NIH GUIDE

For Grants and Contracts

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 17, No. 44
December 30, 1988

Vol. 17, No. 44, December 30, 1988

NOTICES

DATED ANNOUNCEMENTS (RFAs AND RFPs)

ONGOING PROGRAM ANNOUNCEMENTS

NOTICES

SUPERCOMPUTING RESOURCES AVAILABLE TO BIOMEDICAL RESEARCHERS AT THE PITTSBURGH SUPERCOMPUTING CENTER

Division of Research Resources

Grants are available to enable biomedical researchers to use the Pittsburgh Supercomputing Center's (PSC) Cray Y-MP/832 through a program funded by the Biomedical Research Technology Program, Division of Research Resources.

Starter grants of 3 service units are available for feasibility studies or code conversion and optimization. A limited number of larger grants are also available to experienced supercomputing researchers. Prospective grantees should demonstrate a need for supercomputing facilities; the proposed research must be biomedical and non-proprietary; grantees must be faculty members or post-doctoral fellows. Graduate students may be designated as users on any grant. For application forms and additional information, call or send mail to:

Cherolyn A. 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).

DATED ANNOUNCEMENTS (RFAs AND RFPs)

NOTICE OF AVAILABILITY OF SUPPLEMENTAL DRUG ABUSE RESEARCH FUNDS

National Institute on Drug Abuse

The Anti-Drug Abuse Act of 1988 (Public Law 100-690) was signed into law by the President on November 18, 1988. This law contains important provisions for specific new and expanded research initiatives, as well as additional appropriations for intensified research efforts in all basic science, clinical, and epidemiological areas of drug abuse research. The Act provides $30 million dollars in supplemental research funds, of which at least $10 million dollars is to be used for drug development, and the remainder for the enhancement of the general research programs of the Institute including program evaluations and data collection activities.

The availability of these additional funds to expand the scope and depth of drug abuse research comes at a critical time. Developments in several areas of research are either ripe for immediate exploitation, or have surfaced as important areas for the acquisition of new knowledge, fresh clinical approaches to outreach and treatment, and innovations in biomedical science and technology.

The Institute has recently issued (October 1988) a revised General Research Announcement. This Announcement contains important information on extant programs, and on those areas of research the Insitute considers important for increased support and expansion of activities. IMPORTANT: IF YOU INTEND TO SUBMIT AN APPLICATION FOR CONSIDERATION FOR FUNDING WITH SUPPLEMENTAL FUNDS MADE AVAILABLE UNDER THE ANTI-DRUG ABUSE ACT OF 1988 YOU MAY SUBMIT APPLICATIONS UP TO A MARCH 1, 1989 RECEIPT DATE. THIS IS A ONE MONTH EXTENSION OF THE FEBRUARY 1 RECEIPT DATE THAT IS APPLICABLE TO ALL OTHER NIDA PROGRAM ANNOUNCEMENTS. IN ORDER TO QUALIFY FOR THIS EXTENDED DEADLINE, YOU MUST WRITE "ANTI-DRUG ABUSE ACT OF 1988" ON LINE 2 ON THE PHS 398 FORM. This revised NIDA General Research Announcement may be obtained by contacting NIDA's Grants Management Branch at (301) 443-6710. Potential applicants may also write to:

Grants Management Branch
National Institute on Drug Abuse
5600 Fishers Lane, Room 10-25
Rockville, Maryland 20857

In addition to the $30 million appropriated in support of expansion of the ongoing research effort, other new programmatic initiatives are in preparation in response to specific research areas identified in the Act. These new programs will be announced shortly, either through Program Announcements (PAs), Requests for Applications (RFAs), or Requests for Proposals (RFPs). Receipt dates for applications/proposals for these initiatives will be specified in the announcements. For additional information, contact Dr. Kursheed Asghar Chief, Extramural Policy and Project Review Branch, telephone (301) 443-2755.

ADAMHA SMALL INSTRUMENTATION GRANT PROGRAM

Alcohol, Drug Abuse, and Mental Health Administration

The Alcohol, Drug Abuse, and Mental Health Administration is announcing the establishment of an ADAMHA Small Instrumentation Program (ASIP). These grants were authorized by Congress for FY 1989 in Section 501(m) of the Public Health Service Act, as amended by P.L. 100-690, in response to findings that much of the research instrumentation in the Nation's principal universities is either obsolete or poorly maintained. These findings, documented in several reports, identified the need for upgrading equipment currently in use. The most significant need was for relatively low-cost pieces of equipment. To address this problem, ADAMHA is establishing the Small Instrumentation Program. Awards are made under authority of Titles III and V of the PHS Act as amended. Funds will be provided to research-intensive institutions currently receiving ADAMHA research support. The ASIP is not intended to replace requests for equipment in applications for individual research projects. Rather, it is intended to help fund items of equipment which are difficult to justify within the context of an individual research project, but which will upgrade the institution's research infrastructure.

The ADAMHA program has a similar purpose to the National Institutes of Health Small Instrumentation Program, but will operate separately and under slightly different guidelines because of differences in the infrastructure support mechanisms available to the two agencies.

