

NIH GUIDE

For Grants and Contracts

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NOTICES

"OTHER SUPPORT" IN PHS GRANT APPLICATIONS

P.T. 34; K.W. 1014002, 1014006

National Institutes of Health

The PHS 398 (Rev. 9/86) and PHS 2590 (Rev. 9/86) grant application forms include a section on OTHER SUPPORT, where applicants are expected to list all, including both Federal and non-Federal, active support and pending and planned requests for support of research and research-related activities by all key personnel listed for each application. This information is important to PHS review-award processes to help evaluate the compatibility of application requests with investigators' capabilities and responsibilities, and eliminate unwarranted duplication of support for investigators' efforts. Application instructions emphasize the requirement for complete, accurate, and reliable information. In signing the face page of the application the principal investigator/program director and the applicant institution official certify that the application information is accurate and complete.

Applicants are reminded of the necessity to provide the full and reliable information requested. As noted in the instructions, "Incomplete, inaccurate, or ambiguous information about OTHER SUPPORT could lead to delays in review of the application." Further, applicants should be cognizant that serious consequences could result if failure to provide complete and accurate information be construed as an attempt to mislead PHS agency advisory groups and staff in their review and award responsibilities.

"OTHER SUPPORT" IN NIH R&D CONTRACT PROPOSALS

P.T. 34; K.W. 1014002, 1014006

National Institutes of Health

Documentation required in Section J of the NIH uniform Request for Proposal format includes Standard Form 1411, Contract Pricing Proposal Cover Sheet, which instructs offerors to identify any contracts or subcontracts they have been awarded "for the same or similar items" within the past three years. Additionally, offerors are required to provide a Summary of Related Activities, identifying all active federal contracts, cooperative agreements, grants, and commercial agreements, and submitted proposals, including actual and proposed levels of effort for all key individuals in the proposal to NIH.

As for PHS grant applications, mentioned above, offerors should be aware that serious consequences could result if their failure to provide complete and accurate information be construed as an attempt to mislead agency advisory groups and staff in their review and award responsibilities.

NUCLEIC ACID AND PROTEIN SEQUENCE WORKSHOP ANALYSIS FOR BIOMEDICAL RESEARCHERS

P.T. 42; K.W. 0755045, 0760070

Division of Research Resources

Application Receipt Date: February 10, 1989

The Pittsburgh Supercomputing Center (PSC) is conducting a three-day workshop on "Nucleic Acid and Protein Structure Analysis," March 27-29, 1989. This workshop is funded by a cooperative agreement from the Division of Research Resources' Biomedical Research Technology (BRT) Program of the National Institutes of Health (NIH).

The workshop will familiarize biomedical researchers with computational methods and provide practice in applying supercomputing resources to problems of concern in molecular sequence analysis. Practical experience on the Pittsburgh Supercomputing Center's Cray Y-MP/832 will be gained in: (1) the recognition of subsequences representing signals structural patterns and statistical properties of gene and protein sequences; (2) comparisons of sequences for detection of local similarities between pairs and sequences; (3) multiple sequence alignments; and (4) prediction of secondary structure from primary sequence information. Programs such as the IDEAS and Wisconsin packages as well as stand alone programs will be illustrated. Participants are encouraged to bring their own sequence analysis problems. Workshop

leaders: Michael Waterman, University of Southern California; Ruth Nussinov, Tel Aviv University; and Jacob B. Maizel, Jr., National Cancer Institute.

This three-day workshop will include an optional half-day session the morning of March 27 led by PSC staff members. Topics to be covered during the optional session include VAX, VMS, and UNICOS, the Cray version of the AT&T System V Unix operating system.

Travel, meals, and hotel accommodations are covered for U.S. academic participants under the grant. A limited number of openings for industry-based biomedical researchers may be available for a fee of \$1,000. Enrollment is limited to 20 participants. THE DEADLINE FOR SUBMISSION OF APPLICATIONS IS FEBRUARY 10, 1989.

For application forms and further information, call or write to:

Cherolyn Brooks
User Services
Pittsburgh Supercomputing Center
4400 Fifth Avenue
Pittsburgh, Pennsylvania 15213
Telephone: (412) 268-5206, or
1-800-222-9310 (Pennsylvania)
1-800-221-1641 (outside Pennsylvania)

NIH/FDA REGIONAL WORKSHOPS - PROTECTION OF HUMAN SUBJECTS

P.T. 42; K.W. 1014002, 0783005

National Institutes of Health
Food and Drug Administration

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:

o Dates: January 19-20, 1989

Location: Long Beach, California

Title of Workshop:

"Western Regional Workshop on Human Subjects Protection"

Contact:

Dr. Samuel J. Shacks or
Mrs. Mary Quach
Charles R. Drew University
of Medicine and Science
1621 East 120th Street
Los Angeles, California 90059
Telephone: (213) 563-5900

o Date: February 2-3, 1989

Location: Tempe, Arizona

Title of Workshop:

"Ethical Issues Surrounding the Use of Human Subjects in Research"

Contact:

Ms. Carol Jablonski
Human Subjects Coordinator
Office of Research Development
and Administration
Arizona State University
Tempe, Arizona 85287
Telephone: (602) 965-2170

o Dates: March 9-10, 1989

Location: Birmingham, AL

Title of Workshop:

"Institutional Review Board Workshop on Bioethical Considerations in Research with Human Subjects"

Contact:

Ms. Susan Nuckols
Division of Continuing Medical
Education
University of Alabama
at Birmingham
127 CHSB
Birmingham, Alabama 35294
Telephone: (1-800) 292-6508 in Alabama
(1-800) 452-9860 outside Alabama

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

Darlene Marie Ross
Education Program Coordinator
Office for Protection from Research Risks
National Institutes of Health
Building 31, Room 4B09
9000 Rockville Pike
Bethesda, Maryland 20892
Telephone: (301) 496-8101

DATED ANNOUNCEMENTS (RFPs AND RFAs)

COCHLEAR RE-IMPLANTATION: HISTOPATHOLOGY ANNOUNCEMENT

RFP AVAILABLE: NIH-NIDCD-89-13

P.T. 34; K.W. 0715050, 0740030

National Institute of Deafness and Other Communication Disorders

The National Institute of Deafness and Other Communication Disorders (NIDCD), has a requirement and plans to issue a Request for Proposals (RFP) entitled, 'Cochlear Re-Implantation: Histopathology.' Proposals will be solicited for the performance of a study to assess the histopathology associated with implantation, explantation, and re-implantation of cochlear electrode devices in non-human primates.

The Government anticipates one contract award for a performance period of three (3) years.

Prospective offerors are advised that since the performance of work under this project will involve the use of live non-human primates, the awardee shall be required to comply with the DHH/PHS policy and regulations for the "Use and Care of Live Vertebrae Animals." In addition, prospective offerors are expected to have in place and on an in-house basis: 1) the animal and laboratory facilities and equipment necessary for the performance of work; and 2) a senior Ph.D.- or M.D.-level basic or clinical scientist with expertise and experience in the area of neuroscience and cochlear implant surgery.

This is an announcement of an anticipated Request for Proposals. RFP-NIH-NIDCD 89-13 will be issued on or about December 30, 1988, with the closing date for receipt of proposals tentatively set for February 28, 1988. To receive a copy of the RFP, please supply this office with two self-addressed mailing labels. The RFP package will be available upon written request to:

Contracts Management Branch, DEA
National Institute of Neurological Disorders and Stroke
National Institutes of Health
Federal Building, Room 901
7550 Wisconsin Avenue
Bethesda, Maryland 20892
Attn: RFP No. NIH-NIDCD-89-13

PRESOLICITATION: COLLABORATIVE STUDIES FOR DIAGNOSTIC
CENTERS FOR PSYCHIATRIC LINKAGE STUDIES

RFA: MH-88-12

P.T. 34; K.W. 0715177, 0715180, 0755030

National Institute of Mental Health

Anticipated RFA Availability Date: January 15, 1989
Anticipated Application Receipt Date: March 15, 1989

INTRODUCTION

The purpose of this announcement is to alert researchers in the field of mental illness to the issuance of a Request for Applications (RFA) for a collaborative study on the genetics of schizophrenia, bipolar disorder, and Alzheimer's disease. Three extramural research groups per disorder will be chosen from among applicants, and a given site may be designated a research group for more than one disorder. The reason for the presolicitation announcement is to enable interested sites to begin preparation of applications as the amount of time between the issuance of the RFA and the receipt date will be short.

PROJECT GOALS

The overall goal of this project is to provide support for a collaborative study of chromosomal linkage in schizophrenia, bipolar disorder, and Alzheimer's disease. The sites selected and the family types to be assessed will allow for a powerful investigation of the hypothesis that each of these disorders has an associated single abnormal gene. To pursue this hypothesis a modification of the affected sibling pair methodology has been chosen. Each site concentrating on schizophrenia and bipolar disorder will be expected to assess approximately 70 small families with approximately four affected members. Each site working in the area of Alzheimer's disease will be expected to collect about 133 families with affected sibling pairs. Some support for extension of these families into larger pedigrees will be provided. Because of the large number of subjects planned, a significant exploration of presumed genetic heterogeneity can be performed. In addition, a major goal of the project is to create a national resource of clinical material which will allow basic scientists to examine genetic questions.

MECHANISMS OF SUPPORT

This project will be supported by the cooperative agreement mechanism. This is important to note because this mechanism differs significantly from investigator-initiated research grants. Although the awardees are primarily responsible for the conduct of the study, there will be collaboration among the participating groups and NIMH staff will have substantial involvement in planning, coordination, and scientific collaboration during the life of this project.

The responsibilities of the NIMH staff will be outlined in more detail in the RFA. In summary, they will be responsible for activities such as: organizing meetings required to develop the final protocol, arranging for training personnel in diagnostic assessment, coordinating data management at a central site to be supported by a separate contract, and coordinating transfer of lymphocytes to a central cell repository which will also be supported by contract. The responsibilities of the Extramural Research Groups will be described in detail in the RFA. The sites' responsibilities include ascertainment and diagnostic evaluation of patients and their relatives and participation in all phases of scientific decision making about the shared protocol.

