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NIH REGIONAL WORKSHOP - PHS POLICY ON THE HUMANE CARE AND USE OF LABORATORY ANIMALS

P.T. 42; K.W. 0201011, 1014003

National Institutes of Health

The National Institutes of Health, (NIH), Office for Protection from Research Risks (OPRR) announcement which previously appeared in the NIH Guide for Grants and Contracts, Vol. 15, No. 29, December 12, incorrectly identified the Policy on the Humane Care and Use of Laboratory Animals as the NIH Policy. The correct title is the PHS Policy for the Humane Care and Use of Laboratory Animals. For additional information regarding the regional education program contact:

Robert Garfinkle
Director, Animal Welfare Education Program
Office for Protection from Research Risks
National Institutes of Health
Building 31, Room 4B09
9000 Rockville Pike
Bethesda, Maryland 20892
Telephone: (301) 496-7041

DATED ANNOUNCEMENTS (RFPs AND RFAs AVAILABLE)

SMALL GRANTS PROGRAM TO FACILITATE USE OF NEW MOLECULAR BIOLOGIC AND GENETIC TECHNIQUES BY RESEARCHERS IN DIABETES, ENDOCRINOLOGY AND METABOLIC DISEASES

P.T. 34; K.W. 0715075, 0715135, 0785050, 1002008, 1002019

National Institute of Diabetes and Digestive and Kidney Diseases

Application Receipt Date: March 2, 1987

INTRODUCTION

The Division of Diabetes, Endocrinology and Metabolic Diseases (DDEMD) supports basic and clinical research and research training related to diabetes mellitus and its complications, to endocrinology and a variety of endocrine disorders, and to metabolism and various metabolic diseases, including cystic fibrosis. One important area of research supported by the Division includes studies related to the molecular and cellular mechanisms of endocrine disorders including diabetes and of inherited and acquired metabolic diseases. Recent Advisory Panel meetings addressed the concern that the ability of some established investigators in these fields to pursue promising new directions in their research was impaired by their lack of experience in the newest techniques of molecular biology and genetics. The Division therefore wishes to encourage established researchers who are DDEMD supported Principal Investigators (PIs) or, under special circumstances a qualified member of a PI's research team, to obtain first hand experience with new techniques as a "Visiting Researcher" in the laboratory of a "Host" expert in molecular biology or genetics. The new techniques must be an integral part of an original pilot research project conceived by the Host, or by the Visiting Researcher in collaboration with the Host. The proposed research project should result in novel preliminary data which could strengthen a subsequent application for regular grant support.

SCOPE

This Program Announcement should encourage prospective Visiting Researchers to identify Hosts in order to prepare and submit a small, original pilot research grant application. The application must be submitted by the Host's institution with the Host as Principal Investigator. The proposed research project, to be performed in the Host's laboratory, need not be directly related to endocrine or metabolic disease. However the techniques utilized while performing the research project must be directly applicable to the Visiting Researcher's future work in these areas.

This small grants program is intended to provide established researchers supported by the Division with greater flexibility in their research programs and broadened scientific expertise in allied fields. It is hoped that involvement of these PIs in experimental testing of new research ideas or directions in molecular biology and genetics will facilitate transfer of new techniques utilized in this research from the Host to their own laboratories.
OBJECTIVES

This program is requesting short, original pilot research applications designed to utilize one or more of the following techniques:

- recombinant DNA techniques, including but not limited to isolation of mRNA and DNA, preparation of cDNA libraries, in situ hybridization, generation of genetic markers, restriction fragment length polymorphisms and Northern, Southern and Western blotting
- gene transfer techniques, including vector production, transfection and infection,
- production of transgenic cells, cell lines and animals
- hybridoma production
- identification of gene products
- other novel techniques useful in endocrinology

ELIGIBILITY REQUIREMENTS:

The Host must be an established investigator with expertise in molecular biology, genetics or other novel techniques and must also be a current PI of an Institute or Division of the NIH. The proposed Visiting Researcher must be a current PI of NIDDK, DDEMD.

