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

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NOTICES

REVISIONS TO PHS CLAUSES: "PROTECTION OF HUMAN SUBJECTS" AND "CARE OF LIVE VERTEBRATE ANIMALS"

P.T. 34,16; K.W. 0201011, 0783005

National Institutes of Health

The May 24 "Federal Register" (Vol. 52, No. 58) contains the final rule revising two PHS clauses, "Protection of Human Subjects" (PHS 352.280-1) and "Care of Live Vertebrate Animals" (PHS 352.280-2). The changed clauses give the Contracting Officer the right, upon determining that a Contractor is not in compliance with the requirements of each respective clause, to immediately suspend work and further payments until the noncompliance is corrected. Should the noncompliance remain uncorrected, the Contracting Officer may terminate the contract. The exact wording of each added paragraph is set forth below:

PHS 352.280-1, PROTECTION OF HUMAN SUBJECTS

"(c) If at any time during performance of this contract, the Contracting Officer determines, in consultation with the Office for Protection from Research Risks (OPRR), National Institutes of Health (NIH), that the Contractor is not in compliance with any of the requirements and/or standards stated in paragraphs (a) and (b), above, the Contracting Officer may immediately suspend, in whole or in part, work and further payments under this contract until the Contractor corrects such noncompliance. Notice of the suspension may be communicated by telephone and confirmed in writing. If the Contractor fails to complete corrective action within the period of time designated in the Contracting Officer's written notice of suspension, the Contracting Officer may, in consultation with OPRR, NIH, terminate this contract in whole or in part, and the Contractor's name may be removed from the list of those Contractors with approved Health and Human Services Human Subject Assurances."

PHS 352.208-2, CARE OF LIVE VERTEBRATE ANIMALS

"(d) If at any time during performance of this contract, the Contracting Officer determines, in consultation with the Office for Protection from Research Risks (OPRR), National Institutes of Health (NIH), that the Contractor is not in compliance with any of the requirements and/or standards stated in paragraphs (b) and (c), above, the Contracting Officer may immediately suspend, in whole or in part, work and further payments under this contract until the Contractor corrects such noncompliance. Notice of the suspension may be communicated by telephone and confirmed in writing. If the Contractor fails to complete corrective action within the period of time designated in the Contracting Officer's written notice of suspension, the Contracting Officer may, in consultation with OPRR, NIH, terminate this contract in whole or in part, and the Contractor's name may be removed from the list of those Contractors with approved Health and Human Services Human Subject Assurances."

AVAILABILITY OF FISH OIL TEST MATERIALS

P.T. 36; K.W. 0780000, 1003016

National Institutes of Health

SUMMARY AND PURPOSE

There is a growing body of evidence that beneficial effects may be derived from components which exist in seafood or fish oils such as the omega-3 polyunsaturated fatty acids (PUFA). Proper evaluation of such components requires that specific test materials be made available to qualified researchers in adequate amounts and of consistent quality.

In December 1986 a Memorandum of Understanding was signed by the Directors of the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration and the Administrator of the National Oceanic and Atmospheric Administration, Department of Commerce, wherein they agreed to cooperate on a Fish Oil Test Material Program. Congress had previously allocated funds to the National Marine Fisheries Service, DOC, in order to provide for the production of fish oil test materials.

TEST MATERIALS CURRENTLY AVAILABLE - soft gel capsules of:
- o Purified, steam-stripped menhaden oil
- o Commercial preparations of olive, corn and safflower oil

All capsules are 1 gram, opaque and are packaged, 100 capsules per brown glass bottle (each bottle with an internal plastic seal under the screw-cap lid), 12 bottles per shelf-pack, 3 shelf-packs per master case. The fish oils and placebos are packaged identically, and are currently being stored at 5 degrees C. To each kilo of steam stripped fish oil, 1 gm of Tenox 20A (20% TBHQ, 3% citric acid, 30% corn oil, 32% glycerol monooleate, 15% propylene glycol) was added prior to encapsulation. Nitrogen was not used during the preparation/packaging processes. No antioxidant was added to the placebos. Materials will be supplied with actual lot analysis.

TEST MATERIALS AVAILABLE IN THE FUTURE: Concentrates of omega-3 fatty acids from menhaden oil, purified ethyl esters of eicosapentaenoate (20:5w3) and docosahexaenoate (22:6w3) and synthetic deuterated fatty acids are materials planned for production.

