NIH GUIDE

For Grants and Contracts

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

Vol. 19, No. 28
July 27, 1990

NOTICES OF AVAILABILITY (RFPs AND RFAs)

ONGOING PROGRAM ANNOUNCEMENTS

ERRATA

NOTE: The NIH Guide for Grants and Contracts will not be published on August 3, 1990. The next issue will be August 10, 1990.

PROPHET SYSTEM SUPPORT AND ENHANCEMENT

RFP AVAILABLE: NIH-RR-90-16

P.T. 34; K.W. 1004000, 1004004, 0755018, 1010013

National Center for Research Resources

The National Center for Research Resources (NCRR) is soliciting offerors to support and enhance the PROPHET II software system. The PROPHET II software system is an integrated UNIX-based system utilized by the biomedical research community for scientific data management, analysis, and visualization. PROPHET II is currently supported on the following hardware platforms: SUN Microsystems SUN-3 and SUN-4/Sparcstation (UNIX OS); VAXStation, and DECstation 2100/3100 (ULTRIX oS); and, projected for late 1990, the Macintosh II (AUX). The proposed contract will require completion of nine general tasks: User Support, PROPHET II software dissemination, Clinical Data Management, enhanced statistics, implementation of new applications, provision of Programming interfaces, short-term PROPHET core development, long-term PROPHET core development, and special projects. The solicitation will be issued approximately July 27, 1990 with proposals due 60 days thereafter. NCRR expects to award one contract from this solicitation.

To receive a copy of the RFP, please supply this office with two self-addressed mailing labels. The RFP package will be available upon written request to:

Janice G. Brunson
Contracting Officer
Research Contracts Branch
Division of Contracts and Grants
National Institutes of Health
Building 31, Room 1B44
9000 Rockville Pike
Bethesda, MD 20892

EPIDEMIOLOGY OF SPECIFIC LANGUAGE IMPAIRMENT

RFP AVAILABLE: NIH-DC-90-19

P.T. 34; K.W. 0785055, 0715050, 0715055, 0720010, 0410001, 0411005

National Institute on Deafness and Other Communication Disorders

The National Institute on Deafness and Other Communication Disorders has a requirement for a research study to determine the prevalence of Specific Language Impairment (SLI) in five-year-old children within urban, suburban, and rural environments in the United States. Within each of the three environments: 1) ascertain the percentage of SLI with primarily expressive language deficits, primarily receptive language deficits, those with both receptive and expressive deficits, and those with a concomitant phonological disorder; 2) ascertain sex differences in the occurrence of SLI; 3) identify possible risk factors associated with the occurrence of SLI; and 4) identify the percentage of SLI children who have received or are receiving interventions for communication disorders. A three-year, cost-reimbursement contract is anticipated. The scheduled release date for this solication is July 24 with responses due by August 24. All responsible sources may submit a proposal which shall be considered by the agency.

To receive a copy of the RFP, please supply this office with two self-addressed mailing labels. The RFP Package will be available upon written request to:

John P. DeCenzo
Contracting Officer
Research Contracts Branch
Division of Contracts and Grants
National Institutes of Health
Building 31, Room 1B44
9000 Rockville Pike
Bethesda, MD 20892

X-RAY DIFFRACTION SYSTEM FROM MUSCLE FIBERS

RFP AVAILABLE: RFP-NIH-NIAMS-90-2

P.T. 34; K.W. 1002024

National Institute of Arthritis, Musculoskeletal and Skin Diseases

The National Institute of Arthritis, Musculoskeletal, and Skin Diseases (NIAMS), Laboratory of Physical Biology (LPB) has a requirement for a two dimensional X-ray (8 kev) detector system which shall incorporate an imaging plate coated with phosphor crystals plus a high efficiency and low noise readout system. The system should be capable of high quantum efficiency, uniform and stable sensitivity, and high spatial resolution.

This Request for Proposals, RFP No. NIH-NIAMS-90-2, will be issued on or about August 6, 1990, with a closing date of September 24, 1990. NIAMS expects to make one award from this solicitation. To receive a copy of the RFP, please supply this office with two self-addressed mailing labels and cite the RFP number referenced above. Requests must be in writing and addressed to:

Robert Webber
Contract Specialist
National Institute of Arthritis, Musculoskeletal and Skin Diseases
Westwood Building, Room 602
Bethesda, MD 20892

Telephone requests will not be honored. A reasonable number of copies of the RFP have been prepared and will be issued on an as are available basis. This announcement does not commit the Government to make an award.

