

# NIH GUIDE

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## NOTICES

### SUBMISSION OF ADDITIONAL INFORMATION FOR A GRANT APPLICATION

P.T. 34; K.W. 1014006

Division of Research Grants

Once a grant application has been submitted to the National Institutes of Health, any additional information regarding that application may be submitted ONLY to the study section responsible for the review of that application, and ONLY with the concurrence of the executive secretary of that study section. Additional information submitted by mail (or FAX) to the Referral Office, DRG, after a grant application has already been submitted will not be incorporated into the grant application.

To submit additional information, including anything inadvertently left out of the application, the applicant must wait for receipt of his/her notification as to the assignment of the application. This notification will contain the name and telephone number of the executive secretary of the study section. The applicant may then contact the executive secretary to inquire whether additional information may be submitted.

Questions concerning this policy should be directed to:

Referral Office  
Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 248  
Bethesda, Maryland 20892  
Telephone: (301) 496-7447

### IMPLEMENTATION OF GRANTEE REQUIREMENTS FOR DRUG-FREE WORKPLACE

P.T. 34, 22, 44; K.W. 1014006, 0404009

Public Health Service

#### 1. BACKGROUND

Federal regulations implementing the Drug-Free Workplace Act of 1988 (Public Law 100-690, Title V, Subtitle D) were published in the FEDERAL REGISTER, Vol. 54, No. 19, Tuesday, January 31, 1989. The Act requires that, effective March 18, 1989, all grantees receiving grants from any Federal agency certify to that agency that they will maintain a drug-free workplace, or, in the case of a grantee who is an individual, certify to the agency that his or her conduct of grant activity will be drug-free. The governmentwide regulations direct that grantees take steps to provide a drug-free workplace in accordance with the Act.

Implementing regulations for the Department of Health and Human Services are set forth in Title 45, Code of Federal Regulations, Part 76, entitled "Governmentwide Debarment and Suspension (Nonprocurement) and Governmentwide Requirements for Drug-Free Workplace (Grants)."

Until grant application forms are revised to include a specific assurance from applicants that a drug-free workplace will be provided, following are INTERIM procedures regarding (1) the issuance of grants by Public Health Service (PHS) awarding components and (2) the submission of applications by domestic applicants seeking financial assistance from the PHS.

#### 2. ISSUANCE OF GRANTS BY PHS AWARDING COMPONENTS

Beginning MARCH 18, 1989, all grants issued by the PHS as a result of applications not containing the required certification will include the following term and condition:

"This award is issued subject to the grantee's executing and submitting the attached Drug-Free Workplace certification within 10 days of receipt. The grantee may not draw down any funds under this grant until the certification has been executed and submitted."

Grantee ORGANIZATIONS will be provided the certification form entitled "CERTIFICATION REGARDING DRUG-FREE WORKPLACE REQUIREMENTS - GRANTEE OTHER THAN INDIVIDUALS" with the Notice of Grant Award.

Grantees who are INDIVIDUALS (defined in the regulations as meaning "a natural person") will be provided the certification form entitled "CERTIFICATION REGARDING DRUG-FREE WORKPLACE REQUIREMENTS - GRANTEEES WHO ARE INDIVIDUALS" with the Notice of Grant Award. An example of a grantee who is an individual is a "fellow" awarded an Individual Postdoctoral National Research Service Award.

### 3. GRANT APPLICATIONS SUBMITTED BY APPLICANT ORGANIZATIONS

As indicated above, the effective date of the certification requirement is MARCH 18, 1989. Therefore, applicant organizations submitting grant applications to the PHS are required to certify that, as a condition of the grant, it will provide a drug-free workplace. The form entitled "CERTIFICATION REGARDING DRUG-FREE WORKPLACE REQUIREMENTS - GRANTEEES OTHER THAN INDIVIDUALS" found at the end of this issue of the NIH Guide may be used for this purpose.

For grant application purposes, PLEASE REPRODUCE THE FORM and attach it, COMPLETED AND SIGNED, to the application as follows:

- o Behind the CHECKLIST page, for competing applications;
- o Behind the APPLICATION FACE page, for non-competing continuation applications.

### 4. GRANT APPLICATIONS SUBMITTED BY APPLICANTS WHO ARE INDIVIDUALS

As indicated above, the effective date of the certification requirement is MARCH 18, 1989. Therefore, applicants for grants made to individuals are required to certify that, as a condition of the grant, he/she will not engage in the unlawful manufacture, distribution, dispensing, possession or use of a controlled substance in conducting any activity under the grant.

The form entitled "CERTIFICATION REGARDING DRUG-FREE WORKPLACE REQUIREMENTS - GRANTEEES WHO ARE INDIVIDUALS" found at the end of this issue of the NIH Guide may be used for this purpose.

For grant application purposes, PLEASE REPRODUCE THIS FORM and attach it, COMPLETED AND SIGNED, to the application as follows:

- o Behind the CHECKLIST page, for competing applications;
- o Behind the APPLICATION FACE page, for non-competing continuation applications.

### 5. PHS PLANNED ACTIONS

The PHS plans to revise application forms to incorporate the drug-free workplace certification, as well as the certifications regarding delinquent Federal debt and debarment and suspension. It is anticipated that the revised application kits will be available within the next few months.

Also, as soon as possible the Division of Research Grants, National Institutes of Health, will send a copy of the appropriate drug-free workplace certification form to grantees with the non-competing continuation application.