INQUIRIES AND APPLICATIONS

Active investigators may apply for available materials to be used for relevant studies by requesting an application form from:

Fish Oil Test Materials Program
Nutrition Coordinating Committee Office
Building 31, Room 4B63
National Institutes of Health
Bethesda, Maryland 20892

DATED ANNOUNCEMENTS (RFPs AND RFAs AVAILABLE)

BREAST AND OTHER CANCERS FOLLOWING X-RAYS FOR SCOLIOSIS

RFP AVAILABLE: NCI-CP-71107-13

P.T. 34; K.W. 0715035, 0785055, 0404021

National Cancer Institute

The Radiation Epidemiology Branch of the Division of Cancer Etiology, National Cancer Institute, National Institutes of Health, is soliciting proposals from qualified firms to provide the necessary resources to conduct a study on breast and other cancers following x-rays for scoliosis. A feasibility study of cancer morbidity and mortality among scoliotics was initiated in 1983 at four hospitals in Minneapolis-St. Paul, Minnesota. The objectives of the feasibility study were to determine if medical records were available for persons diagnosed with scoliosis between 1935 and 1965, to evaluate the quality of information contained in the medical records, to develop and pretest a medical record abstract form, to identify and tabulate the radiological records for all diagnostic x-rays taken during the course of monitoring scoliosis, to estimate the radiation doses to the breast using data from the radiation records or actual films, to trace and locate patients, and to conduct a mail questionnaire survey. The pilot study was carried out in collaboration with the Scoliosis Research Society.

The objectives of this competition are to obtain managerial, technical, and clerical support services for an expanded epidemiologic followup study of patients treated for scoliosis. In order to obtain sufficient numbers, it will be necessary to enlist subjects from approximately eight different centers across the United States. Emphasis shall be on breast, leukemia, lung and thyroid cancers.

RFP NO. NCI-CP-71107-13 will be available on or about June 10, 1987. Proposals will be due approximately 45 days following the actual date of RFP issuance. The National Cancer Institute will consider proposals from all responsible sources.

Copies of the RFP may be obtained by sending a written request to:

Sharon A. Miller
Contract Specialist
National Cancer Institute
Blair Building, Room 114
9000 Rockville Pike
Bethesda, Maryland 20892

AIRWAY MUCIN: MOLECULAR BIOLOGY AND REGULATION

RFA AVAILABLE: 87-HL-16-L

P.T. 34; K.W. 1002004, 1002008, 0705065, 1002019, 1003002, 0710070, 0710100

National Heart, Lung, and Blood Institute

Application Receipt Date: November 16, 1987

The Division of Lung Diseases of the National Heart, Lung, and Blood Institute invites grant applications to be considered in a single competition for support of molecular biological studies of airway mucins. The primary objective of this special grant program is to stimulate basic research on the structure and biosynthesis of airway mucins in health and disease.

BACKGROUND

Mucins are carbohydrate rich proteins which comprise the major portion of the mucosal layer lining the respiratory epithelium. Mucins provide the first line of defense of the lung from inhaled foreign matter through well-defined functions including mucociliary clearance and prevention of epithelial desiccation. There is increased synthesis and/or secretion of airway mucins during various pulmonary diseases such as asthma, chronic bronchitis, and cystic fibrosis. Mucins associated with disease may be abnormal both in chemical and physical characteristics. Molecular biological techniques have great potential for providing further understanding of the molecular aspects of respiratory mucin synthesis and its regulation in normal and diseased lung. This information should eventually lead to more effective treatment strategies for obstructive lung diseases.

OBJECTIVES AND SCOPE

The overall objective of this initiative is to generate knowledge on the genetic and biochemical mechanisms controlling airway mucin structure and properties in health and disease. Applications are invited for innovative, multidisciplinary studies, combining molecular biology with other approaches, to further understanding of the molecular biology of airway mucins. Among the disciplines and expertise that may be appropriate for this research program are molecular biology, pulmonary cell biology, immunology, biochemistry, pharmacology, molecular genetics, and pulmonary medicine.

MECHANISM OF SUPPORT

The support mechanism for this program will be the traditional, individual research grant. All current policies and requirements that govern the research grant programs of the National Institutes of Health will apply to grants awarded under this RFA. Applications must be received by November 16, 1987. An application not received by this date will be considered ineligible. Awards will be made to foreign institutions only for research of very unusual merit, need, and promise, and in accordance with Public Health Service policy governing such awards.

REVIEW PROCEDURES

All applications submitted in response to this RFA will be evaluated for scientific and technical merit by an initial review group, which will be convened for this purpose, by the Division of Extramural Affairs, NHLBI.

METHOD OF APPLYING

Prospective applicants are asked to submit a letter of intent and include the names of any other participating institutions or investigators. This letter should be received no later than September 15, 1987. Requests for copies of this announcement may be directed to:

J. Sri Ram, Ph.D.
Chief, Airways Diseases Branch
Division of Lung Diseases, NHLBI
National Institutes of Health
Westwood Building, Room 6A15
Bethesda, Maryland 20892
Telephone: (301) 496-7332

The label provided with the full RFA should be affixed to the bottom of the face page of the original completed application. Failure to use this label could result in delayed processing and review of the application.

