

NIH GUIDE

For Grants and Contracts

NOTICE OF MAILING CHANGE

Check here if you wish to
discontinue receiving this
publication

Check here if your address has
changed and you wish to con-
tinue receiving this publication.
Make corrections below and
mail this page to:

NIH Guide
Printing & Reproduction Branch
National Institutes of Health
Room B4BN08, Building 31
Bethesda, Maryland 20892

U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES

OFFICIAL BUSINESS
Penalty for Private Use, \$300

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

Vol. 18, No. 33
September 22, 1989

| |
|----------------------------------------------------------------------------|
| First Class Mail Postages & Fees Paid PHS/NIH/OD Permit No. G-291 |
|----------------------------------------------------------------------------|

NOTICES

NINDS RESTRICTIONS ON REQUESTED BUDGETS FOR PROGRAM PROJECT AND
CLINICAL RESEARCH CENTER APPLICATIONS 1
National Institute of Neurological Disorders and Stroke
Index: NEUROLOGICAL DISORDERS, STROKE

DATED ANNOUNCEMENTS (RFPs AND RFAs)

CYTOGENETIC TESTS IN VITRO AND IN VIVO (RFP) 1
National Institute of Environmental Health Sciences
Index: ENVIRONMENTAL HEALTH SCIENCES

REANNOUNCEMENT OF THE ANIMAL FACILITIES IMPROVEMENT PROGRAMS (RFAs) 2
Division of Research Resources
Index: RESEARCH RESOURCES

THE ROLE OF HEMOSTASIS AND ENDOTHELIAL CELL REACTIVITY IN VASO
OCCLUSION IN SICKLE CELL DISEASE (RFA) 2
National Heart, Lung, and Blood Institute
Index: HEART, LUNG, BLOOD

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES AIDS
INSTITUTIONAL TRAINING GRANTS (RFA) 3
National Institute of Allergy and Infectious Diseases
Index: ALLERGY, INFECTIOUS DISEASES

SPECIALIZED RESEARCH CENTER PROGRAMS IN REPRODUCTION OR CENTER
CORE GRANTS TO SUPPORT REPRODUCTION RESEARCH (RFA) 4
National Institute of Child Health and Human Development
Index: CHILD HEALTH, HUMAN DEVELOPMENT

ONGOING PROGRAM ANNOUNCEMENTS

SMALL GRANTS PROGRAM FOR LABORATORY RESEARCH RELATED TO THE
CLINICAL EVALUATION OF AIDS THERAPIES 5
National Institute of Allergy and Infectious Diseases
Index: ALLERGY, INFECTIOUS DISEASES

BIOLOGY OF TOOTH MOVEMENT AND ERUPTION 8
National Institute of Dental Research
Index: DENTAL RESEARCH

MINORITY HIGH SCHOOL STUDENT RESEARCH APPRENTICE PROGRAM 9
Division of Research Resources
Index: RESEARCH RESOURCES

STUDIES ON CANCER ETIOLOGY IN FINFISH AND SHELLFISH11
National Cancer Institute
National Institute of Environmental Health Sciences
Index: CANCER, ENVIRONMENTAL HEALTH SCIENCES

ERRATA

THE BIOCHEMISTRY OF FIBRINOLYSIS (RFA)13
National Heart, Lung, and Blood Institute
Index: HEART, LUNG, BLOOD

STRUCTURAL BIOLOGY AS APPLIED TO THE PROBLEM OF TARGETED DRUG
DESIGN FOR THE TREATMENT OF AIDS (PA)14
National Institute of General Medical Sciences
Index: GENERAL MEDICAL SCIENCES

NOTICES

NINDS RESTRICTIONS ON REQUESTED BUDGETS FOR PROGRAM PROJECT AND CLINICAL RESEARCH CENTER APPLICATIONS

P.T. 04; K.W. 0785035, 1002030, 0785110

National Institute of Neurological Disorders and Stroke

The National Institute of Neurological Disorders and Stroke (NINDS) announces a new policy of a ceiling amount for applications for program projects and clinical research centers. Effective for the submission deadline of February 1, 1990, such applications may not request more than \$750,000 (direct costs) in each of the five proposed years of support. Applications exceeding this limit will be returned to the applicant without further review.

Also effective February 1, 1990, applications for supplements to NINDS program projects and clinical research centers will not be accepted if the requested amount, added to the amount already approved and committed for that grant, exceeds \$750,000 in any year.

Competing continuation applications for program projects and clinical research centers already received and awaiting review or award may be awarded at amounts in excess of \$750,000 for the first year of continuation support (when appropriately recommended by initial review groups and Council, and meeting current payment criteria), but subsequent years will be reduced to \$750,000.

The NINDS regrets that budgetary constraints have dictated the issuance of this new policy. For additional information, and for NINDS Guidelines for the preparation of program project and clinical research grant applications, please contact:

John C. Dalton, Ph.D.
Associate Director for Extramural Activities
National Institute of Neurological Disorders and Stroke
Federal Building, Room 1016
Bethesda, Maryland 20892
Telephone: (301) 496-9248

DATED ANNOUNCEMENTS (RFPs AND RFAs)

CYTOGENETIC TESTS IN VITRO AND IN VIVO

RFP AVAILABLE: NIH-ES-89-27

P.T. 34; K.W. 1002015, 1002019, 0755010, 0780010

National Institute of Environmental Health Sciences

This is a total setaside for small business.

