

# NIH GUIDE

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## For Grants and Contracts

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NIH GUIDE FOR GRANTS AND CONTRACTS  
Vol. 16, No. 39  
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DATED ANNOUNCEMENTS (RFPs AND RFAs AVAILABLE)

OPERATION OF A PNEUMOCOCCAL POLYSACCHARIDE  
SEROLOGICAL REFERENCE LABORATORY

RFP AVAILABLE: NIAID-88-21

P.T. 34; K.W. 0755010, 0710060, 0780000

National Institute of Allergy and Infectious Diseases

The Development and Applications Branch of the Microbiology and Infectious Diseases Program of the National Institute of Allergy and Infectious Diseases is soliciting proposals from organizations having the capabilities and facilities to operate a reference laboratory for the performance of radioimmunoassay determinations for antibodies to pneumococcal polysaccharide antigens.

Offerors should have the capability of producing all specialized reagents required for performance of radioimmunoassays and should have an interest in the development of new serologic assays for pneumococcal polysaccharide antibodies.

This is an announcement of an anticipated Request for Proposals. RFP-NIH-NIAID-MIDP-88-21 will be issued on or about December 15, 1987, with a closing date for receipt of proposals set for February 1, 1988.

To receive a copy of the RFP, please supply this office with two self-addressed mailing labels. All responsible sources may submit a proposal which will be considered by the agency. Requests for copies of the RFP will be honored if received within 20 calendar days after the scheduled issue date of the RFP. Requests received after this period will be filled on first-come, first-served basis until the supply is exhausted. The RFP package will be available upon written request to:

Contracting Officer  
Contracts Management Branch, NIAID  
National Institute of Allergy and Infectious Diseases  
Westwood Building, Room 707  
5333 Westbard Avenue  
Bethesda, Maryland 20892

SPECIALIZED CENTERS OF RESEARCH IN CARDIOPULMONARY  
DISORDERS DURING SLEEP

RFA AVAILABLE: 88-HL-9-L

P.T. 04; K.W. 0715040, 0715165, 0710030, 1003002, 1002008, 1002019, 0785055

National Heart, Lung, and Blood Institute

Application Receipt Date: April 18, 1988

The Division of Lung Diseases invites grant applications for a single competition for support of research on cardiopulmonary disorders during sleep. The main purpose of this special grant program is to foster a multidisciplinary, concerted effort that involves both basic and clinical research relevant to the pathogenesis, prevention, diagnosis, and management of cardiopulmonary disorders during sleep. This program is initiated in response to the United States Congress, which has recommended that the National Heart, Lung, and Blood Institute provide support for this new centers program in fiscal year 1988. Among the disciplines and expertise that may be appropriate for this research program are pulmonary medicine, cardiopulmonary physiology, pharmacology, sleep physiology, biochemistry, molecular biology, genetics, cardiology, and epidemiology.

It is anticipated that two SCOR grants will be awarded. A letter of intent is requested by January 15, 1988, and the deadline for receipt of applications is April 18, 1988. Awards in connection with this announcement will not be made to foreign institutions.

Requests for copies of this RFA should be addressed to:

James P. Kiley, Ph.D.  
Structure and Function Branch  
Division of Lung Diseases  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 6A07  
Bethesda, MD 20892  
Telephone: (301) 496-7171

The RFA label (found in the 9/86 revision of application form PHS 398) must be affixed to the bottom of the face page of the original copy of the application. Failure to use this label could result in delayed processing of your application such that it will not reach the review committee in time for review.

PATHOBIOLOGY OF BONE MARROW SUPPRESSION IN AIDS OR  
AIDS-RELATED COMPLEX

RFA AVAILABLE: NIH-88-HL-10-B

P.T. 34; K.W. 0765035, 0745040, 0715120, 1002004, 0755030

National Heart, Lung, and Blood Institute  
National Institute of Diabetes and Digestive and Kidney Diseases

Application Receipt Date: April 1, 1988

The Division of Kidney, Urologic and Hematologic Diseases, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and the Division of Blood Diseases and Resources, National Heart, Lung, and Blood Institute (NHLBI), announce the availability of a Request for Applications (RFA) on the above subject. Copies of the RFA are currently available from staff of the NHLBI and the NIDDK.

The purpose of this initiative is to stimulate research on the molecular and cellular mechanisms leading to bone marrow suppression in AIDS or AIDS-Related Complex. In addition, this initiative will address the in vitro or in vivo use of hematopoietic growth factors for increasing blood cell number and/or function. The specific problem of erythroid suppression and severe anemia resulting as side effects of AZT treatment in AIDS patients is of particular interest.