### DATED ANNOUNCEMENTS (RFPs AND RFAs)

#### MICROSTIMULATION OF THE SACRAL SPINAL CORD

RFP AVAILABLE: RFP-NIH-NINDS-89-20

P.T. 34; K.W. 0745047, 1002034, 0710050

National Institute of Neurological Disorders and Stroke

The National Institute of Neurological Disorders and Stroke (NINDS) has a requirement to investigate the feasibility of microstimulation of the sacral spinal cord as a method of controlling micturition and sexual functions. Studies shall be conducted in a non-human male animal model.

Offerors should have experience in electrophysiology including electrical stimulation of neural tissue.

This is an announcement of an anticipated Request for Proposals. RFP-NIH-NINDS-89-20 will be issued on or about April 12, 1989, with a closing

date of June 12, 1989, for receipt of proposals. It is anticipated that one contract award will be made.

To receive a copy of the RFP, you must supply this office with two self-addressed mailing labels. All responsible sources may submit a proposal which will be considered by the agency.

The RFP will be available upon request to:

Contracting Officer  
Contracts Management Branch  
National Institute of Neurological  
Disorders and Stroke, NIH  
Federal Building, Room 901  
7550 Wisconsin Avenue  
Bethesda, Maryland 20892

PRESOLICITATION: AIDS AND ITS BEHAVIORAL CAUSES: CHILDREN'S  
KNOWLEDGE AND EMOTIONS

RFA: 89-HD/MH/DA-07

P.T. 34, AA; K.W. 0715008, 0404000, 0404004, 0502017

National Institute of Child Health and Human Development  
National Institute of Mental Health  
National Institute on Drug Abuse

Anticipated RFA Availability Date: April 27, 1989  
Anticipated Application Receipt Date: July 31, 1989

INTRODUCTION

The purpose of this announcement is to alert the scientific community to the proposed issuance of a Request for Applications for studies on children's knowledge and feelings regarding: (a) Human Immunodeficiency Virus (HIV) infection and mechanisms of its transmission; (b) Acquired Immunodeficiency Syndrome (AIDS) as an illness and its health consequences; and (c) human sexuality and drug abuse.

RESEARCH GOALS AND SCOPE

The proposed Request for Applications will call for developmental research about six-to-twelve year old children's knowledge, attitudes and feelings regarding AIDS, sexuality and substance abuse. The results of this research are intended to inform and guide the planning of AIDS-related educational programs.

Psychological-developmental and physiological-maturational variables are hypothesized to be important determinants of children's capacity for understanding and of their motivation to learn. Research is needed to examine the relationships among children's cognitive development; their physiological development; and their knowledge about HIV infection, AIDS, the behavioral causes of the infection, and its consequences. In addition, research is needed to explore and explain the relationship among developmental/maturational variables and children's knowledge about sexuality and substance abuse.

Environmental variables, such as living in an urban setting or in poverty and cultural variables are hypothesized to shape children's emotions and knowledge regarding AIDS, sexuality and substance abuse. Research is needed to identify the environmental and cultural factors that are most influential and to specify some of the processes by which environment and culture impact on what children think and feel in the domains under inquiry.

The distinction between what children know, believe and feel and what they are capable of understanding is an important one to make. When left to their own resources, children piece together fragments of information to build their knowledge and to form attitudes. This is particularly the case when societal taboos prevent them from finding out what "experts" know or believe. While educators should know what children of a given developmental and maturational level and of a specific sociocultural background know, believe and feel, they should also know what these children are capable of learning. The requested research can provide such information.

Proposed research designs may include both cross-sectional and longitudinal methods. Applicants are invited to develop new methods and new tasks for

studying the development of the above general areas of research. These may include interviews, questionnaires, and problem-solving tasks.

Since no one study can focus on all the above aspects of the needed research, investigators are encouraged to choose a subset of research problems that are closest to their interest and to study these in great depth.

#### MECHANISM OF SUPPORT

Support for this program will be through the traditional research grant (R01), the FIRST Award (R29) and the Small Grant (R03) mechanisms. Policies that govern grant-in-aid award programs of the Public Health Service will prevail.

Issuance of the Request for Applications is contingent on its administrative approval by the Institutes. It is anticipated that up to nine meritorious applications will be funded under this program. The number of awards will depend on the overall merit of the proposals, their relevance to program goals and on the availability of funds.

#### INQUIRIES

To receive a copy of the Request for Applications, please send a self-addressed mailing label to one of the addresses below:

Sarah L. Friedman, Ph.D.  
Health Scientist Administrator  
Human Learning and Behavior Branch  
National Institute of Child Health and Human Development  
9000 Rockville Pike  
Executive Plaza North, Room 633  
Bethesda, Maryland 20892

OR

Leonard Mitnick, Ph.D.  
Chief  
Health and Behavior Research Branch  
National Institute of Mental Health  
Parklawn Building, Room 11C06  
5600 Fishers Lane  
Rockville, Maryland 20857

OR

Rodney R. Cocking, Ph.D.  
Chief,  
Cognition and Learning Program  
Behavioral Sciences Research Branch  
National Institute of Mental Health  
Parklawn Building, Room 11-C-10  
5600 Fishers Lane  
Rockville, Maryland 20857

OR

Zili Amsel, Sc.D.  
Clinical Medicine Branch  
National Institute on Drug Abuse  
Parklawn Building, Room 10A08  
5600 Fishers Lane  
Rockville, Maryland 20857

#### PROGRAM PHYSICIAN SCIENTIST AWARDS (K12)

RFA AVAILABLE: 89-DK-08

P.T. 34; K.W. 0710030, 0715075, 0715135, 0710095, 0715032, 0705030, 0785220

National Institute of Diabetes and Digestive and Kidney Diseases

Application Receipt Date: August 1, 1989

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) announces the availability of a Request for Applications (RFA) for Program Physician Scientist Awards (PPSAs). The NIDDK PPSA program was initiated in competitions held in 1984 and 1985, and 7 grants are currently co-funded by the NIDDK and the National Institute of Arthritis and Musculoskeletal and Skin

Diseases (NIAMS). The NIAMS will not support PPSAs after FY 1989. All 7 currently supported programs are scheduled to terminate their project periods on June 30, 1990.