The purpose of this project is to provide the Government with cytogenetic testing capacity using both in vitro and in vivo assay systems. This will be achieved by conducting approximately 9 in vitro tests and 18 in vivo tests in year 1, and 10 in vitro and 20 in vivo tests per year in years 2 through 5. The in vitro tests consist of testing for the induction of chromosomal aberrations (ABS) and sister chromatid exchanges (SCE) in Chinese Hamster Ovary (CHO) cells (9 in year 1; 10 each in years 2-5). The in vivo tests consist of testing for induction of ABS in mouse bone marrow cells (7 in year 1, and approximately 8 per year in years 2-5) and for the induction of micronuclei (MN) in mouse bone marrow and/or peripheral blood cells (11 in year 1, and approximately 12 per year in years 2-5). This project will be divided into two phases. In Phase I (1st four months of year 1), the Contractor shall demonstrate the ability to perform the protocols required by the Statement of Work and maintain laboratory records in an acceptable manner by conducting 2 in vitro and 4 in vivo tests. If the results of Phase I are determined acceptable by the Project Officer, Phase II shall begin and the Contractor shall test the remaining chemicals for cytogenetic effects. An estimated 50 percent of all studies shall require repeat tests. The Contractor shall test chemicals that are known or potential mutagens, carcinogens, and/or toxins. The Government will provide all test chemicals and all mice for use by the Contractor in the performance of the Statement of Work. All other chemicals, materials, equipment, and facilities will be provided by the Contractor. The contract is expected to cover a five-year performance period. The Government estimates that 1.0 professional

person-year and 3.0 technical person-years of effort are required each contract year. The Request for Proposals (RFP) will be released on or about October 2, 1989, and proposals due December 1, 1989. All responsible sources may submit a proposal which shall be considered by the Agency. The Government plans to award one contract from this solicitation.

Requests should reference RFP NIH-ES-89-27 and should be forwarded to:

National Institute of Environmental Health Sciences
Contracts and Procurement Management Branch, OM
ATTN: Dorothy G. Williams, Contract Specialist
79 T.W. Alexander Drive, 4401 Building
P.O. Box 12874
Research Triangle Park, North Carolina 27709

REANNOUNCEMENT OF THE ANIMAL FACILITIES IMPROVEMENT PROGRAMS

RFA 89-RR-02 - DEVELOPING AND IMPROVING INSTITUTIONAL ANIMAL RESOURCES

RFA 89-RR-03 - ANIMAL FACILITY IMPROVEMENTS FOR SMALL RESEARCH PROGRAMS

P.T. 34; K.W. 1002002, 1014006

Division of Research Resources

This is a reminder of two previously announced Request for Applications (RFAs) concerning the improvement of research animal facilities which are currently available from the Division of Research Resources.

Any domestic public or private institution that receives funds from the Public Health Service (PHS) for the use of animals in research is eligible to apply for funds under RFA 89-RR-02. Matching funds are required.

Only institutions receiving less than \$500,000 annually from PHS for research projects involving the use of animals are eligible for support under RFA 89-RR-03. No matching funds are required.

The size of the award is limited in both programs. The deadline for applications for both RFAs is December 4, 1989. RFA 89-RR-02, Developing and Improving Institutional Animal Resources, was originally announced in the April 28, 1989 issue of the "NIH Guide for Grants and Contracts", Vol. 18, No. 15. RFA 89-RR-03, Animal Facility Improvements for Small Research Programs, was originally announced in the July 7, 1989 issue of the "NIH Guide for Grants and Contracts", Vol. 18, No. 23.

Copies of these RFAs can be obtained by contacting:

Director, Laboratory Animal Sciences Program
Animal Resources Program Branch
Division of Research Resources
National Institutes of Health
5333 Westbard Avenue, Room 853
Bethesda, Maryland 20892
Telephone: (301) 496-5175

THE ROLE OF HEMOSTASIS AND ENDOTHELIAL CELL REACTIVITY IN VASO OCCLUSION IN SICKLE CELL DISEASE

RFA AVAILABLE: 89-HL-18-B

P.T. 34; K.W. 1003002, 1002004, 1002034, 0785070

National Heart, Lung, and Blood Institute

Application Receipt Date: March 15, 1990

The Division of Blood Diseases and Resources of the National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health, announces the availability of a request for applications (RFA) to define the role of hemostasis and endothelial cell reactivity in vaso occlusion in sickle cell disease. Copies of the RFA and Instructions for the Preparation of Applications are currently available from NHLBI staff.

The major goal of this program is to stimulate basic and clinical research to clarify the role of cellular, humoral, and vascular factors of blood coagulation in the pathophysiology of sickle cell disease and to define new

therapeutic strategies that might help to limit or reverse the process of vaso occlusion.

Specific areas of interest are: (a) the role of hemostasis and fibrinolysis, including coagulation proteins, platelets, and endothelial cells in the overall pathophysiology of sickle cell disease, as well as their specific contributions to the pathogenesis of vaso occlusive crises; and (b) the basis of the altered interaction between erythrocytes and endothelial cells in sickle cell disease and to determine the role of this alteration, if any, in the vaso occlusive phenomena of sickle cell disease.

Applications for grants proposing clinical studies should include members of minority groups and women in the study populations. Otherwise, a clear rationale for their exclusion must be provided in the application.