It is estimated that NHLBI will make 8--10 awards under this program and NIDDK will make 10--15.

Requests for copies of the complete RFA announcement should be addresses to either of the following:

Alan S. Levine, Ph.D.  
Chief, Blood Diseases Branch  
Division of Blood Diseases and Resources  
National Heart, Lung, and Blood Institute  
Federal Building, Room 5A12  
National Institutes of Health  
Bethesda, Maryland 20892  
Telephone: (301) 496-5911

or

David G. Badman, Ph.D.  
Hematology Program Director  
Division of Kidney, Urologic, and Hematologic Diseases  
National Institute of Diabetes and Digestive and Kidney  
Diseases  
National Institutes of Health  
Westwood Building, Room 621  
Bethesda, Maryland 20892  
Telephone (301) 496-7458

The RFA label (found in the 9/86 revision of application form PHS 398) must be affixed to the bottom of the face page of the original copy of the application. Failure to use this label could result in delayed processing of your application such that it will not reach the review committee in time for review.

## MOLECULAR BIOLOGY DATA - REPRESENTATION/ANALYSIS BY COMPUTER

RFA AVAILABLE: 88-LM-01

P.T. 34; K.W. 1002008, 1004008, 0790000

National Library of Medicine

Application Receipt Date: February 12, 1988

The National Library of Medicine invites grant applications from investigators who are interested in the computer and information science aspects of molecular biology data management and analysis. The objective is to promote high quality research that has value for furthering our understanding of structure/function relationships in nucleic acids, proteins, and other biologically important molecules, in order to help prevent, diagnose, and treat human disorders. This NLM Request for Application does not supersede the relevant, ongoing program interests of other NIH components as indicated by a similar invitation in May 1987 (Program Announcement - NIH Guide, Vol. 16, No. 18.). However, it is possible that special NLM funds will be available in FY 1988 to support competitive research programs that further the stated goals. Potential applicants are strongly advised to contact NLM staff before submitting applications for support.

### BACKGROUND

The appearance of new experimental methods in the past several years has greatly increased the rate at which data are accumulating about the molecular control of life processes. Restriction enzymes, synthetic molecular probes, efficient microchemical methods for DNA and protein sequence determination, and recombinant DNA technology have developed to the point that it is now feasible to consider large-scale projects, such as the systematic analysis of entire eukaryote genomes. Because of their size and complexity, the data that are generated by such undertakings must be analyzed and compared using computerized techniques for storage, searching, and analysis. The computer databases that hold this information, currently numbered in millions of nucleotide base pairs and thousands of amino acids, are expected to grow by three orders of magnitude to encompass sequences totalling billions of nucleotides. Current methods for structuring, searching, and analyzing such databases need to be enhanced correspondingly.

### RESEARCH GOALS

Research projects which foster the development of new computer-based analysis methods for the interpretation of molecular biological data are invited. Such research will require a diversity of approaches and make use of data from a number of model systems. The research topics of interest described below are intended to illustrate the range of work in computer and information science, as applied to biology, that will be needed to advance our research capabilities in the area of genomic analysis and macromolecular structure and function.

- o Methods and algorithms for improving the efficiency of information retrieval through operations that are computationally intensive (e.g., cannot be performed in linear time).
- o Expert system techniques for automatic generation of annotation information concerning sequence data, creation of linkages among related databases via explicit pointers or common vocabulary.
- o Software algorithms and other database query methods capable of translating natural language questions into appropriate retrievals from multiple related factual databases.
- o Database design, incorporating data representations that are optimal for search, analysis, transmission, and storage of macromolecular data.
- o Algorithms capable of predicting structure and/or function based on primary sequences of nucleotides and amino acids.
- o Methods of pattern recognition based on associative networks and algorithms design optimized for multiprocessor (e.g., parallel processor) machine architectures.

## MECHANISM OF SUPPORT

Support for this program will be through research project grants (R01). Policies that govern research grant programs of the National Institutes of Health apply to this program. Since it is anticipated that potential applicants may wish to enlarge on currently available databases, consortium arrangements are also possible. In addition, collaborative projects between persons with engineering, analytical, and information science skills and molecular biologists are encouraged.

The total amount available for support of grants under this RFA is contingent upon the appropriation of funds for this purpose. The number of awards will be determined by the merit of the proposals and by their relevance to the program goals, as well as by the availability of funds. It is anticipated that in fiscal year 1988 up to one million dollars will be allocated to the research initiatives described in this RFA. This amount may be increased if a large number of highly meritorious applications are received and if funds are available.