The ADAMHA program will be funded in FY 1989 at $2,050,000. The program provides awards which range from $20,000 to $60,000 to eligible institutions. Eligible institutions or institutional components are those that had, in FY 1988, three or more active ADAMHA research grants (types R01, R23, R29, or R37), or cooperative agreements (types U01 or U10) totaling at least $640,000 in direct costs. The amount for which an institution may apply was calculated by a formula based on the $2,050,000 available for the program this year and on the dollar amount of ADAMHA-sponsored research support in the eligible mechanisms at the institution.

Each eligible institution may submit ONLY ONE application that incorporates all appropriate equipment requests from that institution. Thus, it is essential that institutional officials publicize the availability of ASIP funds, so that ADAMHA-supported investigators in need of small research instruments are provided the opportunity to indicate their needs for such equipment to the appropriate institutional official.

The equipment requested must be available for use by more than one project either currently or in the future. The primary user(s) of the equipment must be one or more principal investigators of active ADAMHA-supported research grants, and you must cite the specific projects in your application. No indirect costs will be provided and there will be no future year funding commitment. The requested funds may be for full or partial support of one or more pieces of equipment. In no case, however, may the total purchase price of a requested piece of equipment be less than $5,000 or more than $100,000 regardless of the source(s) of funding. If the total dollar amount of proposed equipment purchases exceeds the amount for which the institution is eligible, a statement must be submitted which indicates that the institution will provide the difference. Support from this program can not be used to purchase items exceeding $100,000 in cost, even if costs are shared. The equipment purchased must be the same as that specified in the ASIP application.

Applications must be received by February 23, 1989. Detailed application procedures have been sent to eligible institutions. Applications will be peer reviewed by a single ADAMHA-wide committee. The review criteria are: Degree of adherence to the terms of the letter of eligibility and adequacy of the justification provided for the equipment requested. The reviewers will determine whether or not the application is recommended for approval; no priority scores will be voted. Applications will be assigned to individual ADAMHA Institutes for consideration by their National Advisory Councils and for funding. The Institutes expect to make the awards during July.

Questions concerning this program, be directed to any of the following persons:

NIAAA
Dr. Louise Hsu
Division of Basic Research
National Institute on Alcohol Abuse and Alcoholism
Room 14C-20
Telephone: (301) 443-4223

NIDA
Dr. Stephen Szara
Division of Preclinical Research
National Institute on Drug Abuse
Room 10A-31
Telephone: (301) 443-6300

NIMH
Mr. James Moynihan
Division of Basic Sciences
National Institute of Mental Health
Room 11-95
Telephone: (301) 443-3107

Dr. Leonard Lash
Division of Clinical Research
National Institute of Mental Health
Room 10-95
Telephone: (301) 443-3264

Dr. Kenneth Lutterman
Division of Biometry and Applied Science
National Institute of Mental Health
Room 18C-26
Telephone: (301) 443-3685

The mailing address for the above individuals is:

5600 Fishers Lane
Rockville, Maryland 20857

DRUG RESISTANCE AND THE HUMAN IMMUNODEFICIENCY VIRUS

RFA AVAILABLE: 89-AI-13

National Institute of Allergy and Infectious Diseases

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

The National Allergy of Allergy and Infectious Diseases (NIAID) is playing a central role in investigating methods to treat viral diseases including the disease known as Acquired Immunodeficiency Syndrome (AIDS). The only drug approved to date for the treatment of AIDS is zidovudine (3'-azido-3'-deoxythymidine, AZT). Since the course of AIDS is usually measured in years, long-term antiviral therapy is anticipated.

Considerable variation in the nucleotide sequence of the human immunodeficiency virus (HIV), the causative agent of AIDS, isolated from a single individual has been observed and continues to be studied in great detail. This genetic diversity is believed to result, in part, from the error prone nature of the HIV reverse transcriptase (RT). It is not known if these variations affect the susceptibility of HIV to therapy with antiviral nucleosides. If differences do exist, the least susceptible strains may be selected for patients undergoing prolonged therapy with antiviral nucleosides.

Given both the error-prone nature of the HIV RT and the anticipated prolonged use of HIV RT inhibitors, the possibility that a drug resistant strain may emerge or has emerged is of concern. This potential problem raises an urgent need to understand the molecular mechanisms associated with HIV resistance to antiviral nucleosides, to devise and utilize methods to screen HIV isolates for antiviral resistance, and to identify therapies or combinations of therapies that overcome resistance.

OBJECTIVES AND SCOPE

The NIAID invites applications for research grants to investigate potential mechanisms by which drug resistant mutants of HIV may be identified and combatted. Investigators are encouraged to: (i) further our understanding of the molecular nature of potential resistance of HIV to zidovudine and other RT inhibitors; (ii) develop and utilize screens to detect the presence of resistant mutants; and (iii) evaluate therapies or combinations of therapies that may overcome acquired resistance in vitro.

Development of methods to screen for the presence of resistant mutants in vitro and in vivo is encouraged under this RFA. Improved DNA hybridization methods may be developed to evaluate susceptibility of HIV isolates to antiviral nucleosides in vitro. Screens based on hybridization techniques with specific probes could be used if specific areas or sequences of the RT gene are consistently associated with drug resistance. Other approaches to

detect the presence of RT mutants in vitro and in isolates from individuals undergoing antiviral therapy are strongly encouraged.

Development of a screen for resistant mutants may first require obtaining resistant mutants. In vitro mutagenesis of the HIV RT open reading frame would comprise one potent and rapid method for establishing structure-function relationships and identifying hot spots and mutations likely to confer drug resistance. Characterization of the kinetic properties of RT mutants in the presence and absence of specific nucleoside antivirals could be accomplished. Other innovative approaches are strongly encouraged.