The requirements and format for application submitted in response to the announcement, and copies of the RFA, may be obtained from:

Charles A. Wells, Ph.D.
Health Scientist Administrator
Sickle Cell Disease Branch
National Heart, Lung, and Blood Institute
Federal Building, Room 508
Bethesda, Maryland 20892

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES AIDS INSTITUTIONAL TRAINING GRANTS (T32)

RFA AVAILABLE: 89-AI-20

P.T. 44; K.W. 0715008, 0720005, 0765033, 1002008, 1002045, 0755025, 0710030

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: November 17, 1989
Application Receipt Date: January 10, 1990

The National Institute of Allergy and Infectious Diseases (NIAID) announces the availability of a Request for Applications (RFA) for development of an institutional training grant to fund long-term training in AIDS research.

Studies of pathogenic mechanisms, and development of vaccines and therapeutics require close collaboration between clinicians and epidemiologists working with HIV-infected patients and basic research scientists in biochemistry, chemistry, immunology, molecular biology, pharmacology, virology, and biostatistics. The collaboration between clinicians and basic research scientists requires individuals appropriately trained in multiple disciplines who have developed an understanding of the requirements and limitations of each discipline. Recognizing this need, the NIAID Division of AIDS is establishing a multi-disciplinary postdoctoral training program in AIDS research. The Division of AIDS anticipates that \$875,000 will be available to support the AIDS Institutional Training Grant Program in FY90.

Applications should focus on the biological mechanisms by which immuno-deficiency viruses cause disease and on mechanisms of prevention and treatment. Strongly encouraged are novel studies addressing the pathogenesis of HIV infection, potential avenues for enhanced and/or selective immune protection, and potential strategies for effective drug development.

The policy of NIAID and National Institutes of Health is to promote broad and systematic efforts to recruit individuals from minority groups currently underrepresented in biomedical research. Applicants must provide a description of special plans or efforts to recruit minorities to the Institutional AIDS Training Program.

Awards will be made as institutional (T32) training grants.

The complete RFA is available from:

Dr. Gregory Milman
Chief, Pathogenesis Branch
Division of AIDS, NIAID, NIH
6003 Executive Boulevard, Room 242P
Rockville, Maryland 20892
Telephone: (301) 496-8378

SPECIALIZED RESEARCH CENTER PROGRAMS IN REPRODUCTION (P50s) OR CENTER CORE GRANTS TO SUPPORT REPRODUCTION RESEARCH (P30s)

RFA AVAILABLE: 89-HD-09

P.T. 04; K.T. 0413002, 0710110, 0710115, 0710030, 0785105, 0760025

National Institute of Child Health and Human Development

Letter of Intent Receipt Date: January 1, 1990

Application Receipt Date: June 11, 1990

The Reproductive Sciences Branch (RSB), Center for Population Research (CPR), National Institute of Child Health and Human Development (NICHD), supports research on human reproduction which relies on a variety of approaches in biomedical sciences. Among the grant mechanisms used to provide research support, the RSB uses:

1) Specialized Research Centers (P50s) which are integrated groups of research projects and supporting core service facilities. The research activities included in such project grants must comprise, by definition, a multidisciplinary approach to biomedical problems in reproduction. Although these research programs may have more than one theme, focus, or emphasis, all of them must be responsive to one or more of the specific areas of reproduction research which constitute the purview of the RSB, CPR, NICHD.

2) Center Core Grants (P30s) which support Center Core facilities designed to enhance existing federally supported research projects within the purview of the RSB, CPR, NICHD. Such project awards require a critical mass of individual, reproduction-oriented awards where coordinated technical support would be cost-effective.

At present, the RSB supports a fixed number of centers with a commitment of five years of support that is competitively renewable for additional five-year periods. Two P50 centers and two P30 centers will seek renewal in FY 1991. One additional center grant (P50 or P30) will be awarded in FY 1991. This Request for Applications (RFA), therefore, represents a competition for a total of five grant awards.

Potential applicants should contact the RSB staff for further information regarding reproductive sciences center grants (P50s and P30s). It is strongly recommended, but not mandatory, that potential applicants send a letter of intent to the RSB staff at the address listed below by January 1, 1990. This letter should outline the organizational structure of the proposed center, list the title of the relevant research projects to be associated with it and the names of the relevant principal investigators. The letter of intent should be received by the RSB no later than January 1, 1990, but applicants are encouraged to send it as soon as they decide to apply for the grant so that the RSB staff can be of maximum assistance in the application process.

Center grant applications must be structured in accord with policy and formatting guidelines established by the NICHD. Such guidelines require, for example, certain tabulations in addition to the usual instructions for the standard NIH grant application forms (PHS-398 rev. 10/88) used to prepare these applications.

Although this solicitation is included in the plans for FY 1991, support for these center grants is contingent upon the receipt of funds for these purposes by the NICHD. The number of grants to be awarded is also contingent upon a sufficient number of applications receiving a high enough level of merit to be considered for an award. It is expected that up to five (5) awards will be made as a result of this announcement.

Applications for grants involving clinical studies should include members of minority groups and women in the study populations. Otherwise, a clear rationale for their exclusion must be provided in the application.

For further information and a copy of the fully described RFA, please contact:

Koji Yoshinaga, Ph.D.
Reproductive Sciences Branch
Center for Population Research
National Institute of Child Health and Human Development
National Institutes of Health
Executive Plaza North, Room 603
Bethesda, Maryland 20892
Telephone: (301) 496-6515

To obtain copies of the NICHD Policy and Formatting Guidelines for P30 or P50 center grant applications, please contact:

Laurance Johnston, Ph.D.
Scientific Review Program
National Institute of Child Health and Human Development
National Institutes of Health
Executive Plaza North, Room 520
Bethesda, Maryland 20892
Telephone: (301) 496-1696

This program is described in the Catalog of Federal Domestic Assistance No. 13.864, Population Research. Awards will be made under the authority of the Public Health Service Act 301 (42 USC 241) and 441 (USC 289d) and administered under PHS Grant Policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 or Health Systems Agency review.