## APPLICATION AND REVIEW PROCEDURES

Prior to initial scientific merit review, a triage mechanism may be employed to screen out applications that are clearly noncompetitive or nonresponsive to the RFA. Such applications would be returned to the applicant. Applications will be evaluated initially by a special NLM peer review committee for scientific and technical merit. A second review will be conducted by the Board of Regents of the National Library of Medicine. Review criteria include the following:

- o Overall scientific merit of the research;
- o Potential value of the research for furthering the understanding and utilization of genomic and other macromolecular information;
- o Feasibility of the research and adequacy of the experimental design;
- o Training, experience, research competence, and dedication of the investigator(s);
- o Adequacy of available facilities; and
- o Appropriateness of the requested budget for the work proposed.

## METHOD OF APPLYING

Applications should be submitted on the new form PHS 398 (rev. 9/86). The RFA label, available in the revised application kit, MUST be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time. Application kits are available at most institutional business or grants offices and from:

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

Applications will be accepted in accordance with the following schedule:

### TIMETABLE

Receipt Date: February 12, 1988

IRG Review: April 1988

Board Review: May 17-18, 1988

Earliest Funding Date: July 1, 1988

It is essential that applicants type "Molecular Biology Data - Representation/Analysis by Computer" and the RFA Number 88-LM-01 on line 2 on the face page of the application form. The original and four copies of the application should be submitted to the following office:

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

To expedite the review process, submit two copies of your application directly to:

Biomedical Information Support Branch  
Extramural Programs  
National Library of Medicine  
Lister Hill Building, Room 5S-522  
Bethesda, MD 20894

Funding decisions will be based on recommendations of the initial review group and the Board of Regents of the National Library of Medicine regarding scientific merit and program relevance and on the availability of funds.

It is strongly recommended, but not required, that potential applicants contact NLM staff to discuss research objectives. Each prospective applicant is strongly advised to submit, by January 4, 1988, a letter of intent which includes a descriptive title of the proposed research and names of key members of the project. This letter is requested to provide NLM staff with an indication of the number and scope of applications to be reviewed. It does not commit the prospective applicant to submit an application nor is it a requirement for submission of an application. For more information, applicants may contact:

Dr. Roger W. Dahlen  
Chief, Biomedical Information  
Support Branch  
Extramural Programs  
National Library of Medicine  
Lister Hill Building, Room 5S-522  
Bethesda, MD 20894  
Telephone: (301) 496-4221

STUDIES FOR DEVELOPING PROCEDURES TO EVALUATE THE SAFETY OF  
BOUND DRUG RESIDUES

RFA AVAILABLE: RFA-FDA-CVM-88-1

P.T. 34; K.W. 1007009, 0755010, 0740025

Center for Veterinary Medicine  
Food and Drug Administration

Application Receipt Date: January 19, 1988

The Food and Drug Administration (FDA), Center for Veterinary Medicine (CVM) is announcing the anticipated availability of approximately \$300,000 for Fiscal Year 1988 for cooperative agreements to support studies for developing procedures to evaluate the safety of drug residues that are bound to tissues of food producing animals. Funds are currently not available for these studies. Accordingly, the government's obligation under this program is contingent upon the availability of appropriated funds from which cooperative agreements will be funded.

The purpose of these agreements will be to provide financial assistance to support research on new models, procedures, or combinations of models and procedures that can contribute to a general approach to evaluating the safety of bound drug residues. Compounds that are known to form covalent bonds, by various mechanisms, to tissue components should be selected as model compounds for the proposed studies. Techniques dealing with the identification or isolation of sufficient quantities of bound residues for toxicological testing and in vitro approaches to the toxicological evaluation of bound residues will also be considered for support under this program. The agency is most interested in complete strategies that will have broad application to the bound residue problems encountered with several classes of animal drugs but will give consideration to proposals addressing significant segments of the problem. FDA anticipates making up to three awards. Support for this program may be for a period of up to three years.