Under special circumstances such as uncancelable prior commitments during the period September 1, 1987 - August 31, 1988, that do not allow the established researcher to visit the Host's laboratory and participate personally in the project, an established researcher and PI of DDEMD may sponsor a qualified member of his/her team as a Visiting Researcher. In such instances it is required that the team member return to the Sponsor's laboratory for at least one year following the visit and effectively work with new molecular biologic and genetic techniques.

The Sponsor must provide documentation countersigned by an authorized institutional representative to vouch both for the research team member's qualifications and the likelihood of his/her return to the sponsor's laboratory. The nature of the special circumstances which preclude the Sponsor's personal participation as a Visiting Researcher must also be thoroughly documented and explained in the application.

All Hosts, Visiting Researchers, or sponsored Visiting Researchers must be citizens or noncitizen nationals of the United States, or have been lawfully admitted to the United States for permanent residence.

All personnel involved in the project must have received a Ph.D., M.D., or equivalent degree from an accredited domestic or foreign institution. The Host and the Visiting Researcher/Sponsor must have had at least seven subsequent years of relevant research or professional experience. Demonstrated research ability must be evidenced by publications and former or current grants from NIH, NSF or research foundations.

PURPOSE AND TERMS OF THE AWARD:

This non-renewable award is intended to provide a maximum of $25,000 (total direct costs) over a three to six months period, to be used for salaries, supply needs in the Host's laboratory, and travel funds for the Visiting Researcher of up to $600. However, the requested period of support may be up to twelve months in order to accommodate scheduling of the proposed activities. Further details on budget will be provided in the special instruction package for preparation of an application to that should be requested from program staff (see below). The proposed activity must be full-time for the Visiting Scientist and must include the conduct of research with supervision provided by the Host, or by the Host in association with an expert member of the Host's staff. The setting may be a U.S. nonprofit private or public institution. The Host institution must be different from the Visiting Researcher's institution.

APPLICATION AND REVIEW PROCEDURES

The format for preparing this abbreviated application is different from that used by NIH for regular research project grants. THEREFORE, BEFORE PREPARING AN APPLICATION, PROGRAM STAFF (listed below) MUST BE CONTACTED REGARDING SPECIAL INSTRUCTIONS. Applications must adhere to this format to be responsive and must be submitted on Form PHS 398, available at most institutional business offices or from the Division of Research Grants, NIH. A single reply date of March 2 will be strictly enforced. An anticipated schedule for review and award is detailed below:
Application NIDDK Special Initial Anticipated Receipt Date Review Committee Award Date
March 2, 1987 March/May 1987 September 1, 1987

REVIEW CRITERIA

A special NIDDK review committee will evaluate the scientific merit of each application based on the following criteria: feasibility of the proposed pilot research project; the potential of the proposed pilot research project to provide meaningful preliminary scientific data; relevance of the techniques proposed in the research project to the Visiting Researcher's (or Sponsor's) future studies in endocrinology, diabetes or metabolism; appropriateness of the Host's research project for communicating the proposed techniques; appropriateness of ALL scientific staff involved; appropriateness of the proposed budget, including degree to which the Visiting Researcher can obtain salary support from other sources.

REPORTING REQUIREMENTS

A Final Progress Report, an Invention Statement and a Financial Status Report must be submitted within ninety days after the termination of the award. This final reporting requirement is the same as that for other types of research grants and is in accord with 42 CFR 52 and 45 CFR 74.

CONSULTATION WITH PROGRAM STAFF

Prospective applicants are strongly encouraged to discuss their ideas with Program staff (see below) to determine whether they fit the definition and guidelines of this announcement. Applications which, in the opinion of staff, do not meet these objectives, scope and eligibility criteria will be returned without review.