ONGOING PROGRAM ANNOUNCEMENTS

SMALL GRANTS PROGRAM FOR LABORATORY RESEARCH RELATED TO THE CLINICAL EVALUATION OF AIDS THERAPIES

P.T. 34; K.W. 0715008, 0785035, 0745000, 0715125, 0755015, 0755010

National Institute of Allergy and Infectious Diseases

Application Receipt Dates: December 12, 1989 and May 4, 1990

The National Institute of Allergy and Infectious Diseases (NIAID) is initiating a small grant award with multiple receipt dates for laboratory research projects related to the clinical evaluation of AIDS therapies.

BACKGROUND

The NIAID has established a clinical trials network to evaluate the safety and efficacy of both antiretroviral and immunomodulatory therapies for the treatment and control of HIV and specific therapies of opportunistic infections and malignancies associated with HIV infection. This network is organized as the AIDS Clinical Trials Group (ACTG) and consists of: 45 funded academic centers or consortiums, termed AIDS Clinical Trial Units (ACTUs), the Division of AIDS/Operations Office, NIAID, and the Clinical Trial Coordinating Center. The ACTG is responsible for developing and conducting therapeutic protocols of the highest scientific priority.

The development of effective therapies depends on information regarding the manifestations of HIV infection, their reproducible and sensitive detection, and on the course and mechanisms of pathogenesis. Since we are in the early stages of an epidemic caused by a new etiologic agent, much of this information is lacking. The Small Grants Program is designed to expand our information base in a responsive, innovative, and timely manner.

RESEARCH GOALS AND SCOPE

This is a one or two year, non-renewable award intended to provide support for small or pilot projects which will obtain timely information that will assist in the development and assessment of effective and appropriate therapies for HIV infection and associated opportunistic diseases.

Research is encouraged in the following areas:

- o the progression of viral infection and organ system pathology, and how test therapies may affect these processes;
- o host factors which affect response to therapy;
- o the development of surrogate markers for clinical endpoints of new trials;
- o the development and application of diagnostics and assays for clinical trial research.

Clinical trials designed to evaluate the safety and/or efficacy of therapies directed against HIV and its sequelae will not be funded under this mechanism.

MECHANISMS OF SUPPORT

ELIGIBILITY

- o Recently trained, or less experienced investigators.
- o Investigators not currently involved in AIDS research who wish to establish collaborations with clinical investigators conducting AIDS research. (The list of AIDS Clinical Trial Units and their principal investigators is available upon request.)
- o Investigators at minority institutions.
- o Established AIDS investigators needing modest support for a pilot or small project.

TERMS OF THE AWARD

The award may be for a 1-2 year time period and will provide a maximum of \$45,000 (direct costs) for technical assistance, supplies, and small equipment required by the project. This is non-renewable award. Dependent on favorable review and contingent on the availability of funds, the Program anticipates to make 10-12 awards in Fiscal year 1990. The earliest start date for successful applications is April 10, 1990, for applications submitted by the December receipt date.

REVIEW PROCEDURES AND CRITERIA

Applications submitted will be reviewed by staff for responsiveness and for eligibility. Non-responsive applications and those applications not meeting eligibility requirements will be returned to the applicant without further consideration. Responsive applications will be subjected to initial scientific review by the Acquired Immunodeficiency Syndrome Research Review Committee (AIDSRRRC) of NIAID.

Because the format for preparing this application is different from that used for regular research grants, ADDITIONAL INFORMATION AND INSTRUCTIONS SHOULD BE OBTAINED FROM THE NIAID DIVISION OF AIDS STAFF CONTACT LISTED BELOW. Applicants must adhere to this format to be responsive.

REVIEW CRITERIA

Applications will be evaluated as to:

- o Significance and scientific merit of the project;
- o Adequacy of the objectives of project to target the research areas listed under RESEARCH GOALS AND SCOPE;
- o Characterization of the proposed project as an innovative or pilot study which provides the basis for more extended laboratory research or contributes to clinical trial investigations of therapies directed against HIV and/or associated opportunistic diseases;
- o Appropriateness of research design and methodology, and feasibility as it relates to Special Considerations listed below;
- o Eligibility of applicant as defined under MECHANISMS OF SUPPORT will be reviewed by the staff of the Division of AIDS, NIAID;
- o Investigators' experience and/or training for carrying out the project;
- o Adequacy of proposed facilities;
- o Appropriateness of proposed budget and adequacy of justification.

SPECIAL CONSIDERATIONS

Both AIDS Clinical Trials Group investigators and scientists not currently involved in the clinical trial effort supported by NIAID are encouraged to apply.

The goal of this Program is to obtain information that will aid in the clinical evaluation of AIDS therapies. The research projects that are proposed, however, must be able to stand alone for evaluation during the peer

review process, and during implementation and data analysis. Therefore, the following guidelines should be adhered to:

- o The research project proposed cannot depend on data that will be generated by unblinding an ongoing clinical trial, either for its development, implementation, or evaluation.
- o If a proposed project requires samples from, or testing of, patients enrolled in ACTG studies, clearance must be obtained from the relevant protocol chairs. This should be documented in a letter submitted with the application.
- o If the feasibility of conducting the proposed project is dependent on the conduct of a clinical trial, assurance must be provided that the clinical trial will take place, i.e., it is already active or completed or that there are no foreseeable impediments to its implementation. Applicants must provide written documentation to this effect.