Questions concerning the programmatic aspects of the RFA should be addressed to:



Dr. David B. Batson  
Center for Veterinary Medicine (HFV-500)  
Food and Drug Administration  
5600 Fishers Lane, Room 8-89  
Rockville, MD 20857  
Telephone (301) 443-6510

Request for copies of the RFA and application kits are available from:

Robert L. Robins  
Grants Management Officer  
State Contracts and Assistance Agreements Branch  
Food and Drug Administration  
5600 Fishers Lane (HFA-520)  
Park Building, Rm. 320,  
Rockville, MD 20857  
Telephone (301) 443-6170

#### ONGOING PROGRAM ANNOUNCEMENTS

##### HYPERTENSION, DIABETES AND THE VASCULATURE

P.T. 34; K.W. 0715115, 0715075, 0705015, 0715040, 0755030

National Heart, Lung, and Blood Institute  
National Institute of Diabetes and Digestive and Kidney Diseases

The Division of Heart and Vascular Diseases of the NHLBI and the Division of Diabetes, Endocrinology and Metabolic Diseases of the NIDDK encourage grant applications on basic and clinical research that will increase our knowledge and understanding of the mechanisms by which hypertension and diabetes mellitus interact in the pathogenesis of vascular disease.

##### BACKGROUND

Considerable evidence indicates that the prevalence of hypertension is increased in patients with both insulin-dependent and noninsulin-dependent diabetes. Also of note is the fact that blood pressure correlates significantly with blood glucose. Such an association has major clinical consequences since it has been reported that the major cause of mortality later in life in insulin-dependent diabetes and in all patients with noninsulin-dependent diabetes is macrovascular disease. Delineation of the precise nature of the association is complicated, however, by such factors as concurrent obesity, renal involvement, type and duration of disease, therapy, and presence of vascular disease.

Although it is uncertain how the two diseases are related etiologically, there are some recent observations indicating possible new research approaches and opportunities that may lead to improved understanding of how diabetes and hypertension intersect to increase the incidence of coronary artery disease, cerebrovascular disease and peripheral vascular disease. One line of investigation suggests that plasma insulin and blood glucose levels can influence blood pressure regulation. Specifically, increases in circulating insulin levels can cause sodium retention and stimulate the sympathetic nervous system. A second line of investigation suggests that hypertension and diabetes accelerate the development of atherosclerosis and its complications. It appears that both conditions enhance arterial permeability, stimulate migration and proliferation of arterial smooth muscle, increase connective tissue deposition, promote entry of blood borne cells into the intima, and induce intimal thickening. In spite of the clinical magnitude of vascular disease that results from both hypertension and diabetes, and in spite of such promising new leads, there is very little extant research aimed at uncovering basic mechanisms by which hypertension and diabetes interact in their contributions to vascular disease.

##### RESEARCH GOALS AND SCOPE

The goal of this program announcement is to stimulate basic and clinical research that will elucidate the fundamental mechanisms by which diabetes mellitus and hypertension interact to contribute to the pathogenesis of vascular disease.

The research scope of this program is broad and will encompass a wide range of basic and clinical research disciplines, such as biochemistry, biophysics, cellular biology, endocrinology, genetics, molecular biology, pharmacology and



physiology. Some examples of relevant research areas are listed below, but applications are not limited to these topics:

1. Development of suitable animal models to examine the influence of both hypertension and diabetes on the micro-and macrocirculation.
2. Determination of the influence of diabetes, insulin, and glucose on the contractile function of vascular segments or vascular reactivity, including the elucidation of the mechanisms responsible for the observed effects. Such studies might address, for example, receptor characterization, sodium-potassium ATPase activity, calcium flux, and second messenger interactions.
3. Delineation of the relative roles of the sympathetic nervous system, the renin-angiotensin-aldosterone system, humoral factors, and renal mechanisms mediating the rise in blood pressure associated with increased insulin levels.
4. Investigation of the single and combined effects of diabetes and hypertension on atherogenesis. Examples of studies could include the effects of ambient insulin and glucose concentration on: endothelial cell function; arterial smooth muscle cell migration, proliferation and responses to growth factors; connective tissue production and glycosylation; and receptor binding and endocytosis of lipoproteins.

#### APPLICATION AND REVIEW PROCEDURES

Applicants should use the regular research grant application (PHS 398, revised 9/86). If applications are not available at the institution's business office or central application control office, an individual copy may be requested by writing to Division of Research Grants (DRG), NIH. There are three receipt dates each year for new applications: February 1, June 1, October 1. All applications will be assigned by the Division of Research Grants for review according to the NIH process for regular research grant applications. Secondary reviews will be by the National Heart, Lung, and Blood Advisory Council and the National Diabetes and Digestive and Kidney Diseases Advisory Council. Applications recommended for approval will compete for available funds with all other approved applications assigned to the two Institutes. However, since the Institutes and their Advisory Councils 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 Councils.