For further information and special instruction on preparation of an application prospective Visiting Researchers or Host applicants should contact:

For Endocrinology Research
Robert Tolman, Ph.D.
Director
Endocrinology Research Program, NIDDK
Room 605A - Westwood Bldg.
NIH, Bethesda, MD 20892
Telephone: (301) 496-7504

For Diabetes Research
Julia Freeman, Ph.D.
Director
Diabetes Research Program, NIDDK
Room 626 - Westwood Bldg.
NIH, Bethesda, MD 20892
Telephone: (301) 496-7731

For Metabolic Research
Robert Katz, Ph.D.
Director
Metabolic Diseases Research Program, NIDDK
Room 607A - Westwood Bldg.
NIH, Bethesda, MD 20892
Telephone: (301) 496-7997

This program is described in the Catalog of Federal Domestic Assistance, No. 13.847, Diabetes, Endocrinology, and Metabolic Diseases. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301, (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations, most specifically at 42 CFR Part 52 and CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

CONSTRUCTION, ALTERATION AND RENOVATION, AND INSTRUMENTATION FOR VISION RESEARCH FACILITIES

P.T. 02; K.W. 0735000, 0780010

National Eye Institute

Application Receipt Date: April 8, 1987

BACKGROUND

The National Eye Institute (NEI) announces that in FY1987 there will be $2,250,000 available for the support of the expansion and improvement of vision research facilities. This program will provide grants for three types of activities:
A. Instrumentation

Support may be requested for a single piece or a collective system of specialized laboratory equipment. The equipment may be project specific or may be shared among investigators who cannot otherwise justify the purchase on an individual grant project. The NEI will provide up to 50% of the total purchase price of major laboratory equipment costing in the range of $25,000 to $300,000, up to a maximum NEI share of $150,000.

B. Alteration and Renovation

Support may be requested for the costs of adapting existing interior space and utilities within a finished structure, to the needs of a vision research group or of an individual researcher. Some examples are: renovation of space to meet the needs of clinical vision research, remodeling laboratory space, redesigning specialized instrumentation space, or upgrading animal care facilities. The NEI will provide up to 50% of the total allowable costs of projects costing in the range of $50,000 to $400,000, to a maximum NEI share of $200,000.

C. New Construction

Support may be requested for the construction of new buildings, additions to existing facilities, or the completion of "shell" space in new or existing buildings. Large-scale Alteration and Renovation projects costing in excess of $400,000 may also be requested under this support mechanism. The NEI plans to provide up to 50% of the total allowable cost of the project, to a maximum NEI share of $500,000.

FUNDING PARTICIPATION

The applicant organization must demonstrate the availability of matching funds from non-Federal sources at the time of application.

ELIGIBILITY

Any domestic public or non-profit institution, organization, or association is eligible to apply.

METHOD OF APPLICATION

Prospective applicants must request additional specific information about application format and other guidelines from the NEI. Applicants are encouraged to discuss with NEI staff the feasibility of the plans before preparing the application.

PHS Form 398 is to be used for Instrumentation and for Alteration and Renovation applications. New Construction applications must be submitted on PHS Form 5162-1.

APPLICATION RECEIPT

Grant applications must be submitted to the Division of Research Grants, National Institutes of Health by April 8, 1987. Applications received after that date will not be accepted for review in this competition.

Specific application guidelines, application forms, and additional program information may be obtained from:

Ms. Gaye Lynch
Grants Management Specialist
National Eye Institute
Building 31, Room 6A48
Bethesda, Maryland 20892
Telephone: (301) 496-5884

The program is described in the Catalog of Federal Domestic Assistance No.13.985, Eye Research Construction Grants. Construction grants made under this program are subject to Executive Order 12372. All awards will be made under the authority of the Public Health Service Act, Title IV, Section 453 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 54.
STUDY CENTERS AND COORDINATING CENTER FOR CHILDREN'S ACTIVITY TRIAL OF CARDIOVASCULAR HEALTH

RFAs AVAILABLE: 87-HL-10-P
87-HL-13-P

P.T. 34; K.W. 0730070, 0705015, 0404000, 0715020, 0745055, 0411005

National Heart, Lung, and Blood Institute

Application Receipt Date: March 16, 1987

The Prevention and Demonstration Research Branch of the Division of Epidemiology and Clinical Applications, National, Heart, Lung, and Blood Institute (NHLBI) announces the availability of Requests for Applications (RFAs) on the above subject. Copies of the RFAs are available from staff of the NHLBI. Note that awards will not be made to foreign institutions.