METHOD OF APPLYING

The prospective applicant is encouraged to submit a one-page letter of intent according to the timetable listed below, indicating the P.I., institution, and a descriptive title. The letter of intent is intended to provide early contact between the investigator and NIH staff, to provide an estimate of numbers of applications expected, and to aid in selection of additional reviewers to the chartered review group, if necessary. It is not binding, will not enter into the review of any application subsequently submitted, and is not a requirement for application. Letters of intent should be addressed to the program staff contact listed below.

Applications should be submitted on form PHS 398, (rev. 10/88) available at most institutional business offices or from the Division of Research Grants, NIH, Bethesda, MD 20892. Mark "Yes" in item 2 of the application and enter the announcement title: "Small Grants Program for Laboratory research related to the Clinical Evaluation of AIDS Therapies: NIAID". Submit the original application and four copies to:

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

Mail 2 exact copies of the application to: Dr. Sally Mulhern (see review staff contact below). If you elect to send appendicies, 2 complete sets are sufficient.

TIMETABLE

The timetable from receipt of applications to award (accelerated process) is as follows:

| Letter of intent receipt date | Application receipt date | Award date |
|----------------------------------|-----------------------------|--------------------|
| November 15, 1989 | December 12, 1989 | April 10, 1990 |
| April 12, 1990 | May 04, 1990 | September 15, 1990 |

As a general guide, application submission dates are four months prior to the funding date for which they are intended.

STAFF CONTACT

For further information regarding the scientific review, prospective applicants should contact:

Dr. Sally Mulhern
AIDS Review Section
Program and Project Review Branch
National Institute of Allergy
and Infectious Diseases
Westwood Building, Room 3A12
Bethesda, Maryland 20892
Telephone: (301) 496-2550

For inquiries regarding the programmatic aspects of the announcement, applicants should contact:

Dr. Robert Eisinger
Treatment Research Program
Division of Acquired Immune Deficiency Syndrome
National Institute of Allergy and Infectious Diseases
6003 Executive Boulevard
Room 212N
Rockville, Maryland 20852
Telephone: (301) 496-0700

This program is described in the Catalog of Federal Domestic Assistance No.13.856 - Microbiology and Infectious Disease Research and 13.855 - Immunology, Allergic and Immunologic Diseases Research. Grants are awarded under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grant policies and Federal Regulations, most specifically at 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

BIOLOGY OF TOOTH MOVEMENT AND ERUPTION

P.T. 34; K.W. 0785040, 0775000

National Institute of Dental Research

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

The Craniofacial Anomalies, Pain Control and Behavioral Research Branch of the National Institute of Dental Research (NIDR) encourages submission of high quality applications for the support of research on the biological mechanisms of tooth movement, tooth eruption and tooth root resorption in order to expand its activities in this area.

BACKGROUND

Tooth movement occurs throughout life, equilibrating the effects of natural forces on the teeth by cellular responses in the surrounding tissues. Orthodontists have exploited this phenomenon by using artificial forces to direct teeth into more desirable positions. Much of orthodontic research has emphasized development of appliances to effect tooth movement. However, tooth movement is mediated by cellular activity and advances in treatment also depend on improved understanding of the biological processes involved. A recent NIDR sponsored conference, entitled "The Biology of Tooth Movement" (Norton L.A., Burstone, C.J. (eds): CRC Press, Boca Raton, Florida, 1989), addressed the key question of how mechanical force application evokes molecular responses in the surrounding tissues. The tissues directly affected by force-induced tooth movement include tooth components, periodontal ligament, alveolar bone, and the gingiva. Vascular, neurological, immunological, endocrine and growth factors in the tissues surrounding the teeth have been implicated as cellular mediators in response to orthodontic forces. Related mechanisms and some of the same mediators may also be involved in excessive root resorption, which is a significant adverse effect of orthodontic treatment.

Many of the biological processes and tissue changes involved in tooth movement are similar to those implicated in the various theories proposed to account for tooth eruption. Several of the theories of tooth eruption implicate propulsive forces generated by extrusion of pulp through the growth of dentin, by growth of the tooth root, by apposition of bone beneath the erupting tooth or by hydrostatic forces derived from blood pressure. Other theories propose that the contractile properties of the periodontal ligament create the eruptive force or that the dental follicle is responsible for initiating bone resorption from the eruption pathway and bone formation beneath the erupting tooth. These theories and the possible mechanisms were critically discussed at another recent NIDR sponsored conference, entitled, "The Biological Mechanisms of Tooth Eruption and Root Resorption" (Davidovitch, Z. (ed), EBSCO Media, Birmingham, Alabama, 1988).

RESEARCH GOALS

The objective of this program announcement is to solicit research grant applications to elucidate the biological mechanisms involved in tooth movement, tooth eruption and root resorption. Applicants are urged to consult the published proceedings of the two conferences mentioned above in order to familiarize themselves with the state of the art at the time of those

conferences. However, applications need not be confined to topics discussed; the differences in the findings and opinions expressed illustrate the need for additional approaches.

MECHANISM OF SUPPORT

Support for this program will be through research grants, including project grants (R01), small grants (R03) and FIRST awards (R29). Policies that govern research grant programs of the National Institutes of Health will prevail.

APPLICATION AND REVIEW PROCEDURES

Applications in response to this announcement will be reviewed in accordance with the usual NIH peer review procedures for research grants (Study Section). Review criteria include the significance and originality of the research goals and approaches; feasibility of the research and adequacy of the experimental design; training, experience, research competence, and dedication of the investigator(s); adequacy of available facilities and availability of appropriate study populations; provisions for the protection of human subjects and the humane care of animals; and appropriateness of the requested budget relative to the work proposed.