When a mutant resistant to one antiviral nucleoside is obtained, the interaction of that mutant with other nucleoside antivirals alone or in combination with other therapies would yield valuable information useful in the design of therapeutic approaches for treating individuals that may harbor resistant strains. The NIAID AIDS Program will provide investigators with current potential treatments for testing against newly developed isolates, clones or RT protein when appropriate.

MECHANISM OF SUPPORT

The NIAID is expected to receive primary assignment on all applications (R01) and to allocate $616,000 (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. Three to five year awards are anticipated to allow for long-term support for the identification and evaluation of resistant strains or clones.

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 "DRUG RESISTANCE AND THE HUMAN IMMUNODEFICIENCY VIRUS" 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: 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:

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

STATISTICAL ISSUES IN AIDS RESEARCH

RFA AVAILABLE: 89-AI-012

National Institute of Allergy and Infectious Diseases

Letter of Intent Date: January 27,1989
Application Receipt Date: March 28,1989

The National Institute of Allergy and Infectious Diseases (NIAID) announces the availability of an RFA for funding statistical research related to the study of AIDS. This RFA (available on request) invites applications which consider research in areas pertaining to clinical trials of treatments or vaccines, epidemiologic studies, or laboratory investigations. Research involving mathematical models to predict the course of the epidemic or to further investigate certain aspects of the epidemic such as the latency period, the effect of behavior modifications, the effect of various types of screening programs, etc., is also within the scope of this announcement.

Awards will be made as individual research project (R01) grants. NIAID has set aside $500,000 in total costs for the initial year's funding, and awards will be made for up to three years. It is anticipated that up to 3 awards will be made. The earliest start date for the initial annual period will be September 30, 1989.

Investigators from any institution, foreign or domestic, are eligible to apply for this funding.

This RFA is available from the following:

Susan S. Ellenberg, Ph. D.
NIAID, AIDS Program
Biostatistics Research Branch
6003 Executive Blvd., Rm. 241P
Rockville, Maryland 20892
Telephone: (301) 496-0694

ANTIBODY DEPENDENT ENHANCEMENT OF LENTIVIRUS INFECTION: IMPLICATIONS FOR AIDS VACCINE DEVELOPMENT

RFA AVAILABLE: 89-AI-09

National Institute of Allergy and Infectious Diseases

Letter of Intent Date: March 17, 1989
Application Receipt Date: May 18, 1989

The National Institute of Allergy and Infectious Diseases (NIAID) announces the availability of an RFA for Antibody Dependent Enhancement of Lentivirus Infection. This RFA (available on request) invites individual research project (R01) grant applications from interested investigators to examine the occurrence and characteristics of antibodies which can enhance infection of monocytes by lentiviruses, particularly human (HIV) or simian (SIV) immunodeficiency viruses.

In vitro studies for both HIV and SIV, and limited in vivo animal studies for SIV, are contemplated. These studies should be directed toward establishing whether there exist specific enhancing epitopes on viral glycoproteins and whether enhancing antibodies are relevant to infection in the animal. Scientific approaches include establishing reliable assays for antibodies which enhance infection, development of assays utilizing primary monocyte/macrophage cells for measuring enhancing antibodies, occurrence of enhancing antibodies in seropositive individuals, specification of enhancing epitopes, determination of the mechanism of enhancement, and in vivo relevance of enhancing antibody.

Awards will be made as individual research project (R01) grants.

Investigators from any institution, foreign or domestic, are eligible to apply for funding. This RFA may be obtained from:

Alan M. Schultz Ph.D.
Chief, Basic Research Section
Vaccine Research and Development Branch
AIDS Program
6003 Executive Blvd., Room 236P
Rockville, Maryland 20892

THE ROLE OF CARBOHYDRATE IN IMMUNOLOGIC RESPONSE TO THE ENVELOPE GLYCOPROTEINS OF HIV OR RELATED IMMUNODEFICIENCY VIRUSES

RFA AVAILABLE: 89-AI-11

National Institute of Allergy and Infectious Diseases

Letter of Intent Date: March 17, 1989
Application Receipt Date: May 18, 1989

The National Institute of Allergy and Infectious Diseases (NIAID) announces the availability of an RFA for funding The Role of Carbohydrate in Immunologic Response to the Envelope Glycoproteins of HIV or Related Immunodeficiency Viruses. This RFA (available on request) invites applications to examine immunological responses to HIV and/or simian immunodeficiency virus (SIV) virions or glycoproteins which possess carbohydrate chains differing from wild type in number or composition. It will be important to obtain well-characterized variant glycoproteins, and then measure a variety of immune responses elicited by these modified antigens, comparing the strengths and extent of responses induced by either the native or variant glycoproteins. The intent is to obtain results on a wide variety of cellular as well as humoral responses, although not all applicants will be expected to propose many different kinds of immunological assays. Data on the effect of the presence or absence of all or part of the carbohydrate of viral proteins will be important in the design of genetically engineered vaccine candidates.