#### RESEARCH GOALS AND SCOPE

The Physician Scientist Awards (PSA) enables individuals with clinical training to undertake up to five years of special study in a basic science coordinated with supervised research experiences. The PSA is intended to be the first intensive research experience at the post-doctoral level. Phase 1 of each individual's course of study (2 to 3 years) must include both didactic work and laboratory experiences conducted under the close sponsorship of an individual with extensive research experience in a fundamental science such as biochemistry, molecular biology, genetics, or immunology. Phase 2 (up to three years) will be to apply laboratory-based research experiences and techniques to disease-related problems in an area of responsibility of the NIDDK, i.e., diabetes, endocrinologic diseases or disorders, metabolic processes and disorders, digestive diseases, nutrition, kidney diseases, urologic disorders, and/or hematologic disorders.

The PPSA represents a mechanism of support which is an alternative to the Individual PSA. Institutions with PPSAs may recruit and select candidates for support without submitting a separate competitive application to the NIH for each individual. Participants supported by Program awards are supported under the same terms and provisions as persons holding Individual PSAs. The NIDDK believes that the PPSA has the potential for providing benefits, both administrative and intellectual, above and beyond those which normally accrue to the Individual award. Not only does a PPSA allow an institution substantial flexibility in recruiting participants but it also makes possible the creation of an extraordinarily rich intellectual environment within which physician-scientists' courses of study may be pursued. Respondents to this solicitation should propose programs which fully exploit the potential benefits of the mechanism within the applicant's institutional context.

It is expected that the scientific range of opportunities for research development described in the application will include a number of the areas of responsibility of the NIDDK and that there will be a major emphasis within one of the principal NIDDK program areas--that is, diabetes, endocrinology and metabolic diseases; digestive diseases and nutrition; or kidney, urologic and hematologic diseases.

#### MECHANISM OF SUPPORT

The mechanism of support for this activity will be the grant-in-aid, awarded under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended, 42 USC 241). The regulations (Code of Federal Regulations, Title 42 Part 52, and Title 45 Part 74) and policies which govern the research grant programs of the National Institutes of Health (NIH) will prevail. The award of grants pursuant to this announcement is contingent upon availability of appropriated funds; however, it is presently anticipated that up to 5 applications will be funded. The total number of participant-slots supported by the NIDDK using the Program PSA mechanism is not anticipated to exceed 25.

#### METHODS OF REVIEW

Applications will be received by the NIH Division of Research Grants (DRG) and assigned to the NIDDK for review and possible funding.

Applications in response to this announcement will be reviewed in nationwide competition and in accordance with usual NIH peer review procedures. They will first be reviewed for scientific and technical merit by an institute review group composed mostly of non-Federal scientific consultants (initial review group). Following this review, the applications will be evaluated by the Institute's Advisory Council.

#### INQUIRIES

For further information and to obtain supplementary instructions critical to the development of applications, please contact:

Walter S. Stolz, Ph.D.  
Director, Division of Extramural Activities, NIDDK  
Westwood Building, Room 657  
National Institutes of Health  
Bethesda, Maryland 20892  
Telephone: (301) 496-7277



## THERAPEUTIC CORRELATES OF DRUG RESISTANCE

RFA AVAILABLE: 89-CA-12

P.T. 34; K.W. 0765012, 0710100, 0785035

National Cancer Institute

Application Receipt Date: July 12, 1989

The Division of Cancer Treatment (DCT) of the National Cancer Institute (NCI) invites grant applications from interested investigators for a tightly focused, integrated research program at the interface of laboratory experimentation and concurrent clinical trials involving the correlation of drug resistance to clinical response and development of clinical treatment to overcome acquired drug resistance.

### BACKGROUND

A formidable obstacle in cancer therapeutics is the emergence and growth of treatment-resistant tumor cells. Recent research efforts concerning this phenomenon have utilized in vitro systems to elucidate the molecular and cellular mechanism(s) operative in resistance to chemotherapy. These efforts have resulted in the determination of a number of genotypic and phenotypic alterations which appear to correlate with the development of drug resistance in tumor cells. However, while there is a substantial amount of ongoing basic research there are relatively few current studies which will determine the clinical relevance of laboratory assays for drug resistance. Research directed at correlating the results of laboratory assays of drug resistance with results of clinical trials is an essential step in the development of effective regimens of cancer therapeutics. In defining the mechanisms of drug resistance, preclinical studies have resulted in the development of therapeutic strategies to overcome acquired clinical drug resistance. These new approaches need to be tested in the clinic and their efficacy correlated to laboratory measures of drug resistance.