Funding decisions will be based on the Study Section's and an appropriate National Advisory Councils' recommendations regarding scientific merit and program relevance, and the availability of appropriated funds.

Questions concerning this announcement may be addressed to Dr. John D. Townsley at the address given below. Applications for research grants should be submitted on form PHS-398 (rev. 10/88), and the special instructions for small grants and FIRST awards should be followed when applicable. Application forms and special instructions are available in the business or grants office at most academic or research institutions, or from the Division of Research Grants, National Institutes of Health, Westwood Building, Room 440, Bethesda, Maryland 20892. Applications will be accepted in accordance with the customary dates for new applications depending upon the funding mechanism.

The phrase "BIOLOGY OF TOOTH MOVEMENT AND ERUPTION" should be typed on line 2 of the face page of the application. The original and six copies should be sent or delivered to:

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

Applicants are encouraged to contact NIDR staff prior to applying. Contact:

John D. Townsley, Ph.D.
Chief, Craniofacial Anomalies, Pain
Control and Behavioral Research Branch
National Institute of Dental Research
Westwood Building, Room 506
Bethesda, Maryland 20892-4500
Telephone: (301) 496-7807

This program is described in the Catalog of Federal Assistance No. 13.122. Awards will be made under authorization of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended), and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

MINORITY HIGH SCHOOL STUDENT RESEARCH APPRENTICE PROGRAM

P.T. 34, FF; K.W. 0710030

Division of Research Resources

Application Receipt Date: December 1, 1989

BACKGROUND AND OBJECTIVES

The Division of Research Resources (DRR), National Institutes of Health (NIH), currently plans to continue the Minority High School Student Research Apprentice Program in 1990.

The purpose of the program is to provide minority high school students with a meaningful experience in various aspects of health-related research in order to stimulate their interest in careers in science.

ELIGIBILITY

Eligible institutions are those that were awarded grants during the latest complete Federal Fiscal Year 1989 from either the Biomedical Research Support Grant (BRSO) Program or the Minority Biomedical Research Support (MBRS) Program, both of which are administered by DRR, NIH. Only one application for the Apprentice Program can be submitted by a component of an institution that is the recipient of both the BRSO and MBRS awards.

Students eligible for support under this program are those who: (1) identify themselves as minority (i.e., Black, Hispanic, American Indian, Alaskan Native, Pacific Islander, or Asian); (2) are U.S. citizens or have a permanent visa; and (3) are enrolled in high school during the 1989-90 academic year. (Students who will graduate from high school in 1990 are eligible, as are students who participated in a previous year, provided they are still enrolled at the high school level.)

MECHANISM OF SUPPORT

The mechanism of support for this program will be the NIH grant-in-aid (Minority High School Student Research Apprentice Program, S03). Support will be provided at a level of \$1,500 for each apprentice position allocated. No indirect costs will be paid. Direct support to the apprentice must be as salary; stipends are not allowed. Within the \$1,500 per student allocation, funds may also be utilized for supplies, extending the research experience through the school year, or if adequate funds exist, for an additional apprentice. However, funds from these grants may only be used for the costs of the apprentice program. The Program Director is responsible for recruitment and selection of the apprentice and assignment of each to an investigator. Recruitment and selection criteria for students should emphasize factors of the students' motivation, ability, scholastic aptitude and accomplishments. In addition, consideration should be given to science teachers' recommendations and, where possible, the degree of parental commitment. Assignments should be made to investigators involved in health-related research who are committed to developing in the high school student an understanding of the research in which they participate and the technical skills needed. Awards will be for one year.

APPLICATION

Eligible institutions should submit an application consisting of no more than:

1. A one-page letter stating the number of student positions requested, plus
2. An original and two signed and completed copies of the Grant Application Form, PHS 398 (Rev. 10/88) face page only.

Mark the "YES" box in item 2 and indicate the announcement title as "Minority High School Student Research Apprentice Program".

Mark items numbered 4, 5, 7, 8b, 10 and 14 as Not Applicable (N.A.). Complete item 8a with the total dollar amount of your request, which is number of student positions requested times \$1,500 per student.

A final progress report, consisting of a one-page Program Director's report, a one-page report for each student, and a Financial Status Report will be required by May 31, 1991.

Please Note: Limited funds and increased requests for such student positions may restrict the final allocations by DRR to three or four students per eligible applicant institution. Upon recommendation of the National Advisory Research Resources Council, DRR will give preference in making awards to those institutions that can support a summer program having a "critical mass" of at least five or six students using institutional as well as DRR funds.

The applications should be submitted to:

Biomedical Research Support Program
Division of Research Resources
National Institutes of Health
5333 Westbard Avenue
Westwood Building, Room 10A11
Bethesda, Maryland 20892

Inquires can be made of Dr. Marjorie A. Tingle at the above indicated address or by calling (301) 496-6743.

The deadline for receipt of applications is December 1, 1989. Awards will be effective March 1, 1990, contingent upon availability of appropriated funds.