Awards will be made as individual Research Project (R01) grants. Investigators from any institution, foreign or domestic, are eligible to apply for funding. This RFA may be obtained from:

Alan M. Schultz Ph.D.
Chief, Basic Research Section
Vaccine Research and Development Branch
AIDS Program
6003 Executive Blvd., Room 236 P
Rockville, MD 20892

MOLECULAR BASIS FOR THE SELECTIVITY OF DIFFERENT ANTIVIRAL THERAPIES

RFA AVAILABLE: AI-89-10

National Institute of Allergy and Infectious Diseases

LETTER OF INTENT: February 1, 1989 APPLICATION RECEIPT DATE: MARCH 28, 1989

The National Institute of Allergy and Infectious Diseases (NIAID) is playing a central role in investigating methods to treat viral diseases including the Acquired Immunodeficiency Syndrome (AIDS). The only drug currently approved for treatment of AIDS is a nucleoside analogue, zidovudine (3'-azido-3'-deoxythymidine, AZT).

Zidovudine and other drugs presently targeted for introduction into clinical trials or already in clinical trials are analogues of endogenous substances. These analogues are metabolized by the same metabolic pathways and utilize the same precursor/cofactor pools as the normal endogenous substances. The optimum therapeutic agent will be that one which produces the highest intracellular concentration of antiviral agent without disrupting the normal function/cycling of the analogous endogenous substances.

The targeted development of optimal nucleoside analogues is dependent upon a thorough understanding of the effect of the therapeutic agent on endogenous purine/pyrimidine pools and activity of enzymes involved in the formation/utilization of these pools. The presence and activity of these components, however, is highly dependent upon cell type and hence aggressive research is required to define the kinetics of metabolism of nucleosides and other endogenous cellular components in various cell types from different research animals and to investigate the complex interrelationship between therapeutic analogues and their endogenous counterparts.

OBJECTIVES AND SCOPE

The NIAID invites applications for research grants to investigate molecular mechanisms of action of potential AIDS therapies and how these agents interact with endogenous metabolic pathways that metabolize the therapeutic agents. Investigators are encouraged to: (a) study kinetics of intracellular metabolism of endogenous substances and how potential therapies affect this normal metabolism; (b) study the metabolism of potential therapeutic agents

and the selective distribution of those metabolites to target tissues in the body; and (c) study the potential interactions that may occur at the molecular level when two or more potential therapies are used in combination.

Our understanding of how therapeutic interventions potentially interact with normal intracellular metabolism and function has been insufficiently studied and only recently appreciated for its potential importance. Thus the feedback inhibition exerted by zidovudine triphosphate on the size and utilization of thymidine triphosphate pools is only now being appreciated for its potential effect on cell viability and function. The difference in such interactions in virus infected and noninfected cells may form the basis for a differential effect of certain specifically targeted antiviral agents. However, prior to the optimum development of specific antiviral therapies, it is necessary to understand the kinetics and mechanics of intracellular metabolites/metabolism which might be affected by the potential therapy. An understanding of such molecular metabolism is the objective of this RFA.

Complicating the development of specifically targeted antiviral therapy drugs is the fact that the size and kinetics of various metabolic pools differs among various cell types. Thus the kinetics of purine metabolism, for example, may differ from bone marrow precursor cells to macrophages to epithelial cells of the gastrointestinal tract. A thorough understanding of the differences in intracellular metabolism among the various target cells of the AIDS virus and thus the target of potential therapies, is essential for any targeted drug development program to succeed.

Letter of Intent: Prospective applicants are encouraged to submit a one-page letter of intent that includes a brief description of the thrust of the research activities and identity of the principal investigator or other key personnel, if known. 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, will not enter into the review of any application subsequently submitted, and is not a necessary requirement for application.

APPLICATION SUBMISSION

Eligibility: Universities, medical colleges, hospitals, and laboratories or other public, private or for-profit institutions are eligible.

Submission: Use the regular research grant application form PHS 398 that is available in business offices of most research institutions or from the Division of Research Grants (DRG), NIH. To identify responses to this announcement, check "yes" and put "MOLECULAR BASIS FOR SELECTIVITY OF DIFFERENT ANTIVIRAL THERAPIES" under item 2 on page 1 of the grant application.

THE RFA LABEL AVAILABLE IN THE 9/86 REVISION OF THE APPLICATION FORM 398 MUST BE AFFIXED TO THE BOTTOM OF THE FACING PAGE.

The complete original application and 32 copies should be mailed to:

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

Applications must be received by March 28, 1989.

MECHANISM OF SUPPORT

The NIAID is expected to receive primary assignment on all applications submitted in response to this RFA and has allocated $440,000 for the initial year of funding of applications received in response to this RFA. Two to four awards are anticipated although the number of awards to be made is dependent upon receipt of a sufficient number of applications of high scientific merit and the uniqueness and diversity of the proposals received. The earliest possible award date is September 30, 1989.