This program will support behavioral, clinical, and biostatistical investigators and supporting staff to collaboratively plan and execute a study to assess the effectiveness of school-based risk reduction interventions involving three components. These components are a cardiovascular curriculum, parent participation, and environmental changes in the school. The program will use the cooperative agreement mechanism. If this Phase I study is successful, it is anticipated that a full-scale field trial will be conducted. Interested institutions may request copies of the RFA for either the Study Center (87-HL-10-P) or the Coordinating Center (87-HL-13-P) or both.

Requests for copies of the RFAs should be addressed to:

Elaine J. Stone, Ph.D.
Division of Epidemiology and Clinical Applications
National Heart, Lung, and Blood Institute
Federal Building, Room 5C-10
7550 Wisconsin Avenue
Bethesda, Maryland 20892
Telephone: (301) 496-3503

GROWTH FACTORS OF THE KIDNEY, GENITOURINARY AND HEMATOLOGIC SYSTEMS

RFA AVAILABLE: 87-DK-03

P.T. 34; K.W. 0760020, 0705075, 0785070, 0765035, 1002004, 1002008, 1002017, 0785050, 0710070, 0710100

National Institute of Diabetes and Digestive and Kidney Diseases

Application Receipt Date: April 1, 1987

The Division of Kidney, Urologic and Hematologic Diseases (DKUHD) of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) announces the availability of a Request for Applications (RFA) on the above subject.

BACKGROUND

Research on growth factors (GFs) affecting the kidney and urologic tract is not as well established as in some other areas. Several factors have been partially characterized in the area of hematopoiesis, but the complex regulatory and pathophysiological roles of these factors has yet to be evaluated. Initial studies into renal, genitourinary and hematopoietic GFs indicate that these are relevant areas for increased scientific interest and research.

RESEARCH GOALS AND SCOPE

This special grant program will support fundamental research on the structure, function and regulation of GFs relevant to the kidney, genitourinary and hematologic systems. The major purpose of this solicitation is to encourage the application of modern cellular and molecular technologies in order to identify, isolate, and purify potential GF(s); to determine their physiological relevance; to develop relevant detection assays; to elucidate regulatory processes governing their activities; and to relate these findings to disease processes.

An emphasis of this initiative is to foster extensive collaboration between individuals in the basic sciences, including biochemistry, cell biology, embryology, endocrinology, hematology, immunology, molecular biology, pathology, pharmacology and physiology. Thus, it is the intent of this solicitation to engage investigators
who currently have diverse research interests but who may wish to apply their
technologies and expertise in elucidating and extending the current knowledge of GFs
in the kidney, urologic and hematologic fields.

MECHANISMS OF SUPPORT

Support for this program will be through the grant-in-aid and will be governed by
the current policies of grant programs of the National Institutes of Health.
Applications may be submitted for traditional, individual research-project grants
(R01s) or First Independent Research Support & Transition Awards (R29s), only.
Although plans for Fiscal Year 1987 include $1.2 million for the total (direct and
indirect) costs of this program, the funding of applications submitted in response
to this RFA is contingent on the actual availability of funds and receipt of
applications deemed worthy of support by the accepted NIH peer review procedure. It
is anticipated that six to eight awards will be made, for up to five years under
this program. Since a variety of approaches would represent valid responses to this
announcement, it is anticipated that there will be a range of costs among individual
awards.

