individual National Research Service Award applications are January 10, May 10, and September 10. The sources of application kits by PHS agency and NRSA program are identified below.

NIH Postdoctoral and Senior Fellowships

Bulk supply of applications (more than five) are available from the Office Services Section, Westwood Building, Room 438, Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20892, Telephone: (301) 496-9797. Individual copies (five or fewer) are available from the Office of Grants Inquiries, Westwood Building, Room 449, Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20892, Telephone: (301) 496-7441. Please indicate whether postdoctoral and/or senior kits.

National Center for Nursing Research

Postdoctoral fellowship applications for the Center (formerly Division of Nursing, Health Resources and Services Administration) are available from the Office of Grants Inquiries identified above. Requestors are asked to specifically identify the Center for Nursing Research. Predoctoral applications are available from the National Center for Nursing Research, Building 38A, Room B2E17, National Institutes of Health, Bethesda, Maryland 20894, Telephone: (301) 496-0526.

Minority Access to Research Career (MARC) Program

Predoctoral, faculty fellowship, and visiting scientist award applications are available from the Director, MARC Program, National Institute of General Medical Sciences, National Institutes of Health, Westwood Building, Room 9A-18, Bethesda, Maryland 20892, Telephone: (301) 496-7941.

Alcohol, Drug Abuse, and Mental Health Administration

Predoctoral and postdoctoral fellowship applications are available from the following offices: Grants Management Officer, NIAAA, Room 16-86, (301) 443-4703; Grants Management Officer, NIDA, Room 10-25, (301) 443-6710; Grants Operation Section, Grants Management Branch, NIMH, Room 7C-05, (301) 443-4414. The mailing address for the above offices is 5600 Fishers Lane, Rockville, Maryland 20857.

DATED ANNOUNCEMENTS (RFPs AND RFAs AVAILABLE)

AVAILABILITY OF REQUEST FOR APPLICATIONS: RFA - 86-HL-23-H

MOLECULAR CHARACTERIZATION OF MYOCARDIAL RECEPTORS, PUMPS, AND CHANNELS

P.T. 34; K.W. 0705015, 0760075, 1002004, 0760070, 0790005, 1002008

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: December 12, 1986

The Cardiac Functions Branch of the Division of Heart and Vascular Diseases, National Heart, Lung, and Blood Institute (NHLBI) announces the availability of a Request for Applications (RFA) on the above subject.

This special grant program will support fundamental research on the structure, function, and regulation of receptors, pumps, and ion channels in the myocardial sarcolemma and sarcoplasmic reticulum. The major purpose is to encourage the application of modern cellular and molecular technologies in order to determine the structure of these important membrane proteins, to correlate structure with physiological function, and to elucidate the regulatory processes governing their activities.

As the major purpose of this solicitation is to encourage the use of gene cloning and related techniques to elucidate structure-function relationships of these important membrane components, the strategies, approaches, and methods of modern molecular biology must constitute an essential portion of the proposed research.

Other relevant areas of expertise include biochemistry, biophysics, cardiology, cellular biology, developmental biology, electrophysiology, genetics, morphology, and pharmacology.

#### TIMETABLE

Letter of Intent	September 12, 1986
Application Receipt Date	December 12, 1986
Technical Review	March 1987
Advisory Council Review	May 21-22, 1987
Award Date	July 1, 1987

#### INQUIRIES

Stephen C. Mockrin, Ph.D.  
Division of Heart and Vascular Diseases  
National Heart, Lung, and Blood Institute  
Federal Building - Room 304  
7550 Wisconsin Avenue  
Bethesda, Maryland 20892  
Telephone: (301) 496-1627

#### ONGOING PROGRAM ANNOUNCEMENTS

##### MECHANISM OF ATHEROGENESIS IN VARIOUS VASCULAR BEDS

P.T. 34; K.W. 0715040, 0755030, 1002034, 0765035, 1002004

##### NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

The Division of Heart and Vascular Diseases, National Heart, Lung, and Blood Institute (NHLBI) encourages meritorious grant applications on the regional biology of the arterial wall. Emphasis is placed on basic research designed to elucidate the cellular and molecular mechanisms causing differences in the extent of arteriosclerosis among different arteries and at specific arterial sites.