BIOLOGICAL AND CHEMICAL STUDIES OF TAXOL

RFA AVAILABLE: CA-90-16

P.T. 34; K.W. 0740020, 0715035, 0765010

National Cancer Institute

Letter of Intent Date: September 17, 1990
Application Receipt Date: October 24, 1990

The Developmental Therapeutics Program of the Division of Cancer Treatment, National Cancer Institute (NCI) announces the availability of a Request for Applications (RFA) for grants related to the further biological and chemical development of taxol as an antitumor agent.

Taxol has shown excellent confirmed activity against refractory ovarian cancer and preliminary activity at other sites, and is one of the most promising new drugs in many years. It has a wholly novel mechanism of action, binding to microtubules and stabilizing them against depolymerization. Investigations of the chemistry, biology, biochemistry, and pharmacology of taxol have been limited and many aspects of drug production in the source plants, Taxus species, as well as many aspects of drug action are not well understood.

The intention of this RFA is to encourage investigators to propose ideas which will increase our knowledge of the drug's properties and which are likely in the long term to contribute to large-scale drug supply and to maximally effective usage of taxol in the clinical setting. The following are undeveloped or underdeveloped areas of interest which merit particular attention: (1) biosynthesis and its regulation in Taxus sp.; (2) plant tissue culture to produce taxol and related compounds; (3) agronomics and plant genetics of taxol to enhance production; (4) evaluation of genetic engineering methods to transfer genes involved in taxol biosynthesis to fast growing plants; (5) identification of the specific taxol binding site on microtubules and of the amino acid sequences involved, leading to high-resolution definition of the binding site and eventually to molecular mimics with simpler structures; (6) frequency, mechanisms, and circumvention of resistance; (7) studies of in vitro combinations of taxol with other cytotoxic agents; (8) human metabolism of taxol; (9) measurements and consequences of tissue distribution of taxol; and (10) in vivo evaluation of combination therapy using taxol in preclinical models. These areas are not restrictive.

The mechanism for this program will be the traditional individual research-project grant. Although the financial plans for fiscal year 1991 include approximately $1,000,000 for the total costs (direct and indirect) of this program, support of grants pursuant to this RFA is contingent upon

receipt of funds for this purpose. It is anticipated that approximately five to eight grants will be awarded under this one-time solicitation.

Inquiries and requests for copies of this RFA should be made to:

Dr. Matthew Suffness
Program Director
Grants and Contracts Operations Branch
Division of Cancer Treatment
National Cancer Institute
Executive Plaza North, Suite 832
Bethesda, MD 20892
Telephone: (301) 496-8783
FAX: (301) 496-8333

NATIONAL RESEARCH SERVICE AWARD-INSTITUTIONAL GRANTS

RFA AVAILABLE: DE-90-02

P.T. 44; K.W. 0720005, 0715148, 0785040

National Institute of Dental Research

Application Receipt Date: December 10, 1990

AUTHORITY AND PURPOSE

Under authority of Section 487 of the Public Health Service (PHS) Act as amended (42 USC 288), the National Institute of Dental Research (NIDR) is awarding National Research Service Award (NRSA) institutional grants (T32) to eligible institutions to develop or enhance research training opportunities for qualified individuals of the institutions's selection who seek to prepare for careers in biomedical and behavioral oral health research. This Request for Applications (RFA) announces the next application receipt date for this program (December 10, 1990) and identifies the training areas of special interest.

The purpose of the NRSA program is to help ensure that highly trained scientific manpower will be available in adequate numbers and in the appropriate research areas and fields to maintain the nation's biomedical and behavioral oral health research agenda. Title 42 of the Code of Federal Regulations, Part 66, is applicable to this program as are the following Catalog of Federal Domestic Assistance numbers: 13.840, 13.841, 13.842, 13.843, 13.844, 13.845, and 13.878.

APPLICANT ELIGIBILITY REQUIREMENTS

Domestic nonprofit private or public institutions may apply for grants to support research training programs. The applicant institution must have the staff and facilities required for the proposed program. The training program director at the institution will be responsible for the selection and appointment of trainees and for the overall direction of the program. Clinical departments or programs should have a significant relationship with basic scientists that will assure trainees with clinical backgrounds the opportunity to acquire the necessary foundation for future independent research.