APPLICATION AND REVIEW PROCEDURES

Applications in response to this RFA will be reviewed for scientific and technical
merit by an initial review group which will be convened by the Division of
Extramural Activities, NIDDK, solely to review these applications. Upon receipt,
applications will be evaluated for their responsiveness to the objectives of this
RFA. If an application is judged unresponsive at this stage, the applicant will be
contacted and given an opportunity to withdraw the application or to have it
considered for the regular research grant program of the NIH. Should the proposal
submitted in response to the RFA be substantially similar to a research application
already under consideration by the NIH, the applicant will be asked to withdraw
either application. Simultaneous submission of identical applications will not be
allowed.

Funding decisions will be based on Initial Review Group and the National Diabetes
and Digestive and Kidney Diseases Advisory Council recommendations and relevance to
the Objectives and Scope of the RFA. Applicants should request a start date of

For further information and copies of the complete RFA, please contact:

M.J. Scherbenske, Ph.D.
Renal Physiology/Pathophysiology Program Director
DKUHD/NIDDK
Westwood Building, Room 621
Bethesda, Maryland 20892
Telephone: (301) 496-7458

KIDNEY DISEASE OF DIABETES MELLITUS: NEW STUDIES ON THE PATHOGENETIC MECHANISMS AND
CLINICAL FEATURES

RFA AVAILABLE: RFA-DK-87-04
P.T. 34; K.W. 0715075, 1002019, 1003002, 0710100, 0765035
National Institute of Diabetes and Digestive and Kidney Diseases
Application Receipt Date: April 1, 1987

The Division of Kidney, Urologic and Hematologic Diseases (DKUHD) of the National
Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) announces the
availability of a Request for Applications (RFA) on the above subject.

BACKGROUND

Renal diseases leading to failure that results in replacement therapy represent an
important public health problem. The largest single cause of renal disease is now
diabetes mellitus. The number of patients with end stage renal disease (ESRD) due
to kidney disease of diabetes mellitus has also risen steadily over the last decade.
At present, nearly 30 percent of new patients entering the ESRD program have kidney
disease of diabetes mellitus. This number is increasing at a rate of approximately
2 percent annually, therefore within the next decade kidney disease of diabetes
mellitus will likely account for more than 50 percent of all patients in the ESRD
program. Thus, kidney disease of diabetes mellitus, being the predominant cause of
ESRD in the United States, represents a significant and growing health problem.
RESEARCH GOALS AND SCOPE

The overall goal of this RFA is to encourage new studies and new investigators to enter this field to broaden the base of research disciplines addressing issues pertinent to kidney disease of diabetes mellitus. The RFA is intended to stimulate the development and submission of projects aimed at understanding the pathogenetic mechanisms of kidney disease of diabetes mellitus and the development of diagnostic measures and approaches to effective prevention, control and treatment. The scope of these projects is intended to include studies of the genetics, physiology, biochemistry, pathology, pharmacology, immunology and clinical features of kidney disease of diabetes mellitus. Research approaches considered appropriate include the use of experimental models and/or clinical studies.

MECHANISMS OF SUPPORT

Applications may be submitted for traditional, individual research-project grants (R01s) or First Independent Research Support & Transition (FIRST) Awards (R29s) only. Although plans for Fiscal Year 1987 include $2.0 million for the total (direct and indirect) costs of this program, the funding of applications submitted in response to this RFA is contingent on the actual availability of funds and receipt of applications deemed worthy of support by the accepted NIH peer review procedure. It is anticipated that approximately seven to ten awards will be made, for up to five years under this program. Since a variety of approaches would represent valid responses to this announcement, it is anticipated that there will be a range of costs among individual awards. The earliest expected starting date for the successful applications will be September 30, 1987.

APPLICATION AND REVIEW PROCEDURES

Applications in response to this RFA will be reviewed for scientific and technical merit by an initial review group which will be convened by the Division of Extramural Activities, NIDDK, solely to review these applications. Upon receipt, applications will be evaluated for their responsiveness to the objectives of the RFA. If an application is judged unresponsive at this stage, the applicant will be contacted and given the opportunity to withdraw the application or have it considered for the regular research grant program of the NIH. Should the proposal submitted in response to the RFA be substantially similar to a research grant application already under consideration by the NIH, the applicant will be asked to withdraw either application. Simultaneous submission of identical applications will not be allowed.