The purpose of this announcement is to stimulate applications to clarify the mechanisms that may explain the development of atherosclerosis in one artery while another artery is spared within an individual or an animal, and to elucidate the mechanisms that may explain the differences in susceptibility of specific arterial sites to atherosclerosis.

There is an extensive literature defining metabolic events that differ between normal and atherosclerotic tissues. Although these studies recognize areas of metabolism that are altered in atherogenesis, they do not identify the changes that occur as a result of the disease and those that play an integral role in the development of the disease. It is of importance to identify the structural and functional factors involved in regional atherogenic pathology within susceptible arteries, and to augment the findings with parallel and comparative studies on resistant vessels in the same animal or species.

Many of the events leading to atherogenesis's need to be pursued at the cellular and molecular levels to identify factors and mechanisms affecting the disease regionally. Questions relating to transcytosis of macromolecules across the endothelium; endothelial cell turnover rates; interaction of blood components with the vascular wall; hemodynamic and rheological influences on atherogenesis; biochemical and metabolic components such as lipolytic enzymes; the prostanoids; arterial connective tissue components; the molecular species of the phospholipids of cell membranes; membrane fluidity; studies on the turnover rates of phosphoinositides and other metabolic events such as protein kinase C, Ca<sup>++</sup> gating, and other related mechanisms; and effect of radicals on prostaglandin synthesis by the vascular tissue are among the possible areas for research investigations.

##### Application, Submission and Review

Applicants should use the regular research grant application (PHS 398). Application receipt dates are the regular NIH receipt dates for new applications of October 1, 1986; February 1, and June 1, 1987. Applications will be reviewed by the Study Section as assigned by Division of Research Grants. Secondary review will be by the

National Heart, Lung, and Blood Advisory Council. Applications recommended for approval will compete for available funds with all other approved applications assigned to the NHLBI. However, since the Institute and NHLBAC have identified this research area to be of particular program interest, applications responsive to this announcement will be brought to the special attention of the council.

In order to identify the application as a response to this program announcement, check "yes" on Item 2 of the application face page with the title "Mechanisms of Atherogenesis in Various Vascular Beds". The original and six copies of the application should be delivered or mailed to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, Maryland 20892

Request for additional information or questions may be directed to:

Montaz K. Wassef, Ph.D.  
Division of Heart and Vascular Diseases  
National Heart, Lung, and Blood Institute  
Federal Building, Room 4A12  
7550 Wisconsin Avenue  
Bethesda, Maryland 20892  
Telephone No.: (301)496-1978

#### RESEARCH GRANTS RELATED TO AIDS DEMENTIA AND OTHER AIDS-ASSOCIATED NEUROLOGICAL DISORDERS

P.T. 34; K.W. 0715120, 0705055, 0715125, 0745020, 0785055

#### NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE

The National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) invites grant applications for support of research on Acquired Immune Deficiency Syndrome (AIDS) dementia and other neurological disorders associated with AIDS.

#### BACKGROUND

The number of adults, children, and infants affected by the AIDS retrovirus (HTLV-III/LAV) is growing, and the associated neurological syndromes are recognized with increasing frequency. Neurological involvement may be apparent before severe immunodeficiency is recognized. The neurological disorders associated with AIDS and AIDS-related complex are of particular concern to the NINCDS.

Dementia is one of the more common and devastating neurological complications of AIDS. As many as 60 percent of patients with AIDS may develop dementia that cannot be attributed to opportunistic infections. The dementia may occur at any stage; it is often manifested very early in the clinical course of the illness. Some of these patients also develop spastic paraplegia and ataxia associated with vacuolar changes in the myelin of the spinal cord.

Infection with the AIDS retrovirus is also associated with the development of peripheral nerve disease in a lesser number of patients. Although neuropathy may affect 10 percent or more of patients with AIDS, the clinical and pathological features are not completely characterized. The spectrum of symptom complexes includes sensory and motor neuropathies and multiple mononeuropathy.