REVIEW SCHEDULE

The schedule (indicated below) is designed to allow Program Directors time to recruit candidates during the fall /winter of the academic year (1991) for appointments to begin the following summer.

Application Receipt Date	Initial Review Meeting	Council Meeting	Earliest Award
December 10 1990	June/July 1991	Jul/Aug 1991	September 1991

ADDITIONAL INFORMATION

The NIDR supports training in all the areas of biomedical and behavioral oral health research. However, for this cycle we are particularly interested in applications proposing training in the basic and clinical sciences pertaining to craniofacial anomalies and dental biomaterials. Application(s) submitted in other program areas also will be considered.

Commensurate with this RFA, the NIDR will modify its guidelines for appointing postdoctoral trainees. Preference must be given to postdoctoral individuals who have received, as of the beginning of their NRSA appointment, a D.D.S., D.M.D., or equivalent dental degree from an accredited domestic or foreign institution. Individuals with a research doctoral degree (Ph.D. or equivalent) may also be appointed to the training grant, although, in general, they are expected to apply for the individual postdoctoral NRSA fellowship award (F32).

The NIDR expects to fund approximately five new and/or renewal institutional training awards in response to this annual RFA.

Applicants should refer to the announcement in the July 15, 1988 issue of the NIH Guide for Grants and Contracts, Volume 17, No. 23, which contains a complete and detailed description of the new structure and administration of our NRSA institutional grants program. A modified version of that document is available from the NIDR (please see below) and should be used in preparing a response to this RFA.

Complete details on the policy and guidelines, the mechanism of the award, application procedure, review criteria, and copies of the RFA may be obtained from:

Thomas M. Valega, Ph.D.
Special Assistant for Manpower
Development and Training
National Institute of Dental Research
National Institutes of Health
Westwood Building, Room 510
Bethesda, MD 20892
Telephone: (301) 496-6324

ONGOING PROGRAM ANNOUNCEMENTS

PILOT PROJECTS OR FEASIBILITY STUDIES FOR GENOMIC ANALYSIS

PA: PA-90-21

P.T. 34; K.W. 1215018, 0755045, 1002058, 1004000

National Center for Human Genome Research

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

The National Center for Human Genome Research (NCHGR) invites applications for pilot projects or feasibility studies to support creative, novel, high-risk/high payoff research that will significantly advance progress toward achieving the goals of the Human Genome Program. These goals are discussed in detail in the document, "Understanding Our Genetic Inheritance - The U.S. Human Genome Project: The First Five Years - FY 1991-1995," available from the Human Genome Management Information System; Oak Ridge National Laboratory; Oak Ridge, TN 37831-6050; telephone (615) 576-6669. A summary of the goals are: completion of a high-density genetic map of the human genome; construction of a high-resolution physical map comprised of large overlapping contigs; development of a "sequence-tagged site" map; development of technology to reduce the expense of DNA sequencing significantly below current cost; development of computer tools to manage and provide access to mapping and sequencing data; examination of the legal, ethical, and social implications of the Human Genome Program; and research training.

RESEARCH OBJECTIVES

Currently, most genomic research utilizes mapping and sequencing techniques that were not developed for large-scale application. Although some reasonable improvements have been made in these techniques and approaches, completion of the Human Genome Program will require considerable increases in efficiency and cost effectiveness of mapping and sequencing techniques, perhaps including the development of completely new approaches.

The purpose of this program announcement is to encourage applications from individuals who are interested in testing novel or conceptually creative ideas that are scientifically sound and may significantly advance progress toward the scientific goals of the Human Genome Program. Some ideas may not be developed fully enough for a standard R01 and can therefore be considered to be in the category of high risk/high payoff. Applications for such pilot

projects or feasibility studies are encouraged in all areas in the five-year plan, which include:

- o construction of high-resolution genetic maps, comprised of DNA markers with an average spacing of 2 centimorgans and gaps no greater than 5 centimorgans, each identified by a "sequence-tagged site;" (Olson et al., Science 245:1434 (1989));
- o construction of high-resolution physical maps of chromosomes in which contigs of at least 2 million base pairs are unambiguously ordered and identified by "sequence-tagged sites," spaced about 100,000 base pairs apart;
- o development of new methods for DNA sequencing that are capable of significantly reducing the cost of sequencing;
- o development of computer tools, information systems, and strategies for collecting, storing, retrieving, analyzing, interpreting and distributing large amounts of mapping and sequencing data.