Among the major criteria used to evaluate applications received in response to the RFA are the following: (1) ability of a site to provide the clinical material required; (2) demonstrated expertise of site staff in clinical and biological characterization of subjects; (3) ability to cooperate with other sites and with the NIMH in the development and implementation of a shared protocol. The cooperative agreement support will be for the diagnostic team at each site as well as some support for travel of subjects and equipment.

Issuance of the RFA for this program is contingent on the availability of funds. It is anticipated that \$1.5 million will be made available for this project in FY 1989. The duration of the awards is 5 years.

INQUIRIES

To receive a copy of the RFA when it is available, please send a letter to either of the addresses listed below. For further information, contact either:

S. Charles Schulz, M.D.
Chief, Schizophrenia Research Branch
Division of Clinical Research
National Institute of Mental Health
10C-06 Parklawn Building
5600 Fishers Lane
Rockville, Maryland 20857
Telephone: (301) 443-3524

or

Mary C. Blehar, Ph.D.
Head, Clinical and Biological Studies of
Mood Disorders Program
Mood, Anxiety, and Personality Disorders
Research Branch
Division of Clinical Research
National Institute of Mental Health
10C-24 Parklawn Building
5600 Fishers Lane
Rockville, Maryland 20857
Telephone: (301) 443-4524

COORDINATING CENTER FOR COLLABORATIVE STUDIES ON THE GENETICS OF ALCOHOLISM

RFA AVAILABLE: 89-AA-01A

P.T. 04; K.W. 0404003, 1002019, 0745020, 0760003

National Institute on Alcohol Abuse and Alcoholism

Application Receipt Date: April 3, 1989

PURPOSE

NIAAA announces the availability of an RFA to support a Coordinating Center for a collaborative research effort to identify the gene(s) which influence susceptibility to alcoholism.

RESEARCH OBJECTIVES

This collaborative study will involve genetic studies of alcoholics and their relatives, the acquisition of immortalized lymphocytes for DNA analysis, and investigations of the association of potential genetic markers with the expression of the alcoholic phenotype(s) in the families being studied.

MECHANISM OF SUPPORT

The study will involve the cooperation of scientists from: (1) a single Coordinating Center, (2) multiple Extramural Research Groups, (3) an NIAAA Intramural Research Group, and (4) the NIAAA Extramural Program. The primary governing body of the study will be the Steering Committee, composed of the principal investigator of the Coordinating Center, the principal investigator of each of the Extramural Research Groups, the principal investigator of the NIAAA Intramural Research Group, the NIAAA Staff Collaborator and any other individuals from participating sites needed to ensure appropriate coverage of subject matter and balance. A Genetics of Alcoholism Collaborative Project Advisory Committee will be formed, composed of experts in the alcohol research field or in the other fields relevant to the project.

Applications for the Coordinating Center will be accepted only from domestic institutions. The award for the Coordinating Center will be made in the form of a cooperative agreement. The Coordinating Center will provide overall study coordination and management; development, refinement, testing and/or training in common diagnostic protocols, as required; a DNA and cell repository; a common data repository; data storage and analysis capabilities; and executive secretariat functions. It may also coordinate laboratory functions, phenotypic testing procedures or linkage analysis if this is deemed desirable in the planning phase. The Coordinating Center may involve a single institution or multi-institution collaboration. Investigators submitting a

proposal to become the Coordinating Center may also submit a separate proposal to function as one of the Extramural Research Groups (RFA 89-AA-01B). NIAAA plans to make multiple awards for the three phases of the project up to five years and has set aside 3.5 million dollars for the initial year's funding.

Prospective applicants are asked to submit a letter of intent by March 1, 1989 to:

Mark Green, Ph.D.
Chief, Extramural Project Review Branch, NIAAA
16-C-20 Parklawn Building
5600 Fishers Lane
Rockville, Maryland 20857
Telephone: (301) 443-4375

The following office may be contacted for necessary application material:

National Clearinghouse for Alcohol and Drug Information
Reference Department
Box 2345
Rockville, Maryland 20852
Telephone: (301) 468-2600

This RFA is a one-time request for applications. Applicants who wish also to apply for consideration as an Extramural Research Group should submit a separate application with the title, "Extramural Research Group for Collaborative Studies on the Genetics of Alcoholism", RFA 89-AA-01B.

THE RFA LABEL FOUND IN THE PHS 398 KIT MUST BE AFFIXED TO THE BOTTOM OF THE FACE PAGE OF THE ORIGINAL COMPLETED APPLICATION FORM, PHS 398. FAILURE TO USE THIS LABEL COULD RESULT IN DELAYED PROCESSING OF YOUR APPLICATION SUCH THAT IT MAY NOT REACH THE REVIEW COMMITTEE IN TIME FOR REVIEW. THERE WILL BE NO OBLIGATION TO REVIEW SUCH APPLICATIONS.