Applicants from institutions which have a General Clinical Research Center (GCRC) funded by the NIH Division of Research Resources may wish to identify the Center as a resource for conducting the proposed research. In such a case, a letter of agreement from the GCRC Program Director should be included in the application material.

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 HYPERTENSION, DIABETES AND THE VASCULATURE. The original and six copies of the application should be mailed to:

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

Applicants are requested to mail a copy of the face page to:

Dr. Robert E. Silverman, Chief  
Diabetes Program Branch  
National Institute of Diabetes and  
Digestive and Kidney Diseases  
Westwood Building - Room 626  
Bethesda, Maryland 20892  
Telephone: (301) 496-7888

AND

Dr. Stephen C. Mockrin, Deputy Chief  
Hypertension and Kidney Diseases Branch  
National Heart, Lung, and Blood Institute  
Federal Building - Room 4C10  
Bethesda, Maryland 20892  
Telephone: (301) 496-1857

Requests for additional information or questions regarding this program may be directed to either of the above.

\*The programs of the two Institutes are identified in the Catalog of Federal Domestic Assistance, number 13.837. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grant policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372, or to review by a Health Systems Agency.

#### MINORITY INVESTIGATOR RESEARCH SUPPLEMENT

P.T. 34, FF; K.W. 0705015, 0705065, 0750010, 0710030

National Heart, Lung, and Blood Institute

#### INTRODUCTION

The purpose of this announcement is to attract minority investigators to careers in heart, lung, or blood research by providing supplemental funds to ongoing research grants supported by the NHLBI.

#### DESCRIPTION

The National Heart, Lung, and Blood Institute (NHLBI) will provide support for members of minority groups underrepresented in biomedical or behavioral research through the Minority Investigator Research Supplement program. This supplement addresses the recruitment of eligible individuals from the full spectrum of minority groups, but with a special emphasis on Blacks, Hispanics, and Native Americans.

Principal investigators who are supported by NHLBI research grants (including R01s, R18s, R37s, P01s, P50s, and P60s) and who are interested in including underrepresented minority investigators in ongoing research may submit a request for an administrative supplement for this purpose.

#### ELIGIBILITY

Any principal investigator with an active R01, R18, R37, P01, P50, or P60 NHLBI grant that has a minimum of two years of research support remaining at the time of a supplemental award is eligible to submit a request for an administrative supplement for the purpose of recruiting a minority investigator to work on the research grant.

- A. **Minority Investigator** - A minority investigator is defined as an individual from a minority group underrepresented in biomedical or behavioral sciences. The minority investigator may be affiliated with the applicant institution or with another nearby institution. The program is intended for the M.D. or Ph.D. who is generally at the junior faculty level, instructor or assistant professor, with at least one year postdoctoral research experience, but who has not received previous funding from NIH as an independent investigator. The minority investigator must make at least a two year commitment and must spend at least 30% time on research supported by the parent grant. This supplement is not intended to support summer-only research.
- B. **Research Experience** - The proposed research experience must be part of the ongoing research of the parent grant. When an award is issued, there should be at least two years of research support remaining on the parent grant. As part of this research experience the minority investigator should have the opportunity to interact with investigators on the parent grant, should be able to contribute intellectually to the research, and should have the opportunity to enhance his/her research skills.

#### PROVISIONS

In order to receive a Minority Investigator Research Supplement there must be, at the time of the supplemental award, a minimum of two years future support remaining on the parent grant. In the first budget period, funds will be provided as an administrative supplement to the ongoing research grant. In future budget periods, funds for the minority supplement will be included in the award to the parent grant. Each annual supplemental budget should not exceed \$30,000 in direct costs, limited to salary, supplies, and travel, and

may not include equipment. The continuation of support for the minority supplement in subsequent years of the grant will depend upon a satisfactory review of progress made, research proposed for the next budget period, and the budget. The minority supplement progress report will be submitted as part of the noncompeting continuation application of the principal investigator. Funding for the supplement always is contingent on funding of the parent grant, and cannot extend beyond the project period of the parent grant. Supplemental awards under this program are for the sole purpose of supporting the research experience of the minority investigator. A minority investigator may receive support under this program on only one grant. The support should be for a minimum of two years duration, and each parent grant can have only one minority investigator at a time. Simultaneous or overlapping Minority Investigator Research Supplements will not be considered.

The funding of this administrative supplement does not preclude the subsequent submission of applications for career development awards (K series) or investigator-initiated research grants by the minority investigator. A minority investigator who previously received a K series award, or an investigator-initiated research project grant from NIH is not eligible to apply for this award.