The sharing of materials and data in a timely manner is essential for progress toward the Human Genome Program. All applicants are expected to discuss in their applications plans for sharing information and data in a timely manner. These plans will be reviewed by the NIH staff and the national advisory council and will become a condition of the award. For additional details, please see the section, "Sharing of Materials and Data", in the Program Announcement entitled "Mapping, DNA Sequencing, and Technology Development in Support of the Human Genome Program," NIH Guide for Grants and Contracts, Vol. 19, No. 28 July 27, 1990.

The NCHGR encourages applications from scientists who have not traditionally been funded by the NCHGR, such as chemists, engineers, physicists, and information scientists, as well as from molecular biologists and other biologists. Applicants must clearly identify the biological problem for which the technology is being developed, and must indicate plans for demonstrating or testing the utility of the technology. Applicants whose expertise is primarily non-biological and who are interested in addressing problems of genome analysis with new, non-biological tools are especially encouraged to interact closely with biologists.

MECHANISM OF SUPPORT

This program will be supported through the exploratory/ developmental grants (R21) mechanism. Applicants may request up to two years of support. In general, projects will be limited to $100,000 (direct cost per annum), although exceptions will be considered. These will be one-time-only awards. Continuation of projects developed under this program will be through the regular grant program.

REVIEW PROCEDURES AND CRITERIA

Applications will be reviewed for scientific and technical merit by an appropriate NIH study section in accordance with the usual NIH peer review procedures. Review criteria that will be used to assess the scientific merit of an application are:

- o Originality of the approach
- o Soundness of the experimental design
- o Track record and commitment of the investigator(s)
- o Resources and environment
- o Appropriateness of the budget

Because this program is designed to support innovative ideas, preliminary data as evidence of feasibility are not required. However, the applicant does have the responsibility for developing a sound research plan. Following initial review, the applications will receive a second-level review by the appropriate national advisory council.

AWARD CRITERIA

Limited funds will be available for this initiative. Applications will compete for available funds with all other approved applications. The following will be considered in making funding decisions:

- o Quality of the proposed project as determined by peer review;

- o Value of the research for achieving the goals of the National Center for Human Genome Research or of the NIH component to which it is assigned;
- o Adequacy of plans for managing data and sharing data and resources in a timely manner;
- o Balance among research areas;
- o Availability of funds.

METHOD OF APPLYING

Applications should be submitted on the grant application form PHS 398 (Rev. 10/88) and will be accepted at the regular application deadlines. Application kits are available at most institutional business and grant/contract offices or may be obtained from the Division of Research Grants, Westwood Building, Room 240, National Institutes of Health, Bethesda, Maryland 20892. The title and number of this announcement should be typed in Item 2 on the face page of the application.

The completed original application and six legible copies should be sent or delivered to:

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

INQUIRIES

Requests for further information should be directed to:

Bettie J. Graham, Ph.D.
Chief, Research Grants Branch
National Center for Human Genome Research
Building 38A, Room 613
National Institutes of Health
Bethesda, MD 20892
Telephone: (301) 496-7531
e-mail: B2G@NIHCU.bitnet
B2G@CU.NIH.Gov.

The program official welcomes the opportunity to discuss the National Center for Human Genome Research's program interests with prospective applicants and encourages telephone, electronic, or written inquiries.

This program is described in the Catalog of Federal Domestic Assistance No. 13.172. Awards will be made under the authority of the Public Health Service Act, Sections 301 (Public Law 78-410, as amended 42 U.S.C. 241) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to Health Systems Agency review.

MAPPING, DNA SEQUENCING, AND TECHNOLOGY DEVELOPMENT IN SUPPORT OF THE HUMAN GENOME PROGRAM

PA: PA-90-20

P.T. 34; K.W. 1215018, 0755045, 1002058, 1004000, 1014004

National Center for Human Genome Research

PURPOSE

The National Center for Human Genome Research (NCHGR) invites applications to support research that will significantly advance progress toward achieving the scientific goals of the Human Genome Program. These goals are discussed in detail in the document, "Understanding Our Genetic Inheritance - The U.S. Human Genome Project: The First Five Years - FY 1991-1995," available from the Human Genome Management Information System; Oak Ridge National Laboratory; Oak Ridge, TN 37831-6050; telephone: (615) 576-6669.