NONTRANSFUSION FORMS OF TREATMENT FOR BLEEDING DISORDERS

RFA AVAILABLE: 87-HL-20-B

P.T. 34; K.W. 0785070, 1003002, 1002008, 0710100

National Heart, Lung, and Blood Institute

Application Receipt Date: November 16, 1987

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.

The program will support basic and clinical studies addressing the development of new modes of treatment for congenital and acquired bleeding disorders. Studies of the mechanism of action of newly-developed products as well as of products already in clinical use will also be encouraged. It is expected that the development of new therapies will include a broad range of approaches requiring expertise in such areas as hematology, biochemistry, molecular biology and pharmacology.

Requests for copies of the RFA should be addressed to:

Pankaj Ganguly, Ph.D.
Blood Diseases Branch
Division of Blood Diseases and Resources
National Heart, Lung, and Blood Institute
National Institutes of Health
Federal Building, Room 5A12
Bethesda, Maryland 20892

The label provided with the full RFA should be affixed to the bottom of the face page of the original completed application. Failure to use this label could result in delayed processing or review of the application.

MOLECULAR SIGNALS IN THE VASCULATURE IN HYPERTENSION

RFA AVAILABLE: NIH-87-HL-21-H

P.T. 34; K.W. 0715115, 0790005, 1002004, 0760075, 1013004, 1002034

National Heart, Lung, and Blood Institute

Application Receipt Date: November 16, 1987

The Hypertension and Kidney Diseases Branch of the Division of Heart and Vascular Diseases, National Heart, Lung, and Blood Institute (NHLBI) announces the availability of a Request for Applications (RFA) on the above subject. Awards will be made for a period up to five years.

Essential hypertension affects 58 million Americans and is a risk factor for heart attack and stroke. The etiology of hypertension is complex and multifactorial, but inevitably involves abnormal responses by cells of the vasculature. Recent work on cellular signal generation and transduction, involving second messengers, has utilized blood vessels or vasoactive substances only infrequently.

The present RFA is designed to encourage research on signal generation and transduction in the plasma membrane and intracellular compartments of cells of the vasculature, such as smooth muscle and endothelium, with particular emphasis on processes involved in vascular hypertrophy, control of ion fluxes, and the possible production of membrane abnormalities associated with hypertension. Such studies are likely to provide insight into mechanisms leading to improved control or prevention of hypertension.

This announcement may be of particular interest to investigators with expertise in several basic disciplines, including molecular and cellular biology, receptor biology and biochemistry, and biophysics and physiology. Awards in response to this announcement will be made to foreign institutions only for research of very unusual merit, need, and promise, and in accordance with PHS policy governing such awards.

TIMETABLE

Letter of Intent: August 14, 1987
Application Receipt Date: November 16, 1987
Technical Review: February, 1988
Advisory Council Review: May 19-20, 1988
Award Date: July 1, 1988

INQUIRIES

Inquiries concerning this program and requests for copies of the RFA should be addressed to:

Dr. David M. Robinson
Deputy Chief
Hypertension and Kidney Diseases Branch
Division of Heart and Vascular Diseases
National Heart, Lung, and Blood Institute
Federal Building, Room 4C10
National Institutes of Health
Bethesda, Maryland 20892
Telephone: (301) 496-1857

The label provided with the full RFA should be affixed to the bottom of the face page of the original completed application. Failure to use this label could result in delayed processing or review of the application.

VASCULAR HEALING: CELL BIOLOGY AND RHEOLOGIC FACTORS

RFA AVAILABLE: 87-HL-18-H

P.T. 34; K.W. 1002004, 0715040, 0785210, 0785070, 0740070, 0710030

National Heart, Lung, and Blood Institute

Application Receipt Date: November 16, 1987

The Devices and Technology Branch, Division of Heart and Vascular Diseases, National Heart, Lung, and Blood Institute invites research grant applications from organizations which are capable of carrying out interdisciplinary, basic and applied research into the mechanisms of vascular healing. The studies should have direct relevance to the clinical problems of restenosis following coronary artery bypass graft (CABG) surgery, percutaneous transluminal coronary angioplasty (PTCA), and carotid endarterectomy, and of occlusion of saphenous vein or prosthetic vascular grafts following peripheral arterial reconstructive surgery.

OBJECTIVES AND SCOPE

The objectives of this RFA are to encourage research into the relative contributions of the following to the pathological consequences of the vascular healing process, specifically vascular stenosis and occlusion: 1) mediators and inhibitors of thrombosis and pseudointimal hyperplasia which include prostaglandins and thromboxanes, plasmatic and platelet factors in hemostasis, complement components, platelet- derived growth factor and related mitogens, interleukin-1, and leukotrienes; 2) rheologic factors, including stasis, recirculation, shear stress, and mass transport; 3) physical properties of the natural or prosthetic vessel wall such as compliance, stress-strain characteristics, and for prostheses, porosity and surface texture; and 4) the chemical composition of vascular prostheses.