STUDIES ON CANCER ETIOLOGY IN FINFISH AND SHELLFISH

P.T. 34; K.W. 0715035, 0755030, 1007001, 1007002, 1007003

National Cancer Institute
National Institute of Environmental Health Sciences

Application Receipt Dates: February 1, June 1, and October 1, 1990

The Division of Cancer Etiology (DCE) of the National Cancer Institute (NCI) and the Extramural Program of the National Institute of Environmental Health Sciences (NIEHS) invite grant applications through a joint Program Announcement (PA) for basic studies intended to provide insights and approaches to an understanding of the possible etiology of neoplasia in finfish and shellfish. This type of solicitation is utilized when it is desired to encourage investigator-initiated research projects in areas of special programmatic interest to the National Institutes of Health (NIH). Applicants funded under the PA are supported through traditional research grants in accordance with Public Health Service (PHS) policies applicable to research grants. It is to be noted that only Research Project (R01) grant applications will be considered to be responsive to this PA.

Applications received in response to this PA by February 1, 1990, may be reviewed by the same NIH Initial Review Group of the Division of Research Grants (DRG). Grant applications in response to this announcement received June 1 or October 1, 1990, will be reviewed in accordance with the usual Public Health Service Peer Review (Study Section) procedures.

I. BACKGROUND

It has become evident that "cancer epidemics," or epizootics can occur in certain fish populations. At present there are at least six areas within the U.S. that appear to present significant epidemics: (1) the Puget Sound Basin in Washington, (2) Torch Lake in Michigan, (3) the Black River in Ohio, (4) the Buffalo River, (5) the Hudson River in New York, and (6) the Pamlico River in Texas. In each case the feral finfish population presents an unusually high prevalence of distinct tumor types. Tumors have been identified in many species of finfish and shellfish at one or more of the following sites: skin, gill, mantle, oral region, pharynx, stomach, carapace, pancreas, liver, kidney, gonads, heart, thyroid gland, nervous system, soft tissues, skeleton, and lymphoreticular and hematopoietic tissues.

Some of these cancers in lower animals may be similar and others dissimilar to those of man. Some cancers, in fact, arise from cells and organs of lower animals that man does not possess. There are large gaps in our knowledge about how neoplasms in aquatic animals conform to what is known about neoplasms of mammals, their morphologic characteristics, biologic course, relation to host-regulating mechanism, and their transplantability and transmissibility. Some neoplastic criteria used in mammalian pathology cannot yet be applied with confidence to many of the tumors or tumor-like lesions of aquatic species. Nevertheless, evolution of the phyla and species has imparted a great deal of biological commonage, particularly at the cellular level, and there are striking similarities in metabolic response to xenobiotics, at least qualitatively, between finfish and mammals. Such commonality serves as the bases for extrapolation of the significance of response at one phyletic level to that at another phyletic level.

Experimental evidence, to date, suggests that some fish species, when compared to rodents, are less sensitive to the toxic and more responsive to the carcinogenic effects of xenobiotics; they react more promptly, with a shorter latency period and with greater specificity. These characteristics, together with the fact that aquatic animals are exposed to a water environment, with all of its solubilized and suspended components, at the level of gill, eye, gut, and skin, suggest that they should serve as major indicators of agents in the environment which may pose a risk to humans. Not only are these aquatic animals obvious candidates to serve as sentinels of carcinogenic pollutants in the environment but the epizootics of cancer which they experience in confined or circumscribed water areas such as lakes and canals or sharply defined areas of rivers, bays and estuaries offer a natural experiment for establishing cause-and-effect relationships, interspecies comparisons, and for establishing target cells at risk.

A request for applications (RFA) for "Studies on the Etiology of Neoplasia in Poikilothermic, Aquatic Animals: Finfish and Shellfish" was issued on January 31, 1986. Fifty-four applications were received in response to the RFA and a total of nine awards were made. The RFA was jointly sponsored by the NCI, NIEHS, and the Department of the Army (Medical Research and Development Command). The Army funds for this initiative are being administered by the NCI through an Interagency Agreement. The NCI and Army funds were used to award seven grants. Two other applications were given NIEHS primary assignment and were awarded by NIEHS early in FY 87.

II. RESEARCH GOALS AND SCOPE

The overall purpose of this PA is to accelerate the development of additional understanding relative to studies on the possible etiology of neoplasia in poikilothermic, aquatic animals: finfish and shellfish. The proposed PA will seek again to make the research community aware of the interests of the NCI and NIEHS in fish carcinogenesis models.

Consistent with the title of this PA are a broad spectrum of studies that would greatly facilitate our understanding of the etiology of neoplasia in finfish and shellfish. Listed below are some commonly identified needs which are intended to express the spectrum of studies of interest but which are not intended as a comprehensive list of possibilities (it will be up to the applicant to determine the scope and objective of the studies proposed):

- a) Evaluation of the similarity of metabolic function in procarcinogen activation among different species of invertebrates and/or vertebrates in regard to Phase I and Phase II reactions. Assessment of the role of fish hepatocytes in metabolism of procarcinogens. Studies on bioavailability and transfer of xenobiotics and their metabolites from invertebrates to fish and from invertebrates and fish to mammals.
- b) Effects of environmental and physiological variables of water temperature, age, sex and gonadal development on bioavailability and metabolism of xenobiotics.
- c) Development of in vitro culture systems for normal and neoplastic cells from invertebrates and vertebrates and analysis of adducts to macromolecules of environmentally relevant xenobiotic metabolites.
- d) Studies on chemical/chemical and chemical/viral interactions in the etiology of aquatic animal neoplasms and the identification of oncogenes in invertebrate and vertebrate species.
- e) Analysis of DNA repair capacity, mitotic index, sister chromatid exchange, cell cycle time, and enzyme pathways for xenobiotic metabolism under various temperature conditions in poikilothermic aquatic animals and determination of the relationship to the persistence of genetic lesions that might lead to tumorigenesis.
- f) Studies of factors involved in promotion or progression of a tumor in aquatic species. Assessment of transplantability of neoplasms.
- g) The effect of chemical pollutants on the immune response in aquatic animals and the role of the immune system in aquatic animal neoplasia.
- h) Expansion of the experimental oncology database on various promising fish species as carcinogen assay subjects. Tumor induction studies with chemical agents which utilize species such as the rainbow trout, the medaka or Japanese killifish, the guppy, the zebrafish, the sheepshead minnow, or other established models. Besides tumor induction, studies might include the further development of data on potency of carcinogenic agents in fishes, utilizing fish molecular, cellular, and tissue responses with screening endpoints such as unscheduled DNA synthesis, liver enzyme induction, chromosomal aberrations, sister chromatid exchange, or detection of altered foci in such target tissues as liver.