Send or deliver the completed application and four (4) signed, exact photocopies of it to:

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

SEND TWO ADDITIONAL COPIES OF THE APPLICATION TO DR. MARK GREEN AT THE ADDRESS LISTED UNDER LETTER OF INTENT. IT IS IMPORTANT TO SEND THESE TWO COPIES AT THE SAME TIME AS THE ORIGINAL AND FOUR COPIES ARE SENT TO THE DIVISION OF RESEARCH GRANTS IN ORDER TO ENSURE THAT THE APPLICATION WILL BE REVIEWED IN COMPETITION FOR THIS RFA.

Applications must be received by April 3, 1989. An application not received by this date will be considered ineligible.

INQUIRIES

For further information contact:

W. Sue Badman Shafer, Ph.D.
Acting Director, Division of Basic Research, NIAAA
14-C-10 Parklawn Building
5600 Fishers Lane
Rockville, Maryland 20857
Telephone: (301) 443-2530

EXTRAMURAL RESEARCH GROUPS FOR COLLABORATIVE STUDIES ON THE GENETICS OF ALCOHOLISM

RFA AVAILABLE: 89-AA-01B

P.T. 34; K.W. 0404003, 1002019, 0760002

National Institute on Alcohol Abuse and Alcoholism

Application Receipt Date: April 3, 1989

PURPOSE

NIAAA announces the availability of an RFA to support two to five Extramural

Research Groups for a collaborative research effort to identify the gene(s) which influence susceptibility to alcoholism.

RESEARCH OBJECTIVES

This collaborative study will involve genetic studies of alcoholics and their relatives, the acquisition of immortalized lymphocytes for DNA analysis, and investigation of the association of potential genetic markers with the expression of the alcoholic phenotype(s) within the families being studied.

MECHANISM OF SUPPORT

This study will involve the cooperation of scientists from: (1) a single Coordinating Center, (2) multiple Extramural Research Groups, (3) an NIAAA Intramural Research Group, and (4) the NIAAA Extramural Program. The primary governing body of the study will be the Steering Committee, composed of the principal investigator of the Coordinating Center, the principal investigator of each of the Extramural Research Groups, the principal investigator of the NIAAA Intramural Research Group, the NIAAA Staff Collaborator and any other individuals from participating sites needed to ensure appropriate coverage of subject matter and balance. A Genetics of Alcoholism Collaborative Project Advisory Committee will be formed, composed of experts in the alcohol research field or in the other fields relevant to the project.

Applications for the Extramural Research Groups will be accepted from domestic and foreign institutions. Awards for the Extramural Research Groups will be made in the form of a cooperative agreement. The final plan for the study will be based on the successful proposals. The Extramural Research Groups will be responsible for the major portion of the performance of the study. Each Extramural Research Group will perform many, if not all, of the different research activities needed for the study. However, a single Extramural Research Group need not necessarily possess the entire range of capabilities needed for the collaborative study, but may contribute some unique capabilities judged by peer review to be necessary to participate in the study. Proposals for the Extramural Research Groups may involve a single institution or a multi-institution collaboration. Investigators submitting a proposal to become one of the Extramural Research Groups may also submit a separate proposal to function as the Coordinating Center (RFA 89-AA-01A). The Extramural Research Groups will be selected as described in RFA 89-AA-01B. The role of NIAAA extramural staff and intramural research group is described in the RFA. NIAAA plans to make multiple awards for the three phases of the project up to five years and has set aside 3.5 million dollars for the initial year's funding.

Prospective applicants are asked to submit a letter of intent by March 1, 1989, to:

Mark Green, Ph.D.
Chief, Extramural Project Review Branch, NIAAA
16-C-20 Parklawn Building
5600 Fishers Lane
Rockville, Maryland 20857
Telephone: (301) 443-4375

The following office may be contacted for necessary application material:

National Clearinghouse for Alcohol and Drug Information
Reference Department
Box 2345
Rockville, Maryland 20852
Telephone: (301) 468-2600

This RFA is a one-time request for applications. Applicants who wish also to apply for consideration as a Coordinating Center should submit a separate application with the title, "Coordinating Center for Collaborative Studies on the Genetics of Alcoholism", RFA 89-AA-01A.

THE RFA LABEL FOUND IN THE PHS 398 KIT MUST BE AFFIXED TO THE BOTTOM OF THE FACE PAGE OF THE ORIGINAL COMPLETED APPLICATION FORM, PHS 398. FAILURE TO USE THIS LABEL COULD RESULT IN DELAYED PROCESSING OF YOUR APPLICATION SUCH THAT IT MAY NOT REACH THE REVIEW COMMITTEE IN TIME FOR REVIEW. THERE WILL BE NO OBLIGATION TO REVIEW SUCH APPLICATIONS.

Send or deliver the completed application and four (4) signed, exact photocopies of it to:

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Westwood Building, Room 240
National Institutes of Health
Bethesda, Maryland 20892**

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Applications must be received by April 3, 1989. An application not received by this date will be considered ineligible.