INQUIRIES

A more detailed RFA may be obtained from:

Charles L. Litterst, Ph.D., Acting Head, Drug Development Section
Developmental Therapeutics Branch, AIDS Program
National Institute of Allergy and Infectious Diseases
6003 Executive Boulevard
Bethesda, Maryland 20892
Telephone: (301) 496-0636

STUDIES OF SUICIDE AND SUICIDAL BEHAVIOR

P.T. 34; K.W. 0404020, 0411005, 0785055, 0404000, 0745027

National Institute of Mental Health

The National Institute of Mental Health (NIMH) is inviting grant applications from interested investigators for research on suicide and suicidal behavior across all age groups. NIMH encourages applications from investigators to study the epidemiology, psychopathology, biological risk factors, clinical course and treatment, and prevention of suicide and suicidal behavior. Applicants may request support for up to 5 years (with the exception of the small grant applications which are limited to 1 year). Applications in response to this announcement will be accepted under the usual Public Health Service receipt dates. Support is available through applications for a traditional research project, small grant, First Independent Research Support and Transition (FIRST) award, Research Scientist Development Award (RSDA), and National Research Service Award (NRSA). Potential applicants wishing to seek further information should contact:

Eve K. Moscicki, Sc.D., M.P.H.
Epidemiology and Psychopathology Branch
Division of Clinical Research
Room 10C-05
Telephone: (301) 443-3774

Irma S. Lann, M.Ed.
Child and Adolescent Disorders Research Branch
Division of Clinical Research
Room 10-104
Telephone: (301) 443-5944

Peter Nuehrer, Ph.D.
Prevention Research Branch
Division of Clinical Research
Room 14C-02
Telephone: (301) 443-4283

Arlene P. Hegg, M.D.
Mood, Anxiety, and Personality Disorders Research Branch
Division of Clinical Research
Room 10C-24
Telephone: (301) 443-4525

Kelly Kelleher, M.D., M.P.H.
Biometric and Clinical Applications Branch
Division of Biometry and Applied Sciences
Telephone: (301) 443-1330

H. Alice Lowery
Schizophrenia Research Branch
Division of Clinical Research
Room 10C-06
Telephone: (301) 443-3524

Nancy E. Miller, Ph.D.
Mental Disorders of the Aging Research Branch
Division of Clinical Research
Room 11C-03
Telephone: (301) 443-3948

Ellen Stover, Ph.D.
AIDS Coordinator
Office of the Director
Room 17C-06
Telephone: (301) 443-7281

The mailing address for all of the above is:

National Institute of Mental Health
Parklawn Bulding
5600 Fishers Lane
Rockville, Maryland 20857

ADAMHA SCIENTIST DEVELOPMENT AWARD and ADAMHA SCIENTIST DEVELOPMENT AWARD FOR CLINICIANS

P.T. 34; K.W. 0404003, 0404009, 0715095, 0785035

National Institute of Mental Health
National Institute on Alcohol Abuse and Alcoholism
National Institute on Drug Abuse

The Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA), which includes the National Institute of Mental Health (NIMH), the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and the National Institute on Drug Abuse (NIDA), announces the ADAMHA Scientist Development Award (SDA) and the ADAMHA Scientist Development Award for Clinicians (SDAC). The SDA and SDAC are awards to foster the development of outstanding scientists and enable them to expand their potential for making important contributions to the fields of alcoholism, drug abuse, or mental health (ADM) research. The SDA is for highly promising developing scientists who need further supervised research experience in order to undertake independent research. The SDA provides 5 years of support; in exceptional circumstances, an established account that the candidate has been trained primarily as a clinician and thus may possess only minimal research skills. Such an individual must show genuine commitment to a research career to justify the need for a 5-year development award.

The SDA and SDAC will each provide the grantee institution up to $45,000 per year toward the employee's full-time salary, excluding fringe benefits, consistent with the percentage of time the candidate proposes to devote to the grant. In addition to salary support, funds up to $35,000 in the aggregate may be requested for each year to pay for research and/or career development support expenses. Please review the announcements for detailed information on salary and research and/or career development expenses.

In FY 1989, approximately $1,900,000 will be available from NIMH, $920,000 will be available from NIAAA, and $1,000,000 will be available from NIDA for SDAs and SDACs.

The SDA and SDAC replace the Research Scientist Development Award - Level I (K01) (ADAMHA), and the Physician Scientist Award (K11) (NIMH) and Clinical Investigator Award (K08) (NIMH). Applications for these three awards will no longer be accepted. The awards will be phased out as presently funded grants terminate.

The initial receipt date for application for these awards will be March 15, 1989. Thereafter, dates for the submission of applications and review cycles will be according to the usual Public Health Service schedule for new applications. Potential applicants interested in obtaining further information should contact one of the following:

NIAAA

Sue Shafer, Ph.D.
Acting Director
Division of Basic Research
Room 14C-10
Telephone: (301) 443-2530

Richard K. Fuller, M.D.
Director
Division of Clinical and Prevention Research
Room 16C-10
Telephone: (301) 443-1207

Mary Dufor, M.D., M.P.H.
Chief, Epidemiology Branch
Division of Biometry and Epidemiology
Room 14C-26
Telephone: (301) 443-4897

NIDA

Marvin Snyder, Ph.D.
Director
Division of Preclinical Research
Room 10A-31
Telephone: (301) 443-6480

Roy W. Pickens, Ph.D.
Director
Division of Clinical Research
Room 10A-38
Telephone: (301) 443-6697

Edgar Adams, Sc.D.
Director
Division of Epidemiology and Statistical Analysis
Kenneth G. Lutterman, Ph.D.
Associate Director
Division of Biometry and Applied Sciences
Room 18C-26
Telephone: (301) 443-3685

Stanley F. Schneider, Ph.D.
Associate Director
Division of Basic Sciences
Room 11-95
Telephone: (301) 443-4347

Leonard Lash, Ph.D.
Associate Director for Research Training
Division of Clinical Research
Room 10-95
Telephone: (301) 443-3264

The mailing address for all of the above is: Parklawn Building, 5600 Fishers Lane, Rockville, Maryland 20857

INVESTIGATIONS INTO THE PATHOLOGY AND PATHOGENESIS OF INTERSTITIAL CYSTITIS: A CHRONIC, INFLAMMATORY DISORDER OF THE URINARY BLADDER.