### RESEARCH GOALS AND SCOPE

The major focus of this RFA is to stimulate clinical trials using new therapeutic strategies to overcome or reverse acquired drug resistance. Studies should be proposed for an integrated research program of laboratory experimentation and concurrent clinical trials involving therapeutic correlates of drug resistance. Studies should be proposed for a clinical trial of antitumor agents which include obtaining malignant tissue to be assessed using measures of drug resistance. Drug resistance assays should include a correlate other than dose responsiveness to the drug in question. Data from the laboratory should be collected to permit statistical analysis so that the measure of drug resistance can be correlated with clinical outcome. Location of the assay laboratory and the target patient population for clinical trials may be at different/multiple institutions.

Examples of potential studies which would be appropriate for this RFA include:

A. A clinical trial which measures drug resistance of human tumor samples obtained prior to treatment and at the time of recurrence or progressive disease in those same patients.

B. A clinical trial involving studies of patients whose tumors are assessed in the laboratory as being drug resistant, and whose treatment includes a specific strategy directed at overcoming or reversing clinical drug resistance. Studies that are directed towards dose intensification or replacement by non-cross resistant drugs are not the focus of this RFA.

### MECHANISM OF SUPPORT

This program will be supported through traditional research grants. Awards may be made to public, private non-profit, and for-profit organizations. All PHS and NIH grant policies will apply to applications received in response to this announcement. Approximately \$1,500,000 in first year total costs will be committed to specifically fund applications which are submitted in response to this RFA. NCI plans to make multiple awards for project periods up to five years. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. The earliest feasible start date for the initial awards will be April 1, 1990.



## INQUIRIES

A copy of the complete RFA describing the research goals and scope, the review criteria, and the method of applying can be obtained by contacting:

Ms. Diane A. Bronzert  
Program Director, Cancer Therapy  
Evaluation Program  
Division of Cancer Treatment  
National Cancer Institute  
Executive Plaza North, Room 734  
Bethesda, Maryland 20892  
Telephone: (301) 496-8866  
FAX: 301-496-9384

Written or telephone inquiries concerning the objectives and scope of this RFA or inquiries about whether or not specific proposed research would be responsive are encouraged and should be directed to Ms. Diane Bronzert at the above address.

## LETTER OF INTENT

Prospective applicants are asked to submit, by May 15, 1989, a letter of intent that includes a descriptive title of the proposed research, the name and address of the principal investigator, the names of other key personnel, the participating institutions, and the number and title of the RFA in response to which the application is being submitted. The letter of intent is requested in order to provide an indication of the number and scope of applications to be reviewed. The letter of intent does not commit the sender to submit an application, nor is it a requirement for submission of an application. Letters of intent should be directed to Ms. Diane Bronzert at the above address.

## ONGOING PROGRAM ANNOUNCEMENTS

### RIBOZYME ANTISENSE MEDIATED CLEAVAGE OF HIV RNA

P.T. 34; K.W. 0715008, 1002008, 1002045, 0790010, 0755025, 0755060

National Institute of Allergy and Infectious Diseases

### BACKGROUND INFORMATION

The National Institute of Allergy and Infectious Diseases (NIAID) is playing a central role in the investigation of Acquired Immunodeficiency Syndrome (AIDS). Research efforts directed toward the pathogenesis, prevention and treatment of the disease and its sequelae have intensified. The NIAID has undertaken a lead role in organizing scientists into National Cooperative Drug Discovery Groups for the Treatment of AIDS (NCDDG/AIDS). NCDDG/AIDS are comprised of scientists from academic, non-profit, and commercial organizations that interact as a unit, with NIAID support, to conduct preclinical research aimed at the discovery of agents which can be used in the treatment of AIDS. Samples of the research areas currently being investigated by NCDDG scientists include molecular biology of HIV and SIV; development of unique cell culture assays, biochemical screens and small animal models; discovery of new lead compounds and biologics; rational drug design; X-ray crystallography of proteins and drugs; characterization and isolation of natural products; development of delivery systems for new drugs; and development of viral vectors for delivery of anti-viral genes, and antisense nucleic acids. Since the inception of the NCDDG/AIDS in 1986, three potential therapies have been discovered and developed. One anti-HIV compound, recombinant soluble CD4 (Biogen, Inc.) has already entered clinical trial and two nucleosides, [azidouridine (CS-87) and dideoxydideohydrothymidine (d4T) are expected to enter clinical trial in 1989. Other potential therapeutics identified through the comprehensive effort of the NCDDG are in earlier states of preclinical development.

The NIAID, through the Developmental Therapeutics Branch of the AIDS Program, will soon launch an NCDDG/OI program to encourage collaborative efforts to discover new therapies targeted to the opportunistic infections associated with AIDS. NIAID also facilitates the acquisition of information on any drug that shows potential in the treatment of HIV infection, fills gaps in the drug development process, provides ancillary information on the rationale of the drug in animal retroviral models, and assists in the transition of promising therapies into clinical trial in NIAID's AIDS Clinical Trial Group program.

The NIAID now wishes to expand the areas of investigator-initiated research currently being funded. This Program Announcement solicits applications from investigators who wish to play an active role in defining the direction of such research. While no funds are specifically set aside for funding grants submitted in response to this Program Announcement, the NIAID regards additional high quality research in this area of high priority.

#### OBJECTIVES AND SCOPE

The objective of this Program Announcement is to stimulate research on the development and use of autocatalytic RNA enzymes for the inactivation of the HIV genome and mRNA transcripts in HIV-infected cells in culture or in small animal models.