INTRODUCTION

The NIH Human Genome Program is envisioned as a fifteen-year project which has very specific goals. The NCHGR was established in October 1989 for the

purpose of planning and supporting the Human Genome Program and coordinating these efforts with other federal agencies and international groups. Recently a joint advisory committee of the NIH and the Department of Energy set forth program goals for the first five years. The goals, outlined in "Understanding Our Genetic Inheritance - The U.S. Human Genome Project: The First Five Years - FY 1991-1995," are:

- construction of high-resolution genetic maps, comprised of DNA markers with an average spacing of 2 centimorgans and gaps no greater than 5 centimorgans, each identified by a 'sequence-tagged site;" (Olson et al., Science 245:1434 (1989);

- construction of high-resolution physical maps of chromosomes in which contigs of at least 2 million base pairs are unambiguously ordered and identified by "sequence-tagged sites," spaced about 100,000 base pairs apart;

- development of new methods for DNA sequencing that are capable of significantly reducing the cost of sequencing;

- development of computer tools, information systems, and strategies for collecting, storing, retrieving, analyzing, interpreting, and distributing large amounts of mapping and sequencing data;

- examination of legal, ethical, and social implications of the Human Genome Program (see Program Announcement in the NIH Guide for Grants and Contracts, Vol. 19, No. 4, January 26, 1990; and

- research training (see Program Announcement in the NIH Guide for Grants and Contracts, Vol. 18, No. 25, July 21, 1989).

The objective of this Program Announcement is to stimulate research that will assist the NCHGR in accomplishing both the short- and long-term scientific goals of the Human Genome Program. This program announcement supercedes the one that was published in the NIH Guide for Grants and Contracts, Vol. 18, No. 26, July 28, 1989.

In planning research projects, applicants should be cognizant of the following: (1) New technologies, strategies, and approaches for mapping, sequencing, and informatics will be needed to reach the final goal of the Human Genome Program. Research projects that focus on technology development in the context of a particular disease gene are appropriate so long as such projects have one or more of the overall objectives of the human genome program as their major research goal. (2) In order to achieve the objectives of the Human Genome Program, collaborations between biologists from various disciplines, including human geneticists and non-biologists, such as chemists, physicists, information scientists and engineers, are essential. (3) The timely sharing of materials and data is expected and is essential for progress toward the Human Genome Program. All applicants are expected to discuss in their applications plans for sharing information and data in a timely manner. (4) The five-year plan supports mapping and sequencing of the DNA of five specific organisms: E. coli; S. cerevisiae; D. melanogaster; C. elegans; and the laboratory mouse. Applicants may propose to study model systems other than those listed but must justify their choice in terms of the overall objectives of the Program. (5) Novel, creative, or high-risk/high payoff research projects are encouraged. Applicants seeking funding to support such studies should submit their applications in response to the Program Announcement "Pilot Projects or Feasibility Studies for Genomic Analysis," (see this issue of the NIH Guide for Grants and Contracts, Vol. 19, No. 28, July 27, 1990).

RESEARCH OBJECTIVES

Research projects are encouraged in the following areas:

Genetic Linkage Maps

- Development of methods to rapidly isolate, identify, and map highly informative markers.

- Expansion of the maps of individual chromosomes with the goal of achieving a high-resolution map comprised of DNA markers with an average spacing of 2 centimorgans and gaps no greater than 5 centimorgans, with each marker identified by a STS. Applications are particularly encouraged for projects addressing those chromosomes or regions of chromosomes where there are presently few markers.

- Improvement of methods for linkage analysis and ordering of markers.

Physical Maps

- Development of methods for isolating large amounts of purified human chromosomes, chromosome segments, or restriction fragments for mapping and sequencing.

- Development of cloning techniques that improve upon current approaches to construct complete physical maps. Attempts should be made to consistently obtain cloned inserts that are stable and are at least one megabase in size.