P.T. 34; K.W. 0715026, 0765033, 0705075, 0760050, 0706030

National Institute of Diabetes and Digestive and Kidney Diseases

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

The Division of Kidney, Urologic and Hematologic Diseases (DKUHD) of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is committed to funding a major research effort in interstitial cystitis (IC). This Program Announcement is to encourage submission of individual research grant (R01) applications in both the basic and clinical sciences which will study, in human and experimental models, the pathology and pathogenesis of interstitial cystitis. Especially encouraged are projects which utilize for comparison both human bladder specimens and non-human experimental models, such as animals or cell cultures.

BACKGROUND INFORMATION

Interstitial cystitis is a chronic, painful, and variably incapacitating disorder of the urinary bladder which affects a significant percentage of the adult population, predominating in women. Pathological findings in the bladder with IC are variable and may include ulcerations, granulation tissue, fibrosis, mononuclear cell and mast cell infiltrates. At the present time the most accurate method of diagnosis is the patient-derived symptom complex.

Numerous theories have been proposed for the etiology of IC but none has been thoroughly substantiated by research data. There is no long-term effective therapy yet available for this unrelenting disorder. A monograph updating the current knowledge of IC was published as a supplement to UROLOGY 29(4): Supplement, April 1987, and the report of a recent NIDDK sponsored Workshop on IC was published in The JOURNAL OF UROLOGY 140(1): 203-206, July, 1988. This later report lists the preliminary diagnostic criteria which should be used to enroll patients in research studies. (These criteria are not meant to be used for the diagnosis of IC in a non-research clinical situation.) Since the criteria were preliminary at the time of publication, investigators should contact the Urology Program Director for the most recent revision of these criteria prior to employing them in a research study.

OBJECTIVES AND SCOPE OF RESEARCH

The objective of this announcement is to encourage research grant applications which will increase the understanding of the etiology of IC, will develop potential areas for therapeutic applications, and will increase the database of patients with IC. Areas of research which should be investigated include, but are not limited to, the following:

o THE FUNCTION OF MUCOSAL BARRIERS IN NORMAL AND ABNORMAL BLADDER PATHOLOGY. Studies have suggested that the layer of glycosaminoglycans (GAG) on the transitional epithelium of the bladder may have a protective function. In theory disruption of this layer would permit toxic substances to initiate and perpetuate an inflammatory response in the submucosal layers of the bladder. Further studies are needed to evaluate the presence and function of GAGs and other mucosal layers on the bladder surface, and to compare the composition and continuity of the mucosal layers in normal bladder and in the bladder with IC. The effect of various types of antibiotics on the integrity of the mucosal layers is also an area which needs investigation.

o THE ROLE OF NEUROPEPTIDES IN THE CHRONIC INFLAMMATION OF THE BLADDER. The neuropeptide transmitters of the afferent (sensory) neurones release neuropeptides which initiate inflammatory changes. The neuropeptides released include substance P, vasoactive intestinal polypeptides, neurokinin A and calcitonin gene-related peptide. Investigation of the role of these substances in the development of chronic inflammation of both animal and human bladders is necessary. Factors which stimulate and inhibit the release of these substances must also be investigated so that potential pharmaceutical agents may be developed for the regulation of the release of these neuropeptides.

o THE UTILIZATION OF MAGNETIC RESONANCE IMAGING (MRI), POSITRON EMISSION TOMOGRAPHIC (PET) SCANNING, RADIONUCLIDES AND OTHER NON-INVASIVE MODALITIES FOR THE DIAGNOSIS AND EVALUATION OF INTERSTITIAL CYSTITIS. At the present time, the diagnosis of IC is made primarily from the symptom complex obtained from the patient. Correlation of these symptoms with cystoscopic or bladder biopsy pathological evaluation is variable and not consistent. In addition, these procedures may require anesthesia and/or hospitalization. Thus the evaluation of the extent of bladder involvement and the response of IC to treatment is difficult and very imprecise. Resolution of symptoms does not mean a complete response of the disease to the therapy. At best, it is a partial response which is enough to temporarily relieve symptoms. If treatment modalities are to be developed, a non-invasive diagnostic modality must be available to detect the extent of the disease and correlate it with the symptoms. Radiological techniques, at the present time, are not used effectively to evaluate IC. Technologies such as MRI and PET scanning, radionuclides and photosensitive injectable dyes with laser light evaluation, should be investigated to determine their effectiveness in the qualitative and quantitative evaluation of IC.

o PROSTAGLANDINS AS MEDIATORS OF CHRONIC INFLAMMATORY DISEASE OF THE BLADDER. Prostaglandin E2 and prostacyelin are hyperalgesic agents. Their detection at sites of inflammation has suggested that they contribute to the erythema and pain at those regions. Both of these agents are also potent vasodilators. These reactions of pain, inflammation and mucosal erythema are variable characteristics of interstitial cystitis. Investigation of the role of prostaglandins in the development of chronic inflammation of the animal and the human bladder is necessary. The investigation of inhibitors of prostaglandin release and their effect on resolution of inflammation should also be investigated.

o FACTORS PRESENT IN THE URINE WITH INTERSTITIAL CYSTITIS. Investigations are needed to evaluate the presence in the urine of factors such as ions, peptides, changes in pH, immunoglobins, antibodies, inflammatory cells, eosinophils, kinins, histamine, uromodulin (Tamm-Horsefall protein), etc., which can be determined to be specific for IC. Studies of patients have sporadically identified these substances in the urine but have not correlated the findings with the presence or resolution of the symptoms or other diagnostic criteria for IC. Well-controlled studies which correlate these findings in IC patients are necessary to acquire a further understanding of the disease and to establish a parameter for evaluation of treatment.