III. MECHANISM OF SUPPORT

This program will be supported through traditional research grants (R01). Awards will be administered under Public Health Service grants policy as stated in the PHS Grants Policy Statement, DHHS Publication No. 82-50,000, revised January 1, 1987. The total project period for applications submitted in response to the PA should not exceed five years.

IV. ELIGIBILITY

Non-profit and for-profit organizations and institutions, governments and their agencies, and individuals are eligible to apply.

V. APPLICATION AND REVIEW PROCEDURES

Applications submitted in response to the PA will be considered by DRG for dual institute assignment to NCI and NIEHS. The primary institute assignment will be determined by DRG based on established institute referral guidelines. If a sufficient number of applications are received for the February 1, 1990, receipt date, they will be reviewed by a special study section to be assembled by the DRG, NIH. Applications received for the June 1 or October 1 1990, deadlines will be assigned by DRG to the most appropriate regular study section. Review criteria include the significance and originality of research goals and approaches; feasibility of research and adequacy of experimental design; adequacy of available facilities and appropriateness of the requested budget relative to the work proposed. Following study section review, further evaluation will be provided by an appropriate National Advisory Board/Council. Funding decisions will be based on the above evaluations and on the availability of funds.

Applications should be submitted on Form PHS-398, revised 10/88, available in the business or grants office at most academic or research institutions, or from the Division of Research Grants, NIH. Applications will be accepted in accordance with the date for receipt of applications on or before February 1, June 1, or October 1, 1990.

The phrase "IN RESPONSE TO PROGRAM ANNOUNCEMENT - FINFISH AND SHELLFISH" should be typed on line 2 of the face page of the application and check "YES" in the box. The original and six copies should be sent to:

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

Additional information related to the background of this program announcement can be obtained by contacting:

Dr. David G. Longfellow
Chief, Chemical and Physical Carcinogenesis Branch
Division of Cancer Etiology
National Cancer Institute
Executive Plaza North, Suite 700
6130 Executive Boulevard
Rockville, Maryland 20892
Telephone: (301) 496-5471

This program is described in the Catalog of Federal Domestic Assistance No. 13.393, Cancer Prevention Research. Awards will be made under authorization of the Public Health Service Act, Title III, Section 301(c) and Section 402 (Public Law 78-410, as amended; 42 USC 241; 42 USC 282) and administered under PHS grant policies and Federal regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

ERRATA

THE BIOCHEMISTRY OF FIBRINOLYSIS

RFA AVAILABLE: 89-HL-16-B

P.T. 34; K.W. 1003002, 0760035, 0790000

National Heart, Lung, and Blood Institute

Application Receipt Date: March 15, 1990

This Request for Applications was published in the NIH Guide for Grants and Contracts on August 25, 1989, Vol. 18, No. 29, which contained incorrect information about funding mechanisms and the anticipated number of awards. This announcement is contains the correct information.

The Blood Diseases Branch of the Division of Blood Diseases and Resources, National Heart, Lung, and Blood Institute (NHLBI), announces the availability of a Request for Applications (RFA) on the above subject. Copies of the RFA are currently available from staff of the NHLBI. Awards will be made to foreign institutions only for research of very unusual merit, need, and promise.

This program will support basic research on the biochemical mechanisms that result in fibrinolysis and thrombolysis with particular emphasis on the thromboselectivity of plasminogen activators and their regulation by plasminogen activator inhibitors. Research elucidating the biochemical basis of resistance of old thrombi towards thrombolytic agents and those thrombi forming after thrombolytic therapy is also relevant to the goals and objectives of this RFA. This announcement may be of particular interest to investigators with expertise in physical and structural biochemistry.

The support mechanism for this five-year program will be the traditional, individual research grant (R01). Although approximately \$1,350,000 (for direct plus indirect costs) for this program is included in the financial plans for fiscal year 1990, award of grants pursuant to this RFA is contingent upon receipt of funds for this purpose.

For further information and to request a copy of the complete RFA, contact:

Diane L. Lucas, Ph.D.
Division of Blood Diseases and Resources
National Heart, Lung, and Blood Institute
Federal Building, Room 5A12
Bethesda, Maryland 20892
Telephone: (301) 496-5911

**STRUCTURAL BIOLOGY AS APPLIED TO THE PROBLEM OF TARGETED DRUG DESIGN
FOR THE TREATMENT OF AIDS**

P.T. 34; K.W. 0715008, 0755025, 1003001, 0710030, 1002045

National Institute of General Medical Sciences

This Program Announcement was published in the NIH Guide for Grants and Contracts on September 8, 1989, Vol. 18, No. 31. It contained incorrect information about the number of copies of the application to submit to the Division of Research Grants. The correct information is to send the original and six (6) copies to:

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

**THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:

5333 Westbard Avenue
Bethesda, Maryland 20816