Funding decisions will be based on Initial Review Group and the National Diabetes and Digestive and Kidney Diseases Advisory Council recommendations and relevance to the Objectives and Scope of the RFA.

For further information and copies of the complete RFA, please contact:

Gladys H. Hirschman, M.D.
Director, Chronic Renal Disease Program
DKUHD, NIDDK
Westwood Building, Room 621
Bethesda, Maryland 20892
Telephone: (301) 496-7571

RESEARCH ON THE NORMAL URINARY TRACT AND IN DISEASES SUCH AS INTERSTITIAL CYSTITIS

RFA AVAILABLE: 87-DK-05

P.T. 34; K.W. 0705075, 0755020, 0715125

National Institute of Diabetes and Digestive and Kidney Diseases

Application Receipt Date: April 1, 1987

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) through the Division of Kidney, Urologic and Hematologic Diseases (DKUHD) invites grant applications for support of research on the structure and function of the urinary tract in normal and disease states such as interstitial cystitis. Structural and/or functional abnormalities of the urinary tract are an essential part of the initiation and progression of urinary tract diseases. Basic research on urinary tract physiology and pathophysiology is considered essential for developing a better scientific understanding of normal and abnormal processes.

BACKGROUND

Disorders of the urinary tract are costly, socially and economically debilitating disorders in children and adults. As an example, interstitial cystitis is a poorly
understood and painful syndrome affecting bladder function and micturition for which there is no effective treatment. Research to date has not uncovered the etiology of interstitial cystitis, although possible roles of bacterial, viral, fungal, inflammatory and immune mechanisms have been studied. The relationship between reflux, infection, adherence and renal dysfunction is poorly understood, but the association is common. The nature of the relationship between urine storage, transport and micturition as related to bacterial infection and as related to interstitial cystitis remains obscure and needs further study.

OBJECTIVES AND SCOPE

To characterize the normal ureteral, bladder and urethral walls with respect to its epithelium, smooth muscle and interstitial aspects. The development of cell lines of the various cell types is a high priority in the study of epithelium and smooth muscle. Determination of changes in the anatomy, physiology and/or neurophysiology of ureterovesical function resulting in ureteral or intrarenal reflux due to diseases such as interstitial cystitis or urinary tract (UT) infection are required. The nature and type of initiating factors and those which may lead to dysfunction require study. Questions such as the site and nature of the permeability barrier, response of the smooth muscle cell to changes therein, and the maturational elements of these phenomena remain to be elucidated. Research is needed to characterize interactive processes responsible for the passage of urine from the renal pelvis to the bladder and eventual micturition. The development of an animal model, or models, would be useful. More understanding is needed on the urgency and frequency for micturition and bladder and UT pain reported in interstitial cystitis, a condition with symptoms mimicking UT infection but without bacteriuria. Characterization of changes is needed in bladder structure and function resulting in the development of the syndrome now commonly diagnosed as interstitial cystitis. Observations have suggested that changes in the bladder mucin layer may be associated with glomerulations, infection and in some instances cancer. The possible role(s) and function of mast cells reported to be present in higher numbers in the bladder muscle of those with interstitial cystitis require further elucidation. Data are needed on whether changes in bladder structure and function may result from urine induced changes or be the result of epithelial/smooth muscle changes or autoimmune factors. The potential role of hormones in effecting lower UT structure, function and sensory phenomena would be important to know. Conditions of the UT that may be conducive to the onset and progression of infection, such as the relation of the urothelium in adherence and/or colonization to the virulence of bacteria leading to infection, require study. Few studies have in turn delineated the effects of bacterial invasion on the structural and functional characteristics of the UT which may well influence the end result of such infections. An overall objective of this announcement is to recruit new investigators into this field so as to expand the breadth and scope of research on the lower UT.