Developmental abnormalities in children with AIDS, characterized by loss of cognitive ability and progressive long-tract signs, are now encountered with increasing frequency. An AIDS-associated dysmorphic syndrome in children due to intrauterine infection has also been described.

The clinical features, course, and pathology of these conditions require elucidation and clarification. An understanding of the etiologies and pathogenesis may provide a rational basis for the development and evaluation of prophylactic and therapeutic strategies. Proposals focusing on AIDS dementia and encephalomyelopathy in infants and children are particularly encouraged.

#### SEARCH GOALS AND SCOPE

There is a paucity of understanding about AIDS-associated disorders of the central and peripheral nervous system in adults, children, and infants; therefore, additional clinical and basic research is essential. Proposals may address clinical or basic science questions. Studies might address nervous tissue response to

HTLV-III/LAV, development of new and more sensitive probes for detection of the virus in the developing and mature nervous systems, development of new animal models with predilection of the HTLV/LAV virus for the nervous system, epidemiology, tests for populations at risk for nervous system involvement, and criteria and tools for early diagnosis.

#### MECHANISMS OF SUPPORT

The support mechanism for this program will be the grant-in-aid. Applications may be submitted for research project grants or for research program project grants.

Research project grants support a specified, circumscribed project in an area representing the interests and competencies of the investigator(s). Applicants may propose any clinical or fundamental investigation relevant to AIDS-related disorders of the developing or mature central and peripheral nervous systems.

Research program project grants support a broadly based, multidisciplinary research program that has a specific major objective or a basic theme. The multifaceted research program proposal may include clinical and experimental approaches. The proposal should provide supportive information regarding technical and professional expertise and resources. Sufficient numbers of patients must be accessible to permit achievement of the desired objectives of clinically based proposals. Applicants should develop a comprehensive research program, each phase of which is directed to a specific aspect of AIDS-associated nervous system disease. Prospective applicants are encouraged to consult with the staff of the Demyelinating, Atrophic, and Dementing Disorders Program early in the planning stage.

Deadlines for receipt of applications in response to this Announcement are February 1, June 1, and October 1.

#### REVIEW PROCEDURES AND CRITERIA

Applications must be prepared on form PHS 398 according to the instructions contained in the application kit. Application kits are available at most institutional business offices or from the Division of Research Grants, NIH. Program projects should conform to the style and format recommended by the NINCDS. This information is available from the staff contact listed below. Program project applications assigned to NINCDS will be reviewed initially and judged for scientific merit by one of the NINCDS program project review committees. Individual research projects are reviewed by the appropriate study section of the Division of Research Grants. These reviews will be conducted in accordance with NIH policy and procedures involving peer review. Applicants may request amounts commensurate with the objectives to be accomplished for a period not to exceed five years. Awards will be made to the applicants who have successfully competed with all those requesting funds from the NINCDS.

The phrase "NINCDS Program Announcement 'AIDS Dementia and other AIDS-Associated Neurological Disorders'" should be typed on line 2 of the face page of the application.

Mail the original application and six exact copies to:

Division of Research Grants  
National Institutes of Health  
Room 240, Westwood Building  
Bethesda, Maryland 20892

#### INQUIRIES AND CORRESPONDENCE

Applicants needing further information, including the format for program project applications, may contact:

Dr. A. P. Kerza-Kwiatecki  
Health Scientist Administrator  
Demyelinating, Atrophic, and Dementing Disorders Program  
Room 702, Federal Building  
Bethesda, Maryland 20892  
Telephone: (301) 496-1431

This program is described in the Catalog of Federal Domestic Assistance number 13.854. Awards will be made under the authority of the Public Health Service Act, Title IV, 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.

## DEVELOPMENT OF NEW METHODS TO COUPLE CYTOTOXIC AGENTS TO MONOCLONAL ANTIBODIES

P.T. 34; K.W. 0760045, 0740015, 0415000, 0740025, 0760080

### NATIONAL CANCER INSTITUTE

The Biological Response Modifiers Program (BRMP), Division of Cancer Treatment (DCT) of the National Cancer Institute (NCI) invites grant applications from interested investigators for basic and applied studies concerned with the development of new methods to couple cytotoxic agents to monoclonal antibodies. 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.