Certain naturally occurring plant viruses and linear satellite RNAs (ribozymes) undergo self-catalyzed cleavage to generate unit-length (+)RNA or (-)RNA as a final step in a rolling circle RNA replication mechanism. Ribozyme-mediated processing of concatenated transcripts has also been identified in the replication of newt's satellite RNA (Epstein and Gall (1987), Cell 48: 535). This property of self-cleavage is imparted by consensus sequences (GU(X)<sub>n</sub>CUGA(U/A)GAG(X)<sub>n</sub>CGAAAC) derived from three distal regions in the molecule; the proposed tertiary ("hammerhead") conformation is thought to bring these sequences into close proximity prior to autocatalytic cleavage. A single ribozyme contains all the structural functions necessary for self-cleavage. Recently, ribozymes were designed and shown to mediate the specific cleavage of the bacterial chloramphenicol transacetylase transcript in vitro (Haseloff and Gerlach (1987), Nature 334:585). Importantly, the consensus domains and secondary structure required for hammerhead-style cleavage can be achieved using two separate strands: a target substrate strand and a ribozyme antisense strand (Uhlenbeck (1987), Nature 328:596). Thus, an appropriately designed ribozyme antisense strand can combine with a specific target substrate containing a minimally conserved consensus sequence and then result in cleavage of the target strand.

A "hairpin" motif, distinct from the hammerhead structure in both sequence and secondary structure, has been proposed for the self-cleavage of (-) strand satellite RNA of the tobacco ringspot virus (Tritz and Hampel (1988), J. Cell Biology 107:321 (Abstract #1819); Buzayan et al (1986), Nature 323:349). The autocatalytic cleavage site of hepatitis delta virus (Sharmeen and Taylor (1988), J. Virol. 62:2674) also does not appear to resemble the hammerhead structure. Other yet undefined types of catalytic RNA structures may exist. Additionally, synthetic forms of antisense, such as a hybrid molecule with an RNA core and flanking DNA sequences or those capable of forming a triple helix, may produce a more stable, nuclease-resistant active ribozyme.

The HIV-1 RNA genome and HIV-1 mRNA's have been found to contain sequences that are potential substrates for cleavage by appropriate ribozyme antisense sequences. Research on the structural requirements of anti-HIV ribozyme antisense sequences (i.e. preferred flanking sequence, length of the flanking stems, sequence of internal loops) and design of an optimal anti-HIV catalyst is needed.

Development and testing of different modalities for the delivery of anti-HIV ribozyme-antisense nucleic acids to target cells would provide important information on the feasibility of ribozyme-mediated, catalytic cleavage as an anti-HIV strategy. At a later date, investigators may want to explore the feasibility of ribozyme-mediated therapy in vivo through collaborations with laboratories with small animal models. The small animal model chosen should be sufficiently defined so as to allow evaluation of the level of activity of the ribozyme construct in blocking expression of a specific retroviral gene or infectious virus. If appropriate, NIAID staff may facilitate small animal studies through the resources of the AIDS Program. A potentially important and unique approach to limit viral replication could emerge. This strategy would have broad implications for the treatment of a variety of infections and other disease states in addition to AIDS and its associated sequelae.

In summary, NIAID wishes to stimulate research in the following areas:

- o Elucidation of the structure-function requirements of the ribozyme antisense strand for cleavage of HIV RNA or mRNAs,
- o Identification and design of optimal anti-HIV ribozyme catalysts,
- o Evaluation of the ability of ribozyme to block HIV-infection in cultured cells, and
- o Testing modalities, such as viral vectors and liposomes, for the delivery of ribozyme antisense molecules to target cells.

The approaches outlined above are not intended to be comprehensive and are not required. Investigations on the use of ribozyme-antisense nucleic acids or other catalytic RNAs that induce the cleavage of retroviral RNAs and that evaluate its therapeutic potential in cell culture and/or small animal models are encouraged under this Program Announcement.

#### METHOD OF APPLICATION

Use the standard research Grant Application Form PHS 398 (Rev. 9/88). For purpose of identification and processing, the words "Auto-Cleavage of Targeted HIV RNA" should be typed in item 2 on the face page of the application. The receipt dates are May 1 and September 1, 1989, and January 1, 1990. In order to comply with the expedited review for AIDS applications, mail the complete application and thirty two (32) exact copies to:

DRG AIDS Coordinator  
Westwood Building, Room 240  
National Institute of Health  
Bethesda, Maryland 20892\*\*

#### REVIEW PROCEDURES AND CRITERIA

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

#### INQUIRIES

Inquiries of a scientific nature may be addressed to:

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

#### NATIONAL RESEARCH SERVICE AWARDS

P.T. 22, 44; K.W. 0720005, 0710030, 1013004, 0710035

National Institute of General Medical Sciences

The National Institute of General Medical Sciences (NIGMS) supports research training in the biomedical sciences under the auspices of the National Research Service Awards (NRSA) Act and through the programs and mechanisms listed below. This announcement is a revision of the 1977 and 1984 NIGMS training announcements with new initiatives in both the predoctoral institutional training grant program and the postdoctoral individual fellowship program in two newly added training fields: Molecular Biophysics and Biotechnology.

#### INSTITUTIONAL TRAINING GRANTS

The NIGMS is currently accepting applications from eligible institutions for support of highly selected, promising individuals who seek biomedical research training in the areas specified.

It is the Institute's goal in the predoctoral programs to provide trainees broad access to thesis research opportunities across disciplinary and departmental lines while not sacrificing the standards of depth and creativity characteristic of the best Ph.D. degree-granting programs. Cooperative involvement of faculty members from several departments or doctoral degree programs as thesis research mentors is considered evidence for such breadth.