- Construction of overlapping sets of cloned DNA, or closely spaced, unambiguously ordered, DNA markers, with continuity over lengths of at least 2 million base pairs.

- Assembly of STS maps of individual human chromosomes with the goal of having the STS markers spaced at approximately 100,000 base pair intervals.

- Development of methods or strategies to solve the problem of closure.

Sequencing

- Improvement of current technologies to significantly reduce present costs.

- Development of new methods, technologies, and strategies for large-scale sequencing, including preparing and sequencing the DNA and assembling the data.

Only applications that aim to develop new or improve current sequence technology should be submitted in response to this Program Announcement. Routine sequencing will generally not be supported unless the region is of extremely high biological interest. Applications to support feasibility studies for large-scale DNA sequencing using advanced state-of-the-art technology should be submitted in response to the Request for Applications, "Feasibility Studies for Large Scale DNA Sequencing," that is currently being developed.

Informatics

- Development of effective software and database designs to support laboratory-based, large-scale mapping, and DNA sequencing projects. Such projects should be undertaken in the context of actual mapping and sequencing efforts.

- Creation of database and/or software tools that provide easy access to up-to-date physical and genetic mapping and DNA sequencing information and provide for linkage of these specific data sets.

- Development of analytical tools that can be used in the assembly and analysis of genomic data.

MECHANISM OF SUPPORT

Support for this program will be through research grants, including research project grants (R01), program project grants, (P01), FIRST awards (R29), Research Career Development Awards (K04), AREA Awards (R15), conference grants (R13), and Small Business Innovative Research grants (R43, R44). As part of this effort the NCHGR encourages the support of minority students and faculty interests in the Human Genome Program through the regular NIH mechanism as well as through minority supplements to ongoing research grants (see Program Announcement in the NIH Guide for Grants and Contracts, Vol. 18, No. 14, April 21, 1989).

Applications to support large complex research programs through the Center Grant mechanism (P30 and P50) should respond to the special Program Announcement (NIH Guide for Grants and Contracts, Vol. 18, No. 36, October 13, 1989) and will not be considered under this Program Announcement.

APPLICATION AND REVIEW PROCEDURES

Applications in response to this announcement will be reviewed in accordance with the usual NIH peer review procedures. In order to achieve the goals of

the Human Genome Program, applications which include the use and extension of state-of-the-art techniques, as well as those which propose creative, novel, high-risk/high-payoff strategies are highly encouraged. All researchers applying for support should: (1) address how the proposed research will help accomplish the five-year goals; (2) address the state-of-the-art in their particular area; (3) approach the problem in a comprehensive manner, irrespective of the size of the project (e.g., in constructing a physical map of a particular chromosome, emphasis should be placed on constructing fully connected contigs, i.e., overlapping units of cloned DNA, rather than just mapping available probes); and (4) demonstrate that there are adequate plans for: (a) data management, (b) interacting and collaborating with the rest of the scientific community working on similar or related objectives, and (c) making data and resources publicly available in a timely manner.

With the exception of program project (P01) and conference grant applications, applications will first be reviewed for scientific and technical merit by the Genome Study Section or another appropriate study section in the Division of Research Grants as deemed necessary. Program project and conference grant applications will be reviewed by an initial review group empaneled for that purpose. Following the initial scientific review, applications will receive a second-level review by the appropriate National Advisory Council.

REVIEW CRITERIA

Review criteria that will be used to assess the scientific merit of an application are: (1) significance and originality of the research and methodological approaches; (2) feasibility of the research and adequacy of the experimental design; (3) training, experience, research competence, and commitment of the investigator(s); (4) adequacy of the facilities and resources; (5) appropriateness of the requested budget for the work proposed; and (6) provisions for the protection of human subjects, the humane care of animals, and biosafety conditions.

AWARD CRITERIA

The following will be considered in making funding decisions: (1) quality of the proposed project as determined by peer review; (2) value of the research for achieving the goals of the NCHGR or of the NIH component to which the application is assigned; (3) adequacy of any plans proposed for managing data and sharing data and resources in a timely manner; (4) balance among research areas; and (5) availability of funds.