### BACKGROUND

The possibility of delivering optimum doses of therapeutic reagents to target tissues in a selective way and developing reagents that are selectively cytotoxic for human tumor cells in vivo without producing detrimental effects on normal cells is of considerable interest. Hybridoma-generated monoclonal antibodies (MoAb) directed against specific antigens expressed on human tumor cells have considerable potential for selective target tissue destruction when they are coupled to cytotoxic agents since they react with a limited number of cell types and can be obtained at high titers. There are reports in the literature that indicate MoAb-toxin, -radioisotope and -drug conjugates can be formed that retain antigenic specificity and cytotoxic reactivity. The possibility exists for developing conjugates with high specificity and affinity for target tumor antigen which and may produce tumoricidal effects in excess of that induced by either antibody or cytotoxic agent alone. At present there are over 300 different murine monoclonal antibodies made against human tumor-associated antigens. The BRMP estimates there are more than 30 that are clinically relevant and could at this time be taken into clinical trials "unarmed" or as immunoconjugates with radioisotopes. The area of chemical coupling of drugs and toxins to monoclonal antibodies has not been as quick to develop in contrast to considerable research activity which is currently underway in the area of monoclonal antibody radioisotope conjugation. At present, procedures to couple a limited number of drugs and toxins exists in only a handful of research labs. The technology is flawed by procedures that have not been standardized and lack reproducibility and potential for clinical scale production. There is a definite need to stimulate new research that will provide the necessary conjugation technology for therapeutically relevant drugs and toxins.

### OBJECTIVES AND SCOPE

This program announcement is intended to foster research that will develop standardized efficient procedures to couple drugs or toxins to monoclonal antibodies directed against tumor associated antigens. Procedures should provide the best ratio of antibody to cytotoxic agent that preserves both antibody specificity and agent toxicity. Assays performed on potentially useful conjugates should include stability, antibody specificity, immunoreactivity and cytotoxicity. Innovative approaches using recombinant DNA technology to couple the toxic agent to the antibody would also be appropriate. In order to be responsive to this announcement, the applicant should demonstrate that the studies are designed to develop therapeutically useful conjugates. At the least, some experiments using a therapeutic end-point should be proposed.

### STAFF CONTACT

For further information, investigators are encouraged to contact:

Dr. Carl M. Pinsky, Chief  
Biological Resources Branch  
Biological Response Modifiers Program  
Division of Cancer Treatment  
National Cancer Institute  
Frederick Cancer Research Facility  
Building 426 - Room 1  
Frederick, MD 21701-1013  
Telephone: (301) 698-1098

### 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 #2 on the first page of this form, indicate the title of the 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, MD 20892

In order to alert the DCT to the submission of applications with primary thrust directed to biological response modifiers research, applicants are encouraged to send a brief letter of intent to Dr. Pinsky.

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 applications will be evaluated for program relevance by an appropriate National Advisory Council/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 apply to applications received in response to this program announcement.

#### DEADLINE

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

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 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.

#### NEUROENDOCRINE EFFECTS ON THE IMMUNE SYSTEM FOR CANCER THERAPY

P.T. 34; K.W. 0710085, 0705040, 0740015, 0415000, 0760075

#### NATIONAL CANCER INSTITUTE

The Biological Response Modifiers Program (BRMP), Division of Cancer Treatment (DCT) of the National Cancer Institute (NCI) invites grant applications from interested investigators for basic and applied studies concerned with application of neuroendocrine effects on the immune system for cancer therapy. 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. Although not participating directly in this announcement, the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) also accepts research grants in the area of neuroimmunomodulation.