The Institute provides support for a small number of postdoctoral research training grants in more clinically related areas of research training and encourages the selection of M.D. degree holders as trainees. For these trainees, at least two years of rigorous research training should be provided, usually in basic science departments. For individuals holding the Ph.D. degree, training should focus on advanced and specialized areas of research and offer appropriate opportunities to study problems of clinical relevance.

Programs for postdoctoral trainees should offer a range of research training opportunities as outlined below.

All training grant applicants are expected to present detailed plans on the training program organization, criteria for trainee recruitment and selection, and mechanisms for quality control. Recruitment of trainees with a variety of undergraduate science backgrounds (or doctoral degree experiences for postdoctoral programs) is encouraged. The application should also give information on the qualifications of the proposed faculty participants, including their experience as trainers and their current research programs and support. Applicants must also describe their program efforts to recruit individuals from underrepresented minority groups.

The NIGMS training grant awards do not provide support for mixed predoctoral and postdoctoral research training. An application must request support for either predoctoral or postdoctoral research training. In general, only one award in each of the areas listed below will be made to an institution. Further information regarding dates of application and notification, tenure, trainee-related expenses, trainee eligibility and required payback provisions may be found in the NIH Guide for Grants and Contracts, Special Edition, Vol. 16, No. 20, June 12, 1987. For current stipend information, see Vol. 17, No. 24, July 29, 1988, and Vol. 17, No. 38, November 18, 1988.

For general information about these institutional NRSA programs, contact Dr. John C. Norvell, Research Training Officer, National Institute of General Medical Sciences, Bethesda, Maryland 20892, telephone (301) 496-7260. Before preparing an application, applicants are strongly urged to contact Dr. Norvell and the staff member who is responsible for the specific area of training.

### Predocutorial Support Areas

#### 1. Cellular, Biochemical, and Molecular Sciences

Training programs should be of a cross-disciplinary nature and involve in-depth study of biological problems at the level of the cellular and molecular sciences. The research training offered should encompass related disciplines, such as biochemistry, biophysics, chemistry, cell biology, developmental biology, genetics, immunology, microbiology, neurobiology, and pathology. These research opportunities should be available in the represented disciplines with faculty mentors from interacting departments or Ph.D. programs.

Dr. Bert Shapiro - (301) 496-7518

#### 2. Genetics

Training programs in genetics should emphasize broad training in the principles and mechanisms of genetics and related sciences. Training in a variety of areas such as classical genetics, molecular genetics, population and behavioral genetics, and developmental genetics should be included. Programs should also include training and research opportunities in related disciplines such as biochemistry, cell biology, and statistics. These programs are generally expected to include faculty members in disciplines other than genetics.

Dr. Joye Jones - (301) 496-7087

#### 3. Pharmacological Sciences

Training programs in this area should be multidisciplinary and emphasize the acquisition of competence in the broad field of pharmacological sciences. Individuals should receive training that will enable them to conduct research on the biological phenomena and related chemical and molecular processes involved in the actions of therapeutic drugs and their metabolites. Thesis research opportunities should be available with faculty members in a variety of disciplines, such as biochemistry, chemistry, genetics, toxicology, medicinal chemistry, physiology and neurosciences, as well as pharmacology.

Dr. Christine K. Carrico - (301) 496-7707

#### 4. Systems and Integrative Biology

Training in this area should be directed toward building broad research competence required to investigate integrative, regulatory, and developmental processes of higher organisms and their functional components. The training program should bring together varied resources, approaches, and thesis research opportunities with faculty mentors of such disciplines/departments as physiology, biomedical engineering, and the neuro- and behavioral sciences, as well as biochemistry and cell and developmental biology. Graduates of the program should be well versed in quantitative approaches to biology.

Dr. Bert Shapiro - (301) 496-7518

## 5. Molecular Biophysics

Multidisciplinary programs in this area are intended to provide training which focuses on the application of physics, mathematics, and chemistry to problems of biological structure, primarily at the molecular level. These programs should bring together faculty members from departments such as chemistry, physics, and engineering with an interest in biologically related research with those faculty in biological science departments whose orientation is to the application of physical methods and concepts to biological systems.  
Dr. Marvin Cassman - (301) 496-7463

## 6. Biotechnology

Training should be multidisciplinary and focus on the applications of engineering, physics, chemistry, mathematics, and biology to those areas of biomedical research related to biotechnology. These programs should involve the participation of faculty members from several departments/ schools whose research emphases are on engineering and mathematical and physical methods applied to the analysis of biological processes. It is expected that trainees will pursue thesis research problems that are of a fundamental nature and that are applicable to the advancement of biotechnology.  
Dr. Luther S. Williams - (301) 496-0186

## 7. Medical Scientist Training Program

Interdisciplinary programs in this training area should provide integrated medical and graduate research training required for investigation of diseases in man. These programs should assure highly selected trainees a choice of a wide range of pertinent graduate programs in the biological, chemical, physical, and social sciences combined with training in medicine leading to the M.D.-Ph.D. degree. The proposed program should be flexible and adaptable in providing each trainee with the appropriate background in the sciences relevant to medicine and be rigorous enough to enable the individual to function independently in both basic research and clinical investigations.  
Dr. Lee Van Lenten - (301) 496-7001