BACKGROUND

Over 600,000 vascular procedures were performed in the U. S. in 1986. These include an estimated 200,000 CABG procedures, 225,000 reconstructive procedures for peripheral vascular disease, 100,000 PTCA procedures, and 85,000 carotid endarterectomies. A significant percentage of these procedures eventually fail, due to thrombosis, pseudointimal hyperplasia, or atherosclerosis. A better understanding of these processes is expected to lead to improved methods of preventing failure. Also the development of a small-diameter (less than 6mm) prosthetic vascular graft which would remain patent for at least 5 years would represent a major advance. In a significant proportion of patients requiring these procedures, a suitable saphenous vein for CABG or peripheral arterial reconstruction is not available and its harvesting requires additional time and discomfort. The internal mammary artery for CABG surgery is clearly preferable to the saphenous vein because of its lower failure rate, but its use is limited to patients with certain types and locations of coronary artery disease. For these reasons a non-occluding prosthetic graft would represent a major advance.

ELIGIBILITY

Applicant organizations are required to have the capacity to perform interdisciplinary research on mechanisms of vascular healing and of natural or prosthetic graft failure: more than one of the four categories of investigation described in OBJECTIVES AND SCOPE should be addressed in their application. It is not required that the proposed research include all four areas.

APPLICATION SUBMISSION AND REVIEW

A potential applicant organization is encouraged, but is not required, to consult with NHLBI staff by telephone before submitting. The letter of intent is requested by August 14, 1987; it will not enter into the review of an application submitted in response to this RFA.

Initial review of proposals will be organized by the Division of Extramural Affairs, NHLBI, with a panel of mostly non-federally employed reviewers with expertise which will include cell biology, rheology and fluid mechanics, surgery, vascular physiology, hematology, materials science and surface chemistry, and biostatistics. Applications will be reviewed in competition with each other on a nationwide basis. This RFA solicitation is a single competition and has one specified deadline for receipt of applications.

MECHANISM OF SUPPORT

The mechanism of support for this program will be the NIH investigator-initiated research grant (R01). Awards may be made to non-profit and profit organizations. An applicant organization may apply for a period of support of up to five years.

Contingent upon the continued availability of funds, and dependent upon the receipt of a sufficient number of applications of high scientific merit, it is anticipated that five to eight awards will be made at an annual total cost of approximately $1,500,000 (direct plus indirect costs).

INQUIRIES

Requests for copies of the RFA in its expanded form, and consultation prior to submitting, should be directed to:

Paul Didisheim, M.D.
Devices and Technology Branch
Division of Heart and Vascular Diseases
National Heart, Lung, and Blood Institute
Federal Building, Room 312
Bethesda, Maryland 20892
Telephone: (301) 496-1586

The label provided with the full RFA should be affixed to the bottom of the face page of the original completed application. Failure to use this label could result in delayed processing and review of the application.

INACTIVATION OF HUMAN IMMUNODEFICIENCY VIRUS (HIV) AND OTHER TRANSFUSION-TRANSMITTED VIRUSES IN BLOOD AND BLOOD COMPONENTS

RFA AVAILABLE: 87-HL-19-B

P.T. 34; K.W. 1002045, 0750010, 0715120

National Heart, Lung, and Blood Institute

Application Receipt Date: November 16, 1987

The Blood Resources 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, NIH-87-HL-19-B, may be obtained from staff of the NHLBI.

The program will encourage basic and applied research on the development and evaluation of procedures to remove or destroy the infectivity of HIV and/or other transfusion-transmitted viruses in blood and blood components while maintaining the therapeutic effectiveness of these preparations. The emergence of the AIDS epidemic has underscored the serious and urgent need to develop effective means of rendering blood and blood components safe for transfusion. Procedures that are developed should be simple, inexpensive and capable of being used in blood banks and blood centers.

Request for copies of the RFA should be addressed to:

Luiz H. Barbosa, D.V.M.
Blood Resources Branch, DBDR
Federal Building, Room 504
National Institutes of Health
Bethesda, Maryland 20892
Telephone: (301) 496-1537

The label provided with the full RFA should be affixed to the bottom of the face page of the original completed application. Failure to use this label could result in delayed processing and review of the application.

EVALUATING ALCOHOL AND COCAINE TREATMENTS AND SETTINGS

RFA AVAILABLE: AA-87-03

P.T. 34; K.W. 0404009, 0404003, 0415000, 0403004

National Institute on Alcohol Abuse and Alcoholism
National Institute on Drug Abuse

Application Receipt Date: October 15, 1987

BACKGROUND

Current research strongly suggests that chemical dependencies are not unidimensional syndromes; rather there appear to be qualitatively and quantitatively different types of alcohol and drug dependent persons. It is evident that for the effective treatment of alcohol dependent persons, cocaine users, and persons who use both substances, development of a basis for careful matching of the type and severity of the dependency and the type of treatment regimen and environment is a necessary next step in treatment assessment research.