APPLICATION AND REVIEW PROCEDURES

Research project (R01) grant applications in response to this announcement will be reviewed in accordance with the usual Public Health Service peer review procedures for research grants (Study Section). Review criteria include: the significance of the research and adequacy of the experimental design; training, research competence, and dedication of the investigator(s); adequacy of available facilities; provision for the humane care of animals; and the appropriateness of the requested budget relative to the work proposed. Funding decisions will be based on the Initial Review Group and an appropriate National Advisory council recommendations.

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, if applicable. In such a case, a letter of agreement from the GCRC Program Director should be included in the application.

Individual research project (R01) grant applications should be submitted on form PHS-398, available in the business or grants research office at most academic or research institutions, or from the Division of Research Grants, National Institutes of Health. Women and minority investigators are encouraged to apply. Applications will be accepted in accordance with the dates for new applications on an indefinite basis: February 1, June 1, October 1.

The phrase "INVESTIGATIONS INTO THE PATHOLOGY AND PATHOGENESIS OF INTERSTITIAL CYSTITIS" should be typed on line 2 of the face page of the application. The original and six copies should be sent or delivered to:

Grant Application Receipt Office
Division of Research Grants
Westwood Building, Room 240
National Institutes of Health
Bethesda, Maryland 20892-4500**

In order to alert the Urology Program to the submission of responses to this announcement, or for further information about this program, persons are encouraged to contact:

Leroy M. Nyberg, Jr., Ph.D., M.D.
Urology Program Director, DKUHD, NIDDK
Federal Building, Suite 102
National Institutes of Health
Bethesda, Maryland 20892
Telephone: (301) 496-8248

RESEARCH ON ECONOMIC AND SOCIOECONOMIC ISSUES IN THE PREVENTION, TREATMENT, AND EPIDEMIOLOGY OF ALCOHOL ABUSE AND ALCOHOLISM

National Institute on Alcohol Abuse and Alcoholism

Application Receipt Dates: April 3, 1989
Regular Receipt Dates for Research Grants Thereafter

Alcohol abuse and alcoholism are major problems in the United States that have profound economic implications. Alcohol is directly or indirectly responsible for approximately 100,000 deaths annually, and more than 20 million adults, adolescents and children are believed to experience alcohol-related problems. The cost of alcohol misuse is estimated to be $117 billion a year. The purpose of this announcement is to stimulate research on economic issues associated with the prevention, treatment, and epidemiology of alcohol abuse, alcoholism, and associated problems.

The statutory authorities for anticipated awards are sections 301 and 510 of the Public Health Service Act (42 USC 241 and 290bb).

PREVENTION RESEARCH ISSUES

This announcement encourages research that examines preventive interventions from an economic perspective, analyzes the effects of alcohol promotion and marketing on consumption patterns, or explores risk-taking behavior in terms of economic models of decision making. Specific examples of research possibilities include:

(1) Investigating the effects of changes in price and availability of alcoholic beverages on alcohol consumption and abuse. Although studies indicate that increases in price and decreases in availability tend to reduce consumption and abuse, further research is needed. Attention could be given to price sensitivities for various alcoholic beverages and population groups, long-run as well as short-run consequences of price and availability changes, and the impact of such factors as the legal drinking age and policies regarding place and hours of sale.

(2) Evaluating the cost effectiveness of business-based alcohol prevention programs. Assessments might be made of various employee assistance and health promotion programs in terms of both business- and worker-oriented goals, taking into account such factors as the structure and regulatory climate of the industries, the philosophies underlying the programs, labor and union involvement, and community support. The alcohol service industry has a unique interest in attending to alcohol problems as evidenced by recent litigation on liability issues. However, the most effective role of the service industry as catalyst for or participant in primary prevention programs (e.g., server intervention, designated driver, and alternative transportation programs) is still undetermined. Economic studies of these types of issues are encouraged.

(3) Exploring the possible effects of mass communications in either promoting or preventing alcohol abuse. Mass communication is widely used both for advertising alcoholic beverages and for discouraging alcohol abuse. Studies could assess the effects of advertising and marketing on alcohol consumption and abuse. Alternatively, research could identify the economic costs and benefits of media prevention campaigns, alone or in combination with

interpersonal communication. How warning labels can most effectively be used as a prevention strategy is another avenue of study.

(4) Examining the relationship of alcohol and risk-taking behavior. There is need to study the use of alcohol as a risk-taking behavior and also to determine the consequences of alcohol consumption on young people's willingness to take risks, especially to drive after drinking. In addition to the building of decision-making models (involving perceptions of benefits and risks associated with alcohol use), the National Institute on Alcohol Abuse and Alcoholism (NIAAA) is interested in laboratory experiments and field studies, which may include survey interviews and observational studies.