METHOD OF APPLYING

Applications should be submitted on the grant application form PHS 398 (Rev. 10/88) except Small Business Innovative Research grant applications which should be submitted on form PHS 6246-1. Applications will be accepted at the receipt dates appropriate for each mechanism. Application kits are available at most institutional business and grant/contract offices or may be obtained from the Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, Maryland 20892. The title and number of this announcement should be typed in Item 2 on the face page of the application. Applications from women and minority scientists are particularly encouraged.

The completed original application and six legible copies should be delivered to:

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

INQUIRIES

The program administrator welcomes the opportunity to discuss the NCHGR's program interests with prospective applicants and encourages telephone, electronic, or written inquiries. For additional information, or for a complete copy of this program announcement, please contact:

Bettie J. Graham, Ph.D.
Chief, Research Grants Branch
National Center for Human Genome Research
National Institutes of Health
Building 38A, Room 613
Bethesda, MD 20892
Telephone: (301) 496-7531
E-mail: B2G@NIHCU.bitnet
B2G@CU.NIH.gov

This program is described in the Catalog of Federal Domestic Assistance No. 13.172. Awards will be made under the authority of the Public Health Service Act, Sections 301 (Public Law 78-410, as amended 42 U.S.C. 241) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to Health Systems Agency review.

DEVELOPMENT AND UTILIZATION OF TRANSGENIC ANIMAL AND CELL MODELS IN STUDIES OF ENVIRONMENTAL MUTAGENESIS AND ASSOCIATED HEALTH EFFECTS

PA: PA-90-22

P.T. 34; K.W. 0755020, 1007003, 1002028

National Institute of Environmental Health Sciences

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

I. BACKGROUND

The impact of environmental chemicals on human health and well-being has been clearly recognized. There are more than 60,000 synthetic chemicals in commercial use, a quarter of which are produced in abundance. New chemicals are introduced at a rate of about 1,000 per year, some of which may pose a significant health risk to humans. Because of their mutagenic potential, exposure to these chemicals is likely to cause genetic changes leading to either inherited or somatic genetic diseases, such as cancer or atherosclerosis.

The development of methods to transfer specific genes (and genes under the control of specific regulatory elements) into the reproductive cell line of mammals and to identify the expression of those genes has the potential to make substantial impact on environmental health research. Transgenic animals-genetically designed animals created by the introduction of DNA coding for specific genes into the genome of pre-implantation embryos - are model systems that should provide us with a better understanding into the mechanisms of environmental agents. For example, they may help determine the basis of mutation and facilitate an identification of chemically induced mutations; they may elucidate the mechanisms responsible for tissue-specific and developmentally regulated gene expression; and they may identify neural and hormonal factors that regulate gene expression. The National Institute of Environmental Health Sciences (NIEHS) recognizes the importance of this methodology, and, therefore, it is the intent of this program initiative to focus on the development and use of transgenic animal model systems as they pertain to environmental health-related issues.

II. RESEARCH GOALS AND SCOPE

This announcement is issued to encourage investigator-initiated research for developing and using transgenic animal and cell model systems to study basic molecular, biochemical, cellular, and physiological mechanisms of toxicology. It is anticipated that these investigations will allow for the production of genetically designed transgenic animals and/or cells, the development of new and novel approaches in understanding the mechanisms of environmental xenobiotic agents at the genomic level, and the establishment of the nature of the xenobiotic-induced expression in specific target organs. Collaborative research efforts between investigators skilled in transgenic techniques and members of the environmental health research community, as well as scientists from closely related disciplines, are especially encouraged.

The following areas of research interest are not intended to be complete, and investigators are encouraged to study these or other topics that meet the objectives of this announcement:

- Research efforts may be directed at the three basic methods that have been successfully used to generate transgenic animals: (1) microinjection of recombinant DNA into the pronucleus, (2) infection of embryos with retroviruses, and (3) gene transfer into embryonic stem cells. Nonetheless, it should be the intent of the application to improve and extend current capabilities in this area by taking advantage of new technologies.

- Studies may involve the creation of animal/cell strains with specific genes that are induced by environmental agents, in which (1) these induced responses are tissue and organ specific; (2) the toxicologic potential of different agents can be compared; and (3) a relationship, or absence of one, between toxicant exposure in

target organs and subsequent development of disease sequelae may be established.