#### REVIEW CRITERIA

The research training committees composed of staff from the heart, lung, and blood programs will review requests for supplemental support under this announcement using the following criteria:

- o Prior research training and experience of the minority investigator,
- o Plans for the proposed research experience in the supplemental request and its relationship to the parent grant, and
- o Assurance from the principal investigator that the experience will enhance the research potential and skills of the minority investigator.

#### APPLICATION PROCEDURES

The principal investigator of the parent grant should submit a request for supplemental funds directly to the NHLBI program division that supports the parent grant. The request should include the following: 1) a letter with the title and grant number of the parent grant and a statement that this is a request for a Minority Investigator Research Supplement, 2) a brief 3-4 page description of the proposed research experience and how it will expand the capabilities and foster the independent research career of the minority investigator, 3) a statement from the minority investigator outlining research objectives and career goals, 4) a biographical sketch of the minority investigator that includes a list of publications and other evidence of scientific achievement, and 5) a proposed budget for the research experience. The request must be signed by principal investigator and the appropriate institutional business official.

Requests may be submitted at any time.

The original and four (4) copies of the request should be sent to the NHLBI program division that supports the parent grant. Division representatives are:

Dr. George A. Hayden  
Research Training and Development Branch  
Division of Heart and Vascular Diseases  
National Heart, Lung, and Blood Institute  
Federal Building, Room 3C01  
National Institutes of Health  
Bethesda, Maryland 20892  
Telephone: (301) 496-1724

or

Ms. Diane L. Aiken  
Prevention, Education, and Research Training Branch  
Division of Lung Diseases  
National Heart, Lung, and Blood Institute  
Westwood Building, Room 640  
National Institutes of Health  
Bethesda, Maryland 20892  
Telephone: (301) 496-7668

or

Dr. Christine Parker  
Program Planning and Prevention Branch  
Division of Blood Diseases and Resources  
National Heart, Lung, and Blood Institute  
Federal Building, Room 5C04  
National Institutes of Health  
Bethesda, Maryland 20892  
Telephone: (301) 496-4186

or

Dr. Katrina W. Johnson  
Prevention and Demonstration Research Branch  
Division of Epidemiology and Clinical Applications  
National Heart, Lung, and Blood Institute  
Federal Building, Room 5C10B  
Telephone: (301) 496-3503

The programs of the National Heart, Lung, and Blood Institute are identified in Catalog of Federal Domestic Assistance, number 13.837, 13.838, and 13.839. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grant policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

### BIOCHEMISTRY OF ANTIVIRAL AGENTS IN EUKARYOTIC CELLS

P.T. 34; K.W. 1002045, 0740020, 1003002, 0760075

National Institute of Allergy and Infectious Diseases

#### BACKGROUND INFORMATION

The National Institute of Allergy and Infectious Diseases (NIAID) currently supports a large number of clinical and basic research projects on the Human Immunodeficiency Virus (HIV), the causative agent of Acquired Immunodeficiency Syndrome (AIDS). These include research directed toward the epidemiology, prevention, pathogenesis and treatment of the disease and its sequelae. NIAID has undertaken a lead role in organizing scientists into the National Cooperative Drug Discovery Groups for the Treatment of AIDS (NCDDG/AIDS). The NCDDG/AIDS are composed of scientists from a combination of academic, non-profit, and commercial organizations, that interact as a unit with NIAID support, to carry out preclinical research aimed at the discovery of agents which can be used in the treatment of AIDS. Although this program has been favorably received, the NIAID wishes to expand the areas of investigator-initiated research currently being funded. This Program Announcement solicits applications from investigators who wish to play a very active role in defining the direction of this research. While no funds are specifically set aside for funding grants submitted in response to this Program Announcement, additional high quality research in this area is of high priority to the NIAID.

#### OBJECTIVES AND SCOPE

The objective of this Program Announcement is to stimulate research on the biochemistry of antiviral agents in eukaryotic cells, particularly cells susceptible to HIV infection. Directions may include elucidation of the metabolic steps involved in activation and inactivation of nucleoside analogues in various HIV-susceptible cells. For example, work on pyrimidine biosynthesis in macrophages has revealed that macrophages have very low levels of deoxythymidine kinase. This would imply that pyrimidine nucleoside analogues may be less active in macrophages than in lymphocytes. Investigators are encouraged but not required to form collaborations with virologists involved in HIV biology so that uninfected and infected cells can be compared. For example, little information is available on the effect of HIV infection on the permeability of infected cells to nucleoside, nucleotide, or oligonucleotide therapeutics. Other approaches may be directed toward elucidation of unique biochemical properties of HIV-infected cells that suggest new anti-HIV therapies. For example, characterization of viral sequence-specific DNA-binding protein(s) may lead to development of an oligonucleotide therapeutic to block HIV replication. Although human cells are of primary interest, comparison of human and animal cells would fall under the scope of this announcement. For example, comparison of human and

chimpanzee proteins regulated by HIV infection may shed light on the mechanism by which replication of HIV is blocked in chimpanzees, even though their cells carry the OKT4 receptor.