INQUIRIES

For further information contact:

W. Sue Badman Shafer, Ph.D.
Acting Director, Division of Basic Research, NIAAA
14-C-10 Parklawn Building, 5600 Fishers Lane
Rockville, Maryland 20857
(301) 443-2530

AIDS THERAPIES TARGETED TO PREVENT THE ESTABLISHMENT OF LATENCY OR SUPPRESS PROVIRUS INDUCTION

RFA AVAILABLE: 89-AI-06

P.T. 34; K.W. 0715008, 1002045, 0715125, 0760015

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: February 1, 1989
Application Receipt Date: March 28, 1989

NIAID is playing a central role in the investigation of methods to treat the Acquired Immunodeficiency Syndrome, or AIDS. Molecular processes associated with the establishment of latency and with subsequent induction of HIV expression play a pivotal role in the progression of AIDS. If the onset of latency can be prevented, or if the latent stage can be extended indefinitely, the host may be spared cell destruction and various immune system impairments. New modalities for treatment of HIV infection that consider the reservoir of the virus in latently infected cells and the process(es) by which HIV latency and activation occurs need to be developed.

OBJECTIVES AND SCOPE

NIAID invites applications for individual research project (R01) grants to elucidate the viral and cellular factors involved in the establishment of latency and events contributing to the progression from dormant to productive infection which impact on anti-HIV therapy. Aggressive research is necessary to: (i) delineate the events leading to establishment and maintenance of latent HIV infection; (ii) define the processes associated with activation of gene expression from a dormant state which culminate in productive infection; (iii) define the viral and cellular genes and gene products necessary for these processes; (iv) design and develop in vitro model systems for delineating events associated with the establishment of latency and those involved in the induction of HIV expression; and (v) utilize the knowledge gained from this research to design and develop new modalities for anti-HIV therapy that may prevent the integration of HIV provirus, block activation of the provirus from a dormant state or otherwise impede virus replication. Research plans solely to evaluate various compounds for their ability to block the establishment of latency or suppress HIV activation are not considered responsive to this announcement.

Several HIV genes have been implicated in the establishment of latency and/or in the activation of HIV gene expression from latently infected cells. These include Integrase, Nef, tat and rev genes. Cellular factors may also play a role in the regulation of HIV expression. Examples of cellular activators/repressor include: (i) UBP-1, a HeLa cell nuclear factor, recently shown to bind to TAR and presumed to play a role in Tat-mediated transactivation; (ii) EBP-1 and LBP-1, also HeLa cell nuclear factors, which bind to the HIV enhancer and leader sequence, respectively, and have been implicated in virus activation; and (iii) NF-kB, a known activator that binds directly to the viral enhancer sequence. Identification and analysis of these and other viral and cellular genes or factors and their interplay in the

establishment of HIV latency or activation of HIV replication are necessary to allow a targeted anti-viral approach devoid of cytotoxicity.

The information gained through this research should be exploited to design new modalities for anti-HIV therapy that may prevent the establishment of latency and/or the activation of HIV expression.

MECHANISM OF SUPPORT

The NIAID is expected to receive primary assignment on all applications (R01) and to allocate \$704,000 (total costs) for the initial year of funding of applications received in response to this RFA. The award of grants pursuant to this RFA is contingent upon the continuing availability of funds for this purpose and upon receipt of a sufficient number of applications of high scientific merit.

APPLICATION SUBMISSION

Eligibility: Any domestic or foreign institution, university, medical college, hospital, and laboratory or other public, private or for profit institutions are eligible.

Letter of Intent: Prospective applicants are asked to submit, by February 1, 1989, a letter of intent that includes a descriptive title and a description (not to exceed one page) of the proposed research.

Submission: The regular research grant application form PHS-398 (rev. 9/86) must be used in applying. These forms are available at most institutional business offices or from the Division of Research Grants, NIH, 9000 Rockville Pike, Bethesda, Maryland 20892. To identify responses to this announcement, check "yes" and put "AIDS THERAPIES TARGETED TO PREVENT THE ESTABLISHMENT OF LATENCY OR SUPPRESS PROVIRUS INDUCTION" under item 2 on page 1 of the grant application. The RFA label provided with the instructions must be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of your application such that it may not reach the review committee in time for review.

The completed original application and thirty two (32) copies should be mailed to:

DRG AIDS Coordinator
Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, Maryland 20892**

Applications must be received by March 28, 1989. Awards will be based on scientific merit and the uniqueness of the proposed project. Funding around September 30, 1989, is anticipated.

INQUIRIES

A more detailed RFA may be obtained from:

Nava Sarver, Ph.D
Developmental Therapeutics Branch
AIDS Program, NIAID, NIH
6003 Executive Boulevard
Rockville, Maryland 20892
Telephone: (301) 496-8197

DEVELOPMENT OF SMALL ANIMALS EXPRESSING HUMAN IMMUNODEFICIENCY VIRUS GENES AS MODELS FOR THERAPY

RFA AVAILABLE: 89-AI-05

P.T. 34; K.W. 0715008, 1002002, 0765033, 0740023, 0760015

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: February 1, 1989
Application Receipt Date: March 28, 1989

The National Institute of Allergy and Infectious Diseases (NIAID) is playing a central role in the investigation of methods to treat the disease known as Acquired Immunodeficiency Syndrome or AIDS. Non-human primate systems are essential for the evaluation of potential therapies. Small animal viruses

currently employed in these systems differ from HIV and may not be fully predictive of drug efficacy in humans. Additional research is required to develop new small animal models that contain and express the HIV genome or portions of the genome to facilitate evaluation of potential therapies and to further our understanding of the pathogenesis of AIDS.