RESEARCH GOALS AND SCOPE

This announcement seeks research grant applications to compare the treatment efficacy of residential or inpatient vs. outpatient settings for one or more of the following categories of chemically dependent persons: (a) persons who meet a primary diagnosis of alcohol dependence with no other clinically significant drug abuse, (b) persons with a primary diagnosis of cocaine dependence [may include crack], with no other clinically significant drug abuse, and (c) persons who primarily use/abuse both alcohol and cocaine at dependence-producing levels with no other clinically significant abuse of drugs. Proposals may address one or more of these three categories of chemically dependent persons, but must address a comparison between inpatient or residential vs. outpatient settings in which equivalent treatment regimens are offered.

It is the intent of the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the National Institute on Drug Abuse (NIDA) to support studies evaluating and comparing the treatment efficacy of residential or inpatient vs. outpatient settings among commonly used treatment regimens at one or more facilities. This announcement is not for the purpose of developing new treatment regimens or assessing the efficiency of a particular facility per se. The primary aim of research projects sought under this announcement is to study the careful matching of the type and severity of substance dependency with the type of treatment regimen and setting.

ELIGIBILITY

Applications may be submitted by public or private nonprofit or for-profit organizations such as universities, colleges, hospitals, laboratories, units of State or local governments, and eligible agencies of the Federal Government. Women and minority investigators are encouraged to apply. Applications are especially encouraged from State governments with research units and/or State governments collaborating with university-based research units.

APPLICATION PROCESS

Potential applicants may obtain a more detailed RFA by contacting:

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

State and local government agencies should use form PHS 5161-1 (Rev. 3/86). All other applicants should use the research grant application form PHS 398. The title of this announcement "EVALUATING ALCOHOL AND COCAINE TREATMENTS AND SETTINGS" AA-87-03 should be typed in item number 2 on the face page of the PHS 398 application form.

The label provided with the full RFA should be affixed to the bottom of the face page of the original completed application. Failure to use this label could result in delayed processing and review of the application.

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

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

o Letter of Intent and Further Information

Applications will undergo expedited review procedures. As a notice of intent to apply, or for further information, it is suggested that prospective applicants call either Dr. Tims at NIDA (301/443-4060) or Dr. Lettieri at NIAAA (301/443-4223) or send a "Letter of Intent" (a brief letter indicating their intention to submit an application for the October 15, 1987 submission deadline) to the NIAAA, Office of Scientific Affairs at the address given below. It would be helpful if these calls or letters were received prior to September 15, 1987.

o Completed Grant Application

The completed grant application should be submitted by October 15, 1987. The signed original and four (4) permanent legible copies of the completed application (original and two copies, if using form PHS 5161-1) should be sent to:

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

To assist in the expedited review, two (2) copies of the application should be sent by October 15, 1987 directly to:

National Institute on Alcohol Abuse and Alcoholism
Office of Scientific Affairs
5600 Fishers Lane, Room 16-C-20
Rockville, Maryland 20857

REVIEW PROCESS

Applications received under this announcement will be reviewed for scientific and technical merit by an initial review group convened by NIAAA or NIDA. Review criteria include significance and originality from a scientific or technical standpoint of the goals of the proposed research; adequacy of the methodology proposed to carry out the research; feasibility of the proposed research; qualifications and research experience of the principal investigator and other key personnel; availability of adequate facilities, other resources, and collaborative arrangements necessary for the research; appropriateness of budget estimates for the proposed research activities; and adequacy of provisions for the protection of human subjects and the welfare of animal subjects, as applicable. Notification of the review recommendations will be sent to the applicant after the initial review. Applications will receive a second-level review for merit, policy, and program relevance by the National Advisory Council on Alcohol Abuse and Alcoholism or the National Advisory Council on Drug Abuse.

Alcohol and drug abuse research grants are described in the Catalog of Federal Domestic Assistance No. 13.273 and 13.279. Grant awards are made under the authority of Sections 301, 510, and 515 of the Public Health Service Act (42USC 241, 290bb and 290cc). Applications submitted in response to this announcement are not subject to the intergovernmental review requirements of Executive Order 12372, as implemented through Department of Health and Human Service regulations at 45 CFR Part 100.