- It is anticipated that the development of transgenic models will play a role in determining the concordance between in vivo and in vitro systems; therefore, research efforts may also include areas such as the following: (1) development of transgenic cell lines that will serve as indicators of exposure to xenobiotic agents, defining the organs and tissues most susceptible to a given agent; (2) identification and characterization of alternate helical DNA structures formed in the cell's genome, which may contribute to somatic mutation; (3) study of chemical-oncogene interactions, i.e., investigations into the relationships among mutagenesis, oncogene activation and tumor development; (4) study of oncogenes that collaborate in the development of malignancies; (5) analysis of the molecular mechanism(s) involved in sequence directed mutagenesis; (6) investigation into the role of spontaneous and induced homologous recombination in somatic and germline cells; and (7) study of the role of tumor promoters and exogenous agents that cause chronic cell proliferation as cancer or toxicological risk determinants.

- Studies may be designed to gain a better understanding of the molecular basis of tissue-specific and stage-specific gene expression following xenobiotic exposure, e.g., to identify and characterize DNA sequences that control cell specificity of gene expression and to utilize these cell-specific elements to explore the physiological consequences of overexpression or inappropriate expression of foreign gene products.

III. MECHANISM OF SUPPORT

The mechanism of support for this activity will be the individual research grant - Research Project Grant and FIRST Award as applicable.

IV. APPLICATION AND REVIEW PROCEDURES

A. Deadline

Applications will be accepted in accordance with the usual receipt dates for new research grant application; i.e., February 1, June 1, and October 1. The earliest possible award dates will be approximately nine months after the respective receipt dates. Applications received too late for one cycle of review will be held until the next receipt date.

B. Method of Applying

Applications will be received by the NIH's Division of Research Grants (DRG) and referred to an appropriate study section for scientific and technical merit review. Institute assignment decisions will be governed by normal programmatic considerations. The review criteria customarily employed by the NIH for regular research grant applications will prevail. Following the initial scientific review, the applications will be evaluated by an appropriate National Advisory Council.

Applications should be submitted on form PHS-398 (revised 10/88) available in the business or grants and contract offices at most academic and research institutions or from the DRG. To identify the application as a response to this announcement, check "yes" in Item 2 on the face page of the application and enter the title, "Development and Utilization of Transgenic Animal and Cell Models in Studies of Environmental Mutagenesis and Associated Health Effects, PA-90-22."

The original and six (6) copies of the application should be directed to:

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

Prior to submitting an application and for further information, investigators are strongly encouraged to contact the following program staff:

Dr. William A. Suk
Program Administrator
Scientific Programs Branch
Division of Extramural Research and Training
National Institute of Environmental Health Sciences
P. O. Box 12233
Research Triangle Park, NC 27709
Telephone: (919) 541-0797

ERRATA

PERINATAL EMPHASIS RESEARCH CENTERS

RFA: HD-90-10

P.T. 04; K.W. 0775020, 0775025, 0403020, 0775015, 0411005, 0710030

National Institute of Child Health and Human Development

This Request for Applications was announced in the NIH Guide for Grants and Contracts on June 8, 1990, Vol. 19, No. 21.
The receipt date has been changed from September 19, 1990 to November 21, 1990.

Any questions contact:

Dr. Charlotte Catz
Chief, Pregnancy and Perinatology Branch
Center for Research for Mothers and Children
National Institute of Child Health and Human Development
National Institutes of Health
Executive Plaza North, Room 643
9000 Rockville Pike
Bethesda, MD 20892
Telephone: (301) 496-5575

CVD NUTRITION EDUCATION FOR LOW LITERACY SKILLS

RFA: HL-90-11-P

P.T. 34; K.W. 0710095, 0502028, 0715040, 0411005

National Heart, Lung, and Blood Institute

This is to correct the dates for review by the National Heart, Lung, and Blood Advisory Council and anticipated award for the RFA "CVD Nutrition Education for Low Literacy Skills" released in the July 6, 1990, NIH Guide for Grants and Contracts (Vol. 19, No. 25). The correct dates are as follows:

Review by the National Heart, Lung, and Blood Advisory Council: May 1991

Anticipated Award Date: August 1, 1991

Inquiries regarding this RFA may be directed to:

Dr. Nancy C. Santanello
Prevention and Demonstration Research Branch
National, Heart, Lung, and Blood Institute
Federal Building, Room 604
Bethesda, MD 20892
Telephone: (301) 496-2465

**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

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