OBJECTIVES AND SCOPE

The NIAID invites applications for research grants to develop and investigate small animal models that contain and express the HIV or SIV genome or portions thereof for evaluation of the role of the HIV genome and/or specific HIV genes in the pathogenesis of AIDS and for testing potential AIDS therapies. Development and utilization of models such as: (i) transgenic animals that introduce the HIV or SIV genome or portions of the genome into small animals; (ii) rabbits infected with HIV; and (iii) mice with severe combined immunodeficiency disease (SCID) reconstituted with human cells and infected with HIV are considered responsive to this RFA and are expected. Investigators, however, are not constrained to these approaches. Development of any small animal model which expresses an HIV gene product or products (particularly tat, rev, reverse transcriptase, integrase, and proteinase alone or in combination), or which results in expression of HIV- or SIV-induced cytopathology is encouraged. It may also be possible to utilize certain enhancers that allow the targeted expression of genes within tissues infectable by HIV, particularly T cells and monocytes/macrophages. Models which include control of HIV gene expression by an inducible promoter may be particularly advantageous. Since this RFA further encourages the use of these small animal models for testing potential drugs, immunomodulators, biologics, and other therapies, it is critical that viral or gene expression be sufficient to allow monitoring of drug effectiveness; it may be necessary to include a reported gene or other methods to facilitate detection.

Investigators responding to this RFA will be encouraged to: (i) make available to the U.S. Government the developed models for the purpose of government-sponsored screening and analysis of potential therapies for AIDS, and (ii) evaluate their model for potential use by testing in a double-blind study 2 or more key drugs or biologics per year provided by the NIAID. Principal Investigators funded under this RFA will be required to attend a meeting at NIH once a year. Applications which involve collaborative scientists or institutions are encouraged but not required. Research must be performed according to established NIH guidelines.

MECHANISM OF SUPPORT

The NIAID is expected to receive primary assignment on all applications (R01) and has allocated \$900,000 for the initial year of funding of applications received in response to this RFA. The award of grants pursuant to this RFA is contingent upon the continuing availability of funds for this purpose. Three to five year awards are anticipated, to allow for long-term support for the development and evaluation of the new models.

APPLICATION SUBMISSION

Eligibility: Any domestic or foreign institution, university, medical college, hospital, and laboratory or other public, private or for-profit institutions are eligible.

Letter of Intent: Prospective applicants are asked to submit, by February 1, 1989, a letter of intent that includes a descriptive title and a description (not to exceed one page) of the proposed research.

Submission: The regular research grant application form PHS 398 (rev. 9/86) must be used in applying. These forms are available at most institutional business offices or from the Division of Research Grants, NIH, 9000 Rockville Pike, Bethesda, Maryland 20892. To identify responses to this announcement, check "yes" and put "DEVELOPMENT OF SMALL ANIMALS EXPRESSING HUMAN IMMUNODEFICIENCY VIRUS GENES AS MODELS FOR THERAPY" under item 2 on page 1 of the grant application. The RFA label provided with the instructions must be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of your application such that it may not reach the review committee in time for review.

The completed original application and thirty two (32) copies should be mailed to:

DRG AIDS Coordinator
Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, Maryland 20892**

Applications must be received by March 28, 1989. Awards will be based on scientific merit and the uniqueness of the proposed techniques and projects. Several different models are expected to be funded. Funding on or around September 30, 1989, is anticipated.

INQUIRIES

A more detailed RFA may be obtained from:

Margaret Johnston, Ph.D.
Head, Targeted Drug Discovery Section
Developmental Therapeutics Branch
AIDS Program, NIAID
6003 Executive Boulevard
Bethesda, Maryland 20892
Telephone: (301) 496-8197

PROGRAM PROJECTS IN TRANSPLANTATION IMMUNOLOGY

RFA AVAILABLE: 89-AI-07

P.T. 34; K.W. 0710125, 0710065, 0745040

National Institute of Allergy and Infectious Diseases

Letter of Intent Date: April 17, 1989
Application Receipt Date: June 14, 1989

BACKGROUND INFORMATION

The Genetics and Transplantation Biology Branch of the Allergy, Immunology and Transplantation Program* of the National Institute of Allergy and Infectious Diseases (NIAID) supports fundamental studies and applied research in immunogenetics and transplantation immunology. Program Projects in Transplantation Immunology are intended to stimulate collaboration between transplant clinicians and basic immunologists to evaluate the immune response to organ and bone marrow allografts, elucidate the important cellular and molecular events of both the induction and effector phases of the alloimmune response and to develop improved immunosuppressive therapeutic procedures. This Request for Applications (RFA) is intended to encourage the development of proposals from collaborating investigators and to coordinate the submission and review of new program project applications. Three such Program Projects are currently funded. In 1990, NIAID plans to award at least two new Program Projects in Transplantation Immunology.