APPLICATION RECEIPT AND REVIEW SCHEDULE

Letter of Intent	September 15, 1987
Receipt of Application	October 15, 1987
Initial Scientific/Merit Review	January 1988
Advisory Council Review	February 1988
Earliest Award Date	February 1988

AVAILABILITY OF FUNDS

Applications submitted in response to this announcement will compete for approximately $2.3 million in new grant money that has been made available for this purpose in FY 1988 by Section 1923 of the Public Health Service Act, which was added by the "Anti-Drug Abuse Act" of 1986. The size and number of possible awards will depend on the complexity of the projects proposed and selected for funding.

It should be noted that research evaluating alcohol and drug treatment is an ongoing priority within the regular research grant programs of the NIAAA and the NIDA. Consequently, applications of high scientific merit which cannot be funded under this announcement could be considered for funding under the Institutes' regular research grant programs. Also, future applications of this type are encouraged under the regular programs.

ONGOING PROGRAM ANNOUNCEMENTS (PAs)

COMPUTER-BASED REPRESENTATION AND ANALYSIS OF MOLECULAR BIOLOGY DATA (PA)

P.T. 34; K.W. 1002008, 1004000, 1004005, 1004008, 1004017, 0790010, 0760070

National Institutes of Health

This announcement is complementary to the announcement, "New Approaches to the Analysis of Complex Genomes," published in this issue. Interested applicants may wish to consider both announcements as they plan projects.

INTRODUCTION

The National Institutes of Health (NIH) invites grant applications from investigators who are interested in the computer and information science aspects of molecular biology data management and analysis. The long term goal of this initiative is to promote high quality research that has value for furthering our understanding of structure/function relationships in nucleic acids, proteins, and other biologically important molecules, in order to help prevent, diagnose, and treat human disorders. Although no special pool of funds has been set aside, the NIH is committed to support of competitive research programs that further these objectives.

BACKGROUND

The appearance of new experimental methods in the past several years has greatly increased the rate at which data are accumulating about the molecular control of life processes. Restriction enzymes, synthetic molecular probes, efficient microchemical methods for DNA and protein sequence determination, and recombinant DNA technology have developed to the point that it is now feasible to consider large-scale projects, such as the systematic analysis of entire eukaryote genomes. Because of their size and complexity, the data that are generated by such undertakings must be analyzed and compared using computerized techniques for storage, searching, and analysis. The NIH currently supports several computer databases, including GenBank and the National Biomedical Research Foundation (NBRF) Protein Sequence Database, through grant and contract mechanisms. Additionally, research into mathematical algorithms for analysis of macromolecular sequences is supported by intramural and extramural programs. The computer databases that hold this information, currently numbered in millions of nucleotide base pairs and thousands of amino acids, are expected to grow by three orders of magnitude to encompass sequences totalling billions of nucleotides. Current methods for structuring, searching, and analyzing such databases need to be enhanced correspondingly.

RESEARCH SCOPE

This program announcement is intended to emphasize the commitment of the National Institutes of Health to foster the development of new computer-based analysis methods for the interpretation of molecular biological data. Such research will require a diversity of approaches and make use of data from a number of model systems. The research topics of interest described below are not intended to limit the types of applications that can be submitted under this announcement, but rather to illustrate the range of work in computer and information science, as applied to biology, that will be needed to advance our research capabilities in the area of genomic analysis and macromolecular structure and function. Additionally, it is recognized that the development of computational methods may be based in the context of a specific biologic problem (e.g., use of immunological sequence data to explore genetic aspects of the immune response).

- Database design, incorporating data representations that are optimal for search, analysis, transmission, and storage of macromolecular data.
- Software algorithms and other database query methods capable of translating natural language questions into appropriate retrievals from multiple related factual databases.

- Man-machine interface methods that are optimally suited to laboratory researchers without prior training in database searching and computational analysis methods.
- Methods of pattern recognition based on associative networks and algorithm design optimized for multiprocessor (e.g., parallel processor) machine architectures.
- Expert system techniques for automatic generation of annotation information, creation of linkages among related databases via explicit pointers or common vocabulary.
- Specialized computer hardware for economical and rapid comparison of large volumes of biological data.
- Mathematical methods and algorithms for improving the efficiency of comparison operations that are computationally intensive (e.g., cannot be performed in linear time), such as rigorous high speed multiple alignments of macromolecular sequences.
- Algorithms capable of predicting structure and/or function based on primary sequences of nucleotides and amino acids.

MECHANISM OF SUPPORT

Support for this program will be through research grants, including project grants (R01), small grants (R03), program projects (P01), FIRST awards (R29), Small Business Innovation Research Grants (R43 and R44), and the Biomedical Research Technology resource grants (R24, P41). Policies that govern research grant programs of the National Institutes of Health apply to this program. Since it is anticipated that potential applicants may wish to enlarge on currently available databases, consortium arrangements are also possible. In addition, collaborative projects between persons with engineering, analytical, and information science skills and molecular biologists are encouraged.