(5) Evaluating attempts to reduce drunk driving through deterrence-based legal interventions. Economic analysis of these interventions is necessary to test the validity of deterrence theory as well as to formulate wise public policy. Deterrence-based programs could be compared with other drunk driving prevention stategies (e.g., price and availability constraints) in terms of their respective costs and benefits. Analyses, including "natural experiments," should distinguish between interventions focused on severity, on swiftness, and on certainty of threatened punishment.

(6) Assessing the impact of prevention within the context of primary medical care. Primary care providers are in key positions to identify and provide guidance and referral services to individuals at risk of alcohol problems, including "anticipatory guidance" to children, adolescents, and their parents. Studies could address the cost-benefits and cost-effectiveness of integrating these types of prevention efforts into the variety of primary care settings.

Investigators may also apply economic theory and methods to other prevention research topics. Communities as well as individuals might constitute the units of analysis.

TREATMENT RESEARCH ISSUES

Research is needed on the cost, financing, access to, and utilization of alcohol treatment services. There are a number of different possibilities for research on the economics of alcohol treatment. For example, research could describe the alcoholism treatment system, including the distribution, availability, and costs of various treatment alternatives. Cost-offset studies would be welcomed. Identification of the determinants of use of or access to treatment services, including economic and nonmonetary factors influencing the willingness to seek treatment, is another important area for research. The fit between population needs and available services could be examined.

Other relevant research questions include: What kinds of people demand which services? What are the implications of various strategies of public

financing? What are the implications of alcoholism treatment beyond the consequences for individual patients? How do strategies for financing alcohol treatment affect the organization and delivery of care? What are the effects of alternative financing and reimbursement strategies on the organization, cost, delivery, availability, or outcomes of alcoholism treatment? What are the determinants of insurance benefits; and what determines alcoholism services provided in Health Maintenance Organizations and other managed care systems?

EPIDEMIOLOGICAL RESEARCH AND DATA BASES

A variety of epidemiological topics could be addressed under this program announcement. Variations in alcohol use and abuse could be related to economic conditions as measured by rates of employment and unemployment, income levels and earnings, the proportion of women in the labor force, and similar indices. NIAAA supports both bibliographical and empirical data bases capable of aiding research stimulated by this program announcement. For example, ETOH, a bibliographical data base of scientific materials related to alcohol and alcohol problems, is available to researchers through BRS Information Technologies. Empirical data from numerous agencies are also available through the Alcohol Epidemiologic Data System (AEDS), which permits, among other possibilities, estimations of the magnitude, characteristics, and trends of alcohol problems nationwide, as well as specific consequences of alcohol use (including health problems, reduced longevity, casualties, and economic costs).

REVIEW PROCEDURES AND CRITERIA

The standard review procedures of the Alcohol, Drug Abuse, and Mental Health Administration will be followed for applications received in response to this

announcement. Criteria to be used in the merit review include:

(1) Evidence that the applicant will utilize economic theory, data, or analytic methods in the proposed research;
(2) Potential of the research for enhancing the science of prevention, treatment, and epidemiology in the area of alcohol abuse and alcoholism;
(3) Evidence that the investigators are familiar with the state-of-the-art and existing knowledge gaps in their proposed area of research;
(4) Degree of scientific rigor in the design and implementation of the study;
(5) Adequacy of the methods used to collect and analyze data;
(6) Qualifications and research experience of the principal investigator and other key research personnel;
(7) Evidence of availability of facilities, resources, collaborative arrangements, and subjects appropriate to the goals of the research;
(8) Adequacy of procedures to protect human subjects;
(9) Appropriateness of budget estimates for the proposed research activities.

Applicants are urged to include females and ethnic and racial minorities in study populations and at sufficient numbers to generalize the results. If females and minorities are excluded, a clear rationale should be provided.

ELIGIBILITY

Applications may be submitted by public or private non-profit or for-profit organizations such as universities, colleges, hospitals, research institutes and organizations, units of state and local governments, and eligible agencies of the Federal Government. Women and minority investigators are encouraged to apply.

APPLICATION PROCEDURES

The standard research grant application form PHS 398 (revised 9/86) must be used to apply for these awards. When applying, type the name of this announcement, "Research on Economic and Socioeconomic Issues in the Prevention, Treatment, and Epidemiology of Alcohol Abuse and Alcoholism," on page 1, item 2, of PHS 398. State and local government agencies should use form PHS 5161-1 (revised 3/86).

Application kits containing the necessary forms and instructions (PHS 398) may be obtained from institutional business offices or offices of sponsored research at most universities, colleges, medical schools, and other major research facilities. Application forms may also be obtained from:

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

The signed original and six permanent, legible copies (original and two copies if using form PHS 5161-1) of the complete application and any appendices should be submitted to:

Division of Research Grants, NIH
Westwood Building, Room 240
Bethesda, Maryland 20892**

Potential applicants are encouraged to obtain a copy of the complete announcement and to seek preapplication consultation. Please contact:

H. Laurence Ross, Ph.D.
Prevention Research Branch
National Institute on Alcohol Abuse and Alcoholism
5600 Fishers Lane, Room 16C-03
Rockville, Maryland 20857
Telephone: (301) 443-1677

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