### Postdoctoral Support Areas

#### 1. Genetics

Training programs should provide advanced and specialized research training in the principles of genetics with the goal of understanding human genetic disorders. Trainees should be drawn from diverse backgrounds and should be offered opportunities for conducting research with faculty who represent a variety of approaches to genetics ranging from molecular genetics to human population genetics. Programs should provide rigorous training in basic or applied research, with an emphasis on human or medical genetic problems. For holders of the M.D. or other professional degrees, the program should provide training and research opportunities in area of basic genetics. This training should build on, and complement, the trainee's clinical background. For holders of the Ph.D. degree, the research and training should emphasize the application of the trainee's basic genetics background to problems in human and medical genetics.  
Dr. Joye Jones - (301) 496-7087

#### 2. Clinical Pharmacology

Individuals in these training programs should receive experience in the methodology and in the conduct of clinical and basic research to qualify them to investigate the effects and mechanisms of drug actions in humans. Trainees, who would usually have the M.D. degree, should have the opportunity to acquire fundamental scientific knowledge and learn research techniques in areas such as basic pharmacology, biochemistry, physiology, biostatistics, and other biomedical subdisciplines.  
Dr. Christine K. Carrico - (301) 496-7707

#### 3. Trauma and Burn Research

Multidisciplinary research training should be offered to postdoctoral scientists seeking to improve the understanding of the body's systemic responses to major injury and to foster the more rapid application of this knowledge to the treatment of trauma and burn-injured victims. The supervisory staff should include trauma surgeons and/or burn specialists as well as basic scientists. Trainees, most of whom would hold the M.D. degree, will be expected to spend at least two years in the training program and to apply such basic disciplines as biochemistry, physiology, immunology, microbiology, cell biology, molecular biology, biomedical engineering, or behavioral sciences to the study of trauma.  
Dr. Yvonne T. Maddox - (301) 496-7001

#### 4. Anesthesiology

Training programs should offer training support to individuals with the M.D. degree who seek a better understanding of the fundamental mechanisms of anesthetic action. Trainees will be expected to spend at least two years in such basic science departments as pharmacology, physiology, or biochemistry to enable them to study the effects of anesthetic agents on the body at the level of the organ system as well as at the molecular and cellular level.  
Dr. Paul Velletri - (301) 496-7707

#### INDIVIDUAL FELLOWSHIPS

The National Institute of General Medical Sciences is currently accepting individual postdoctoral fellowship applications from eligible individuals who seek advanced biomedical research training in broad areas related to the scientific programs of the Institute. Individuals holding an M.D. degree, as well as those holding a Ph.D. degree, are encouraged to apply.

Information regarding dates of application and notification, tenure, stipend, eligibility, and payback requirements may be found in the NIH Guide for Grants and Contracts, Special Edition, Vol. 13, No. 1, January 6, 1984. Current stipend information may be found in Vol. 17, No. 24, July 29, 1988.

For additional general information about the individual National Research Service Awards, contact Dr. David Wolff, National Institute of General Medical Sciences, Bethesda, Maryland 20892, telephone (301) 496-7063. For information specific to the listed program areas, call the indicated staff member.

1. Biophysics and Physiological Sciences
  - Biomedical Engineering: Dr. Helen Sunshine - (301) 496-7309
  - Molecular Biophysics: Dr. Helen Sunshine - (301) 496-7309
  - Physiological Sciences: Dr. Yvonne Maddox - (301) 496-7001
  - Trauma and Burn Research: Dr. Yvonne Maddox - (301) 496-7001
2. Biotechnology
  - Dr. John C. Norvell - (301) 496-7260
  - Dr. Luther S. Williams - (301) 496-0186
3. Cellular, Biochemical, Molecular Sciences
  - Dr. Warren Jones - (301) 496-7621
  - Dr. Marian Zatz - (301) 496-0334
4. Genetics
  - Dr. Stephen Fahnstock - (301) 496-7137
  - Dr. Barbara Williams - (301) 496-7087
5. Pharmacological Sciences
  - Anesthesiology, Bio-related Chemistry, Pharmacology:  
Dr. Paul Velletri - (301) 496-7707

#### MINORITY ACCESS TO RESEARCH CAREERS PROGRAM

The Minority Access to Research Careers (MARC) Program supports several research training programs. Its goals are to increase the number and capabilities of scientists from underrepresented minorities that are engaged in biomedical research. These training programs are intended to strengthen science curricula and student research opportunities at institutions with substantial minority enrollment in order to prepare minority students for research careers.

##### 1. MARC Honors Undergraduate Research Training Awards

These awards are offered to 4-year colleges, universities, and health professional schools with substantial enrollment of such ethnic minorities as American Indians, Blacks, Hispanics, and Pacific Islanders. These grants support research training for honors undergraduate students in their third and fourth years and are intended to prepare these students to compete successfully for entry into graduate programs leading to the Ph.D. degree in a biomedical science. Honors programs should be designed to augment and enhance science curricula, faculty skills, and student laboratory experiences. In addition to a stipend, tuition, fees, and limited travel costs for trainees, funds are provided for consultants, personnel, staff travel, and essential research equipment and supplies. Arrangements should be made for special training during summer recesses at research universities and laboratories other than those of the grantee institution. (See the NIH Guide for Grants and Contract, Vol. 6, No. 7, March 17, 1977. Current stipend information may be found in Vol. 17, No. 38, November 18, 1988.)

## 2. MARC Predoctoral Fellowships

These fellowships are individual National Research Service Awards made to outstanding graduates of the MARC Honors Undergraduate Research Training Program to help them pursue a Ph.D. degree in the biomedical sciences. Support is not available for individuals enrolled in medical or other professional schools unless they are enrolled in a combined-degree (e.g., M.D.-Ph.D.) program. A maximum of five years of support may be requested. NIGMS will also provide tuition, fees, and trainee-related expenses to the predoctoral fellow's sponsoring institution to help defray such trainee expenses as research supplies and equipment. (See the NIH Guide for Grants and Contracts, Vol. 10, No. 1, January 2, 1981.)