APPLICATION AND REVIEW PROCEDURES

Applications in response to this announcement will be reviewed in accordance with the usual NIH peer review procedures. They will first be reviewed for scientific and technical merit by a special review group organized for this purpose by the Division of Research Grants and composed mostly of non-Federal scientific consultants. Following this initial review, the applications will be secondarily evaluated by the appropriate National Advisory Board or Councils. Review criteria include the following:

- Significance and originality of the research goals and approaches as they relate to the computer-based management and analysis of molecular biological data;
- Potential value of the research for furthering the understanding and utilization of genomic and other macromolecular information;
- 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
- Appropriateness of the requested budget for the work proposed.

METHOD OF APPLYING

Applications should be submitted on the new form PHS 398(rev. 9/86). Application kits are available at most institutional business offices and from:

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

Applications will be accepted in accordance with the usual NIH receipt dates for new applications--October 1, February 1, and June 1. It is essential that applicants type "Computer-based Representation and Analysis of Molecular Biology Data," in item 2 on the face page of the application form. The original and six copies of the application should be submitted to the following office.

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

The conventional presentation for grant applications should be utilized.

Funding decisions will be based on recommendations of the initial review groups and the BID Advisory Council regarding scientific merit and program relevance and on the availability of funds. No special funds are set aside for this program.

INQUIRIES

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B/I/D	CONTACT	BUILDING	ROOM	TELEPHONE
NIDDK	Robert Katz, Ph.D.	Westwood	607	496-7997
NCI	Alan S. Rabson, M.D.	31	3A03	496-4345
FIC	Jack R. Schmidt, Ph.D.	38A	616	496-1415
DRR	Charles Coulter, Ph.D.	31	5B41	496-5411
NICHD	Delbert H. Dayton, M.D.	Landow	7C08	496-5541
NINCDS	N.C. Myrianthopoulos, Ph.D.	Federal	8C16A	496-5821
NLM	Arthur J. Broering	38A	5N503	496-4621
NIDR	John D. Townsley, Ph.D.	Westwood	506	496-7807
NIGMS	James C. Cassatt, Ph.D.	Westwood	909	496-7309
NIAMS	Steven J. Hausman, Ph.D.	Westwood	403	496-7495
NHLBI	Carol Letendre, Ph.D.	Federal	518	496-8966
NIA	Huber R. Warner, Ph.D.	31	5C19	496-6402
NIAID	Mildred S. Warfield	31	7A19	496-6752

Mailing Address for the above offices: Bethesda, Maryland 20892
All Bethesda telephone numbers are area code 301

NIEHS	Michael J. Galvin, Ph.D.	Research Triangle Park North Carolina 27709	(919) 541-7825

NEW APPROACHES TO THE ANALYSIS OF COMPLEX GENOMES (PA)

P.T. 34; K.W. 1002019, 1004000, 0790010, 0760080, 0755035, 0755045, 1004005

National Institutes of Health

This announcement is complementary to the announcement, "Computer-based Representation and Analysis of Molecular Biology Data," published in this issue. Interested applicants may wish to consider both announcements as they plan projects.

INTRODUCTION

The National Institutes of Health (NIH) invites research grant applications from investigators who are interested in developing new ideas and innovative approaches for analyzing complex genomes. The long-term goal of this initiative is to promote high-quality research that has actual or potential value for furthering our understanding of structure/function relationships within the human genome and utilizing human genomic information to prevent, diagnose, and treat human disorders. Although no special pool of funds has been set aside, the NIH is committed to support competitive research programs that further these objectives.

BACKGROUND INFORMATION

Within the past year, discussions about research priorities for various aspects of genomic analysis or "genomics" have begun among many scientists and various public and private agencies. The Advisory Committee to the Director of the National Institutes of Health recently discussed research priorities regarding human genomic analysis. The Committee concluded that the current state of knowledge and technology dictates the continued support of diverse research activities drawing from many disciplines in the biological sciences but also recognized a need to foster new initiatives and approaches to genomic analysis. The National Institutes

of Health currently funds this effort through individual research projects, program projects, centers, and research training grants, as well as through many research resources, including GenBank--The DNA Sequence DataBank, BIONET, the Repository of Human DNA Probes and Libraries, and the Human Genetic Mutant Cell Repository. In addition, the NIH is committed to fostering new technological approaches for studying complex genomes. NIH support of research and resource activities in genomic analysis has already led to greatly improved strategies for studying human genetic disorders. NIH has also supported much research on the causes, diagnoses, and treatments of specific disorders, such as Huntington's disease, cystic fibrosis, and muscular dystrophy. Similar understanding of many common disorders, such as diabetes, atherosclerosis, and cancer, will depend on continued support of this field.