The approaches outlined above are not intended to be comprehensive or required. Any investigations on a biochemical pathway or biomolecule present in cells susceptible to HIV that is altered by HIV infection or that is involved in the metabolism or mechanism of action of a potential AIDS therapeutic are encouraged under this Program Announcement.

#### METHOD OF APPLICATION

Use the standard research Grant Application Form PHS 398 (Rev. 9/86). For purposes of identification and processing, the words "NIAID Biochemistry of Antiviral Agents in Eukaryotic Cells" should be typed in item 2 on the face page of the application. The receipt dates will be the usual receipt dates of Feb. 1, June 1 and Oct. 1 (as shown on pg 11 of the PHS 398 application instructions). Mail the complete application and six (6) exact copies to:

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

Send a copy of the face page of the application to the individual listed below under INQUIRIES.

#### REVIEW PROCEDURES AND CRITERIA

Support for this program will be through the traditional research grant. Applications will be reviewed by the appropriate Study Sections designated by the Division of Research Grants. A second review will be made by the National Advisory Allergy and Infectious Diseases Council. Review criteria will be the same as those for traditional research grant applications.

#### INQUIRIES

Additional information may be obtained from:

Margaret I. Johnston, Ph.D.  
Head, Molecular Mechanisms Section  
Developmental Therapeutics Branch  
AIDS Program, NIAID  
National Institutes of Health  
Bethesda, Maryland 20892  
Telephone: (301) 496-8197

#### EXPRESSION OF THE HUMAN OKT4 ANTIGEN ON THE SURFACE OF NON-LYMPHOID CELLS

P.T. 34; K.W. 1002019, 0710065, 0715120

National Institute of Allergy and Infectious Diseases

#### BACKGROUND INFORMATION

The National Institute of Allergy and Infectious Diseases (NIAID) currently supports a large number of clinical and basic research projects on the Human Immunodeficiency Virus (HIV), the causative agent of Acquired Immunodeficiency Syndrome (AIDS). These include research directed toward the epidemiology, prevention, pathogenesis and treatment of the disease and its sequelae. NIAID has undertaken a lead role in organizing scientists into the National Cooperative Drug Discovery Groups for the Treatment of AIDS (NCDDG/AIDS). The NCDDG/AIDS are composed of scientists from a combination of academic, non-profit, and commercial organizations, that interact as a unit with NIAID support, to carry out preclinical research aimed at the discovery of therapies for AIDS. Although this program has been favorably received, the NIAID wishes to expand the areas of investigator-initiated research currently funded. This Program Announcement solicits applications from investigators who wish to play an active role in defining the direction of this research. While no funds are specifically set aside for funding grants submitted in response to this Program Announcement, additional high quality research in this area is of high priority to the NIAID.

## OBJECTIVES AND SCOPE

The NIAID wishes to stimulate research on the generation, testing and subsequent application of animals and cells which express the human OKT4 receptor, in whole, in part, or as a hybrid protein. A major limitation in studies on AIDS is the inability to efficiently grow HIV in cell lines or animals. It appears that HIV strains are capable of replication only in cells that express the human OKT4 receptor. At present, cultivation of isolated human cells is expensive and requires skills other than those required for utilization of continuous cell lines. The availability of cell lines that express an active HIV receptor would promote the study of HIV by scientists who do not have experience in the techniques of lymphocyte cultivation. Further insight into the preferential tropism of certain HIV isolates for some cell types would also be possible. Most importantly, establishment of cell lines competent to carry out any one or more of a variety of steps of HIV replication may facilitate testing of inhibitors of each step of HIV replication, allow a more thorough understanding of the mechanism of action of each potential therapeutic, and thereby provide valuable information on the design of new therapies or combinations of therapies.