*formerly Immunology, Allergic and Immunologic Diseases Program

RESEARCH GOALS AND SCOPE

Applications should heavily emphasize collaboration in research between transplant clinicians and immunologists, and the application of the most up-to-date concepts and techniques of immunology to the evaluation of the immune system of recipients in all circumstances attendant to the transplantation. The application should describe a multidisciplinary research program that has a well-defined central research focus or objective. As with other program projects, the individual projects of which they consist should be interrelated, all contributing to the program objective.

The objectives of the research should be: (a) the characterization of the status of the immune systems, specifically of the immunoregulatory balance (1) prior to transplantation in its relatively normal state, or, if the transplant is occasioned by a disturbance of the immune state, in the causative disordered state, (2) in the course of transplant preparation which consists of the reduction of responsiveness (immunosuppression) or the induction of tolerance, (3) postoperatively during maintenance immunosuppression as the graft becomes established, (4) during rejection episodes, and (5) during treatment of rejection; and (b) the modulation of immunological activity on the basis of the information so obtained.

MECHANISMS OF SUPPORT

Program project grants are awarded to an institution in behalf of a program director for the support of a broadly-based multidisciplinary, long-term, research program which has a specific major objective or basic theme. A program project generally involves the organized efforts of groups of investigators who conduct research projects related to the overall program objective.

The grant can provide support for the projects and for certain core resources shared by individuals in a program where the sharing facilitates the total research effort. Each component project supported under a program project grant is expected to contribute to and be directly related to a common theme; the projects should demonstrate an essential element of unity and interdependence. In fiscal year 1990, NIAID plans to award at least two new program projects at approximately \$500,000 direct costs for the initial year.

METHOD OF APPLYING

Before preparing an application, the prospective applicant should request a copy of the Information Brochure: Program Project and Center Grants, NIAID, from:

Dr. Nirmal K. Das
Executive Secretary
Allergy, Immunology and Transplantation
Research Committee
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Westwood Building, Room 3A-07
Bethesda, Maryland 20892
Telephone: (301) 496-7966

STAFF CONTACT

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

William R. Duncan, Ph.D.
Chief, Genetics and Transplantation Branch, AITP
National Institute of Allergy and Infectious Diseases
Westwood Building, Room 754
National Institutes of Health
Bethesda, Maryland 20892
Telephone: (301) 496-5598
Telefax Number: (301) 480-3780

Prospective applicants are encouraged to submit a one-page letter of intent that includes a descriptive title and identification of any other participating institutions. The Institute requests such letters by April 17, 1989, for the purpose of providing an indication of the number and scope of applications to be received. Letters of intent should be directed to Dr. Duncan at the address shown.

THE RFA LABEL AVAILABLE IN THE 9/86 REVISION OF APPLICATION FORM 398 MUST BE AFFIXED TO THE BOTTOM OF THE FACE PAGE. FAILURE TO USE THIS LABEL COULD RESULT IN DELAYED PROCESSING OF YOUR APPLICATION SUCH THAT IT MAY NOT REACH THE REVIEW COMMITTEE IN TIME FOR REVIEW.

LONG TERM CULTIVATION AND PRESERVATION OF HUMAN IMMUNOCYTE PROGENITORS

RFA AVAILABLE: 89-AI-08

P.T. 34; K.W. 0780005, 0780015

National Institute of Allergy and Infectious Diseases

Letter of Intent Date: April 17, 1989
Application Receipt Date: June 14, 1989

BACKGROUND INFORMATION

The National Institute of Allergy and Infectious Diseases (NIAID) is soliciting regular research project grant (R01) applications that are designed to successfully isolate, cultivate, characterize and preserve human lymphoid progenitor cells. Both the totipotent hematopoietic stem cells and immunocyte-lineage-committed progenitor cells are of interest. The availability of such ancestral cells, in homogeneous or near-homogeneous condition (e.g., 50 percent "pure"), along with the methodology to prepare highly enriched ancestral cells should offer enormous therapeutic potential. Some examples include: (a) lymphocyte replacement therapy in certain immunodeficiency disorders resulting from genetic, viral, neoplastic or geriatric causes; (b) selective in vitro immunization to obtain antigen-primed lymphocytes that could be used therapeutically in cases of infections with weakly immunogenic or cryptic pathogens; (c) acquisition of B lymphocytes in numbers suitable for appropriate antigen stimulation/selection, or selective gene transfection, preparatory to fusion with human myelomas for the purpose

of developing human, monoclonal antibody producing hybridomas; and (d) preparation of monoclonal antibodies against stage-specific, and possibly clone-specific, antigens that could be used for therapeutic enhancement or deletion of designated subsets of immunocytes. Furthermore, the ability to cultivate lymphocyte ancestors should lead rapidly to answers to fundamental questions concerning the lineage and differentiation of various subsets of lymphocytes and the precise roles of essential cytokines in lymphocyte differentiation and growth.