#### BACKGROUND

There is an increasing body of information indicating bidirectional communication between the immune and nervous systems. Neuropeptides have recently been shown to be important mediators in regulating the function of diverse immunocompetent cells. Exposure of an animal to opioid-inducing stress over a period of days can reduce the number of NK cells in the animal and reduce survival following injection of a transplantable tumor. Injection of stressed animals with opiate antagonists reverses the immune defects and prolongs survival. Different neuropeptides are capable of activating and inhibiting mast cell and basophil functions in immediate hypersensitivity. B- and T-cell lymphocytes have specific receptors for neuropeptides which can effect their proliferation and synthetic functions in a positive or negative manner and may influence their tissue distribution. On the other side, molecules produced by immunocompetent cells may produce specific effects on the nervous system. Polypeptides of thymic origin profoundly modify some neurophysiologic functions and may induce abnormal neurologic activities. It has also been shown that lymphocytes, macrophages and basophils produce factors which are antigenically similar to neuropeptides and neuroendocrine hormones. Furthermore, recent studies have demonstrated the presence of receptors for various lymphokines on the cells of the central nervous system. In addition, lymphocytes and neurons share several important antigenic structures. Studies conducted at NIH have shown that primate brain expresses a T4-like epitope, which could account for the dual infectivity of HTLV-III for T-cells and the CNS. Neuropeptides have been



shown to have direct effects on growth of tumor cells; Bombesin, for example, has been shown to be a growth factor for small cell lung cancer cells and also a chemotactic factor.

#### OBJECTIVES AND SCOPE

There is a need to assess the effects of mediators that act between the immune and nervous system, the cells they act upon, their receptors, and target cell effects to determine possible application for enhancement of the immune response for cancer therapy. Studies directed toward a therapeutic endpoint may involve, but not be limited to, identification of responsiveness of immune cells to neuroendocrine mediators in vitro and in vivo, administration of mediators to animals bearing spontaneous, transplantable, and autochthonous tumors for therapeutic evaluation, and direct intervention to inhibit tumor growth promoting activities of neuroendocrine mediators by administration of antibodies directed against neuroendocrine peptides or cell receptors.

#### STAFF CONTACT

For further information, investigators are encouraged to contact:

Dr. Carl M. Pinsky, Chief  
Biological Resources Branch  
Biological Response Modifiers Program  
Division of Cancer Treatment  
National Cancer Institute  
Frederick Research Facility  
Building 426 - Room 1  
Frederick, MD 21701-1013  
Telephone: (301) 698-1098

#### 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 2 on the first page of this form, indicate the title of the 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, MD 20892

In order to alert the DCT to the submission of applications with primary thrust directed to biological response modifiers research, applicants are encouraged to send a brief letter of intent to Dr. Pinsky.

Applications in response to this announcement will be evaluated by the Division of Research Grants with regard to suitability to the NCI. Those which may be judged more suitable to other components of the National Institutes of Health (NIH) will be so assigned. All applications will be reviewed in accordance with the usual NIH peer review procedures, including an initial review for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants. Following the initial review, the applications will be evaluated for program relevance by the appropriate National Advisory Council or 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 apply to applications received in response to this program announcement.

#### DEADLINE

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

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 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.

ERRATUM

THE ROLE OF CAMPYLOBACTER PYLORIDIS IN GASTRODUODENAL DISEASE

P.T. 34; K.W. 0715125, 0715085, 0745020, 1002027, 0785055, 0785165, 0755030

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES  
NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

A line was omitted from the above program announcement in the June 6 issue of the Guide (Vol. 15, No. 7). The second paragraph under "Background" should read as follows:

The exact role of C.P. in these diseases of the stomach requires clarification. The NIAID/NIDDK believe that longitudinal studies of patients with and without these symptomatic GASTRODUODENAL DISORDERS IS NECESSARY AND DESIRABLE TO CONFIRM OR REJECT AN ETIOLOGIC ROLE FOR C.P. and to describe the natural history of this newly recognized infection of the stomach which may affect millions of Americans. Research into Campylobacter pyloridis and associated diseases offers a means of improving the diagnosis and treatment of this putative gastroduodenal infection. To pursue these studies in depth the NIAID/NIDDK favor collaborative research among multiple disciplines: microbiology, epidemiology, gastroenterology, and pathology. Institutions with demonstrated expertise in both clinical and basic sciences, with strong ongoing research programs and resources, and with the ability to mount a multidisciplinary and collaborative effort will be considered most favorably for research support under the provisions of this program.