## 3. MARC Faculty Fellowships

Awards are made to selected full-time faculty members of four-year colleges, universities, and health professional schools with substantial enrollment of ethnic minorities. Awards support predoctoral or postdoctoral research training in the biomedical sciences. Fellows may train at any private or public institution in the United States with suitable research facilities, but they are expected to return to their sponsoring institutions after completion of their fellowships. Annual stipends are based on the current salary of the applicant. (See the NIH Guide for Grants and Contracts, Vol. 5, No. 15, September 15, 1976.)

## 4. MARC Visiting Scientist Fellowships

Fellowships are offered for periods of several weeks to one year to support outstanding scientist-teachers serving as visiting faculty at eligible minority institutions. Stipends are determined on an individual basis. (See the NIH Guide for Grants and Contracts, Vol. 6, No. 1, January 7, 1977.)

For additional information about the MARC Program, contact Mr. Elward Bynum, Director, MARC Program, or Ms. Dolores Lowery, National Institute of General Medical Sciences, Bethesda, Maryland 20892, telephone (301) 496-7941.

### ERRATUM

#### RESEARCH TRAINING RELATED TO ALZHEIMER'S DISEASE & RELATED DISORDERS

P.T. 44; K.W. 0715180, 0720005, 0785130

National Center for Nursing Research

This Program Announcement was published in the NIH Guide for Grants and Contracts on March 10, 1989 (Vol. 18, No. 8). The telephone number listed with the address is incorrect. The correct address and telephone number are below:

Division of Extramural Programs  
Extramural Programs  
National Center for Nursing Research  
National Institutes of Health  
Building 31, Room 5B13  
Bethesda, Maryland 20894  
Telephone: (301) 496-0523



U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
CERTIFICATION REGARDING DRUG-FREE WORKPLACE REQUIREMENTS  
GRANTEES OTHER THAN INDIVIDUALS

By signing and/or submitting this application or grant agreement, the grantee is providing the certification set out below.

This certification is required by regulations implementing the Drug-Free Workplace Act of 1988, 45 CFR Part 76, Subpart F. The regulations, published in the January 31, 1989, FEDERAL REGISTER, require certification by grantees that they will maintain a drug-free workplace. The certification set out below is a material representation of fact upon which reliance will be placed when HHS determines to award the grant. False certification or violation of the certification shall be grounds for suspension of payments, suspension or termination of grants, or governmentwide suspension or debarment.

The grantee certifies that it will provide a drug-free workplace by:

(a) Publishing a statement notifying employees that the unlawful manufacture, distribution, dispensing, possession or use of a controlled substance is prohibited in the grantee's workplace and specifying the actions that will be taken against employees for violation of such prohibition;

(b) Establishing a drug-free awareness program to inform employees about:

- (1) The dangers of drug abuse in the workplace;
- (2) The grantee's policy of maintaining a drug-free workplace;
- (3) Any available drug counseling, rehabilitation, and employee assistance programs; and
- (4) The penalties that may be imposed upon employees for drug abuse violations occurring in the workplace;

(c) Making it a requirement that each employee to be engaged in the performance of the grant be given a copy of the statement required by paragraph (a);

(d) Notifying the employee in the statement required by paragraph (a) that, as a condition of employment under the grant, the employee will:

- (1) Abide by the terms of the statement; and,
- (2) Notify the employer of any criminal drug statute conviction for a violation occurring in the workplace no later than five days after such conviction;

(e) Notifying the agency within ten days after receiving notice under subparagraph (d)(2) from an employee or otherwise receiving actual notice of such conviction;

(f) Taking one of the following actions, within 30 days of receiving notice under subparagraph (d)(2), with respect to any employee who is so convicted:

- (1) Taking appropriate personnel action against such an employee, up to and including termination; or
- (2) Requiring such employee to participate satisfactorily in a drug abuse assistance or rehabilitation program approved for such purposes by a Federal, State, or local health, law enforcement, or other appropriate agency;

(g) Making a good faith effort to continue to maintain a drug-free workplace through implementation of paragraphs (a), (b), (c), (d), (e), and (f).

**ACCEPTANCE**

In accepting this grant, I hereby certify that a drug-free workplace will be provided according to the requirements described above.

Grant No. \_\_\_\_\_

\_\_\_\_\_  
Grantee Organization

\_\_\_\_\_  
Date of Signed Certification

\_\_\_\_\_  
Name/Title of Signing Official

(\_\_\_\_\_) \_\_\_\_\_  
Telephone No. of Official

\_\_\_\_\_  
Signature of Above Official

U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
CERTIFICATION REGARDING DRUG-FREE WORKPLACE REQUIREMENTS  
GRANTEES WHO ARE INDIVIDUALS

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The grantee certifies that, as a condition of the grant, he or she will not engage in the unlawful manufacture, distribution, dispensing, possession or use of a controlled substance in conducting any activity under the grant.

ACCEPTANCE

In accepting this grant award, I hereby certify that I will not engage in the unlawful manufacture, distribution, dispensing, possession or use of a controlled substance in conducting any activity under the grant.

Grant No. \_\_\_\_\_ Name of Grantee \_\_\_\_\_

\_\_\_\_\_ Date of Signed Certification \_\_\_\_\_ Signature of Grantee \_\_\_\_\_

( ) \_\_\_\_\_  
Telephone No.