Production of transgenic cells and or animals is also expected to be useful in defining specific human genes and epitopes required for uptake of HIV, for replication of HIV, and for the immunopathogenic response to HIV. For example, HIV does not appear to replicate in animals other than the chimpanzee, in which HIV does not appear to produce an immunodeficiency disorder. Availability of a chimeric rodent or other non-primate animal in which the human HIV retrovirus produces an immunodeficiency syndrome would open a new arena of research into the efficacy and mode of action of potential therapies for AIDS. Stringent precautions should be instituted if it is anticipated that the approach taken may generate another animal reservoir for HIV.

The approaches outlined above are not meant to be comprehensive or required. Any investigations on production, testing, and application of transgenic cells or animals that express antigen(s) required for one or more steps of HIV replication or the pathogenic effects of HIV are encouraged under this Program Announcement.

## METHOD OF APPLICATION

Use the standard research Grant Application Form PHS 398 (Rev. 9/86). For purposes of identification and processing, the words "NIAID Expression of the Human OKT4 Antigen on the Surface of Nonlymphoid cells" should be typed in item 2 on the face page of the application. The receipt dates will be the usual receipt dates of Feb. 1, June 1 and Oct. 1 (as shown on pg 11 of the PHS 398 application instructions). Mail the complete application and six (6) exact copies to:

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## INQUIRIES

Additional information may be obtained from:

John J. McGowan, Ph.D.,  
Chief, Developmental Therapeutics Branch, AIDS Program,  
NIAID,  
National Institutes of Health,  
Bethesda, Maryland 20892  
Telephone: (301) 496-8197

CHILD AND ADOLESCENT MENTAL HEALTH ACADEMIC AWARD

P.T. 34, AA; K.W. 0715095, 0414000

National Institute of Mental Health

The National Institute of Mental Health announces the Child and Adolescent Mental Health Academic Award. The purpose of this award is to assist in the development of a resource person in academic settings who is oriented toward research in child and adolescent mental disorders. The award, made to an institution, provides a faculty member with opportunity for 3 years of special study and supervised experience to prepare for a faculty leadership role in child and adolescent mental health research. Applications are encouraged from women and minority faculty or from historically minority institutions. Salary support is based on a full-time, 12-month staff appointment, consistent with the established salary structure at the institution. The award may not be renewed. Applications in response to this announcement will be accepted under the usual Public Health Service receipt dates for new applications, beginning February 1, 1988. Potential applicants interested in obtaining further information should contact:

Jon A. Shaw, M.D.  
Chief, Child and Adolescent Disorders Research Branch  
or  
Eleanor Dibble, D.S.W.  
Program Director, Clinical Research Training  
Child and Adolescent Disorders Research Branch

The address for both of the above is:

Division of Clinical Research  
National Institute of Mental Health  
Room 10-104, Parklawn Building  
5600 Fishers Lane  
Rockville, Maryland 20857  
Telephone: (301) 443-5944

GERIATRIC MENTAL HEALTH ACADEMIC AWARD

P.T. 34; K.W. 0710010, 0715095

National Institute of Mental Health

The National Institute of Mental Health has revised its announcement for the Geriatric Mental Health Academic Award. The purpose of this award is to assist in the development of academically situated, research-oriented persons in the area of mental disorders of the aging. The award, made to an institution, provides a faculty member who is a psychiatrist or a psychiatric nurse with the opportunity for 3 years of special study and supervised experience to prepare for a faculty leadership role in geriatric mental health research. Applications are encouraged from women and minority faculty or from historically minority institutions. Salary support of up to \$45,000 may be provided. The total amount of funding will depend on appropriated funds and program priorities at the time of the award. Applications in response to this announcement will be accepted under the usual Public Health Service receipt dates for new applications, beginning February 1, 1988. Potential applicants interested in obtaining further information should contact:

Barry D. Lebowitz, Ph.D.  
Chief, Mental Disorders of the Aging Research Branch  
Division of Clinical Research  
National Institute of Mental Health  
Room 11C-03, Parklawn Building  
5600 Fishers Lane  
Rockville, Maryland 20857  
Telephone: (301) 443-1185



ERRATUM

RESEARCH CENTERS FOR AIDS DEMENTIA AND OTHER  
RETROVIRUS-ASSOCIATED NEUROLOGICAL DISORDERS

P.T. 04; K.W. 0715120, 0710085, 1003002, 0785110, 0414000

National Institute of Neurological and Communicative Disorders and Stroke

In the above-captioned RFA, published in the November 13, 1987 issue of this Guide, no telephone number was given for the staff contact for the RFA, Dr. A.P. Kerza-Kwiatecki. Dr. Kerza-Kwiatecki may be reached at (301) 496-1431.