RESEARCH GOALS AND SCOPE

Recent publications have demonstrated that murine hematopoietic stem cells can be isolated in homogeneous condition and that they can be maintained for long periods in vitro. Human bone marrow hematopoietic stem cells have been enriched several hundred-fold. Furthermore, new methods permit the growth and differentiation of human stem cells and lymphoid progenitors in severe combined immunodeficient (SCID) mice. Most of the major technical problems that might prevent successful, long-term storage, at ultra-low temperature, of stem cells and lymphoid progenitors have been solved, although there is need for further refinement of the procedure. Thus, there is the real possibility that healthy stem cells could be isolated, grown in vitro and stored for as long as necessary awaiting their use in a therapeutic procedure. What is needed now are concerted and dedicated efforts to: (a) determine the most effective and efficient procedure for enriching progenitor cells having various differentiative potentialities; (b) achieve enrichment on, at least, a moderately large scale; (c) improve and optimize in vitro cultivation media and procedures; and (d) define and characterize, both morphologically and functionally, distinct subsets and differentiative stages of lymphoid ancestral cells.

MECHANISMS OF SUPPORT

The support mechanism for this program will be the individual research project grant. The NIAID plans to support at least five awards at a direct cost of approximately \$150,000 each for the first year. Up to five years of support is anticipated. Support is contingent upon receipt of applications of substantial scientific merit and availability of funds.

LETTER OF INTENT

Prospective applicants are encouraged to submit a one-page letter of intent that includes a descriptive title and identification of any other participating institutions. The Institute requests such letters for the purpose of providing an indication of the number and scope of applications to be received. A letter of intent is not binding. It will not enter into the review of any application subsequently submitted and is not a necessary requirement for application. If submitted, the letter of intent should be received no later than April 17, 1989.

Inquiries and letters should be directed to:

Joseph F. Albright, Ph.D.
Chief, Basic Immunology Branch, AITP
National Institute of Allergy and Infectious Diseases
Westwood Building, Room 757
Bethesda, Maryland 20892
Telephone: (301) 496-7551
Telefax Number: (301) 480-3780

REVIEW PROCEDURES AND CRITERIA

The receipt date for applications will be June 14, 1989. They will undergo initial peer review in October by an initial review group to be convened by the Program and Project Review Branch, Extramural Activities Program, NIAID, and subsequent review by the National Advisory Allergy and Infectious Diseases Council in January 1990. March 1, 1990, will be the earliest starting date for approved applications.

CONSEQUENCES OF LACK OF RESPONSIVENESS TO THE RFA OR LATE SUBMISSION

Formal applications that are not received by June 14, 1989, or are considered to be non-responsive to the RFA will be entered into the next review cycle as regular competing applications.

METHOD OF APPLYING

Use the standard research grant application form PHS 398 (rev. 9/86) which may be obtained from the institution's business office or from the Division of

Research Grants, NIH. THE RFA LABEL AVAILABLE IN THE 9/86 REVISION OF THE APPLICATION FORM 398 MUST BE AFFIXED TO THE BOTTOM OF THE FACE PAGE. FAILURE TO USE THIS LABEL COULD RESULT IN DELAYED PROCESSING OF YOUR APPLICATION SUCH THAT IT MAY NOT REACH THE REVIEW COMMITTEE IN TIME FOR REVIEW. For purposes of identification and processing, the RFA number "89-AI-08" and the words "LONG TERM CULTIVATION AND PRESERVATION OF HUMAN IMMUNOCYTE PROGENITORS" should be typed in item 2 on the face page of the application. The original application, including one set of the appendix, and four copies should be submitted to:

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

To expedite the review, two exact copies of the application and four sets of the appendices should be sent directly to:

Dr. Nirmal K. Das
Executive Secretary
Transplantation Biology and Immunology Subcommittee
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Westwood Building, Room 3A-07
Bethesda, Maryland 20892

ERRATUM

SPECIALIZED CENTERS FOR NURSING RESEARCH (RFA 89-NR-01) EXPLORATORY CENTERS FOR NURSING RESEARCH (RFA 89-NR-02)

P.T. 04; K.W. 0785130, 0710030

National Center for Nursing Research

These two RFAs were announced in the NIH Guide for Grants and Contracts on November 18, 1988 (Vol. 17, No. 38). This erratum is to correct a section in the Request for Application that was distributed by the National Center for Nursing Research. Please substitute the following paragraph for item II, B (page 4).

B. Eligibility for Submission of Applications

Institutions eligible for Specialized Center Grants are schools of nursing or departments of nursing within clinical settings at which there are at least three principal investigators with any PHS, or comparable peer reviewed research project (R01, P01) grants with a minimum of \$200,000 per year in research project funds in a specific area of nursing research. The Specialized Center Grant will have at least two new research projects proposed as part of this application. No more than one Specialized Center Grant will be made to any one institution (or, for multi-campus institutions, no more than one to each campus). Joint applications may also be submitted by neighboring institutions which demonstrate a high degree of multidisciplinary collaboration.

CLINICAL INVESTIGATOR AWARD IN GERIATRIC OTOLARYNGOLOGY (K08)

P.T. 34; K.W. 0785160, 0710010, 0715050

National Institute on Aging
National Institute of Neurological and Communicative Disorders and Stroke

This announcement is to correct the application deadline for the Clinical Investigator Award in Geriatric Otolaryngology (K08) which was published in the NIH Guide for Grants and Contracts, Vol. 17, No. 37, page 5, November 11, 1988. Applications for the CIA must be received by February 1, June 1 (rather than July 1 as erroneously stated), and October 1. All other information contained in the original announcement remains the same.