RESEARCH SCOPE

This program announcement is intended to emphasize the ongoing commitment of the National Institutes of Health to analyses of complex genomes, including both model systems and the human genome, and to encourage investigators to pursue new approaches to studies of molecular genetics and gene expression. The NIH will continue to support a broad spectrum of research from the most fundamental and non-categorical research to clinical studies and applications development. Such research will require a diversity of approaches and make use of a number of model systems as well as human material. The research topics of interest described below are not intended to limit the types of applications that are encouraged by this announcement, but rather to illustrate the range of work that will be needed to advance our knowledge and research capabilities in the broad area of genomic analysis and its applications.

Methods Development

- Improving methods for fragmenting DNA, including the isolation and characterization of new restriction enzymes, studies of the mechanism of action of restriction enzymes, and the development of sequence-specific chemical cleavage methods;

- Improving large-scale separation and purification of specific DNA fragments, including techniques for purification of DNA fragments based on sequence and techniques for obtaining pure preparations of individual human chromosomes and their fragments;

- Cloning large (more than 100,000 base pairs) fragments of DNA, with special emphasis on mammalian DNA fragments, and including the development of new cloning vehicles for large DNA fragments;

- Improving methods for ordering sets of DNA fragments in the genome, including the development of supporting mathematical and computer methodologies;

- Improving sequencing technologies, including automation of DNA isolation and purification, automation of gel preparation and scanning, and enhancement of the speed and accuracy of sequencing methods;

- Developing alternative approaches to cloning DNA regions that are refractory to currently available cloning techniques;

- Improving electron microscopic techniques for analyzing large chromosome fragments and for molecular mapping; and

- Improving storage methods which preserve the integrity of long DNA fragments, including studies on the stability and selective loss of cloned DNA fragments and associated vectors.

Mapping and Sequencing

- Mapping and/or sequencing selected chromosomal segments with the goals of finding new functional relationships of genomic elements such as reading frames, control regions, protein binding sites, highly repetitive sequences, and with the goal of understanding the role of DNA sequence in determining chromosome structure;

- Expanding the genetic and physical maps of the human genome, including mapping of specific genes and studies to determine the relationships between these two maps;

- Determining the amount and significance of variation among human genomes, with special emphasis on variation in DNA sequences within and among human populations; and

- Developing genetic and physical maps of model systems, including sequencing where that would be useful, studies of the relationships of these maps, development of mapping strategies, comparison of maps and sequences both within and among species, and studies of the evolution of chromosome structure.

Applications of Genomic Information

- Exploring new strategies for using genetic tools and information for the diagnosis, prevention, and treatment of human genetic disorders; and

- Applying information about the genetic and physical maps of the human genome to genetic epidemiological research, including linkage analysis, with the goal of understanding multifactorial genetic disorders.

MECHANISM OF SUPPORT

Support for this program will be through research grants, including project grants (R01), small grants (R03), program projects (P01), FIRST awards (R29), biomedical research technology resource grants (R24, P41), and Small Business Innovation Research (SBIR) grants (R43 and R44). Policies that govern research grant programs of the National Institutes of Health apply to this program. Consortium arrangements and collaborative projects between molecular biologists and persons with engineering, analytical and information science skills are encouraged.

APPLICATION AND REVIEW PROCEDURES

Applications in response to this announcement will be reviewed in accordance with the usual NIH peer review procedures. They will first be reviewed for scientific and technical merit by a special review group organized for this purpose by the Division of Research Grants and composed mostly of non-Federal scientific consultants. Following this initial review, the applications will be secondarily evaluated by the appropriate National Advisory Board or Councils. Review criteria include the following:

- Significance and originality of the research goals and approaches as they relate to the analysis of complex genomes;

- Potential value of the research for furthering the understanding and utilization of information about the human genome;

- Feasibility of the research and adequacy of the experimental design;

- Training, experience, research competence, and dedication of the investigator(s);

- Adequacy of available facilities;

- Provisions for the protection of human subjects and the humane care of animals; and

- Appropriateness of the requested budget for the work proposed.

METHOD OF APPLYING

Applications should be submitted on the new form PHS 398 (rev.9/86). Application kits are most institutional business offices and from:
Office of Grants Inquiries
Division of Research Grants
Westwood Building, Room 449
National Institutes of Health
Bethesda, Maryland 20892

Applications will be accepted in accordance with the usual NIH receipt dates for new applications--October 1, February 1, and June 1. It is essential that applicants type "New Approaches to the Analysis of Complex Genomes," in item 2 on the face page of the application form. The original and six copies of the application should be submitted to the following office.

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

The conventional presentation for grant applications should be utilized.

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NEI	Jack A. McLaughlin, Ph.D.	31	6A51	496-5983

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**THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS 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 STREET ADDRESS FOR THE WESTWOOD BUILDING IS:

5333 Westbard Avenue
Bethesda, Maryland 20816

*U.S. G.P.O. 1987-181-289:40043