MECHANISM OF SUPPORT

Support for this program will be through the traditional research grant. Policies that govern research grant programs of the National Institutes of Health will prevail. Financial plans for FY 1987 include $600,000 for the total costs of this program. It is anticipated that four to six awards will be made, contingent upon receipt of funds for this purpose. The specific amount to be funded will depend on the merit and scope of the applications received.

APPLICATION AND REVIEW PROCEDURES

Applications in response to this RFA will be reviewed for scientific and technical merit by an initial review group which will be convened by the Division of Extramural Activities, NIDDK, solely to review these applications. Upon receipt, applications will be evaluated for their responsiveness to the objectives of this RFA. If an application is judged unresponsive at this stage, the applicant will be contacted and given an opportunity to withdraw the application or to have it considered for the regular research grant program of the NIH. Should the proposal submitted in response to the RFA be substantially similar to a research application already under consideration by the NIH, the applicant will be asked to withdraw either application. Simultaneous submission of identical applications will not be allowed.

Funding decisions will be based on Initial Review Group and the National Diabetes and Digestive and Kidney Diseases Advisory Council recommendations and relevance to the Objectives and Scope of the RFA. Applicants should request a start date of September 30, 1987.

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

Charles H. Rodgers, Ph.D.
Urology Program Director, DKUHD, NIDDK
Westwood Building, Room 609C
Bethesda, MD 20892
Telephone: (301) 496-7573
ERYTHROPOIETIN REGULATED EXPRESSION, RECEPTION, AND MODULATION OF CELLULAR DIFFERENTIATION

RFA AVAILABLE: 87-DK-06

P.T. 34; K.W. 0760020, 1002004, 1002008, 0760075, 0760025, 0790000, 1002019, 0765015

National Institute of Diabetes and Digestive and Kidney Diseases

Application Receipt Date April 1, 1987

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) through the Division of Kidney, Urologic and Hematologic Diseases (DKUHD) invites grant applications for support of research on fundamental questions of erythropoietin regulated expression, reception, and modulation of cellular differentiation. The recent availability of pure recombinant erythropoietin makes it possible to pursue studies aimed at understanding this important growth factor in normal and pathologic functioning of the hematopoietic system. Such work could contribute to the prevention and alleviation of the anemia of chronic diseases. Clinical trials are not requested.

BACKGROUND

Erythropoietin, a growth factor produced primarily by the kidney, causes both proliferation and differentiation of cells of the hematopoietic system in response to renal cell oxygen concentration. The study of erythropoietin has been hampered by difficulties encountered in measuring this growth factor, and by the limited amount of pure erythropoietin available. Recent isolation of the erythropoietin gene and the commercial production of erythropoietin in vitro, coupled with a highly sensitive and specific radioimmunoassay, now makes it possible to examine the regulation of erythropoietin expression, interaction with its receptor, and signal transduction at the cellular and molecular level.

The purpose of this initiative is to seek proposals in which the regulated expression, reception, post-receptor modulation of cell activities, role in differentiation of erythropoietin, and limitation of effect are examined at the cellular and molecular level. Particular encouragement is offered to investigators well-trained in pertinent technologies who currently may be pursuing other research interests.

RESEARCHOBJECTIVES

Circulating levels of erythropoietin are modulated in response to changes in the oxygen tension of the blood by undetermined mechanisms. Patients with severe kidney dysfunction have significantly reduced plasma erythropoietin levels, often have chronic anemia, and require frequent blood transfusions. The anemia of chronic renal failure appears to be due to a lack of erythropoietin, along with the possible accumulation of uremic inhibitors of erythropoiesis. Studies of the clinical use of erythropoietin are under way.

Central questions include which kidney cells are responsible for erythropoietin production, regulation of erythropoietin production at the molecular level, and cellular conversion of the signal of lowered oxygen tension into the stimulus for increased erythropoietin transcription and translation. Factors which have been demonstrated to affect the plasma erythropoietin level include decreased renal blood flow, hypoxia, anemia, or increased hemoglobin affinity for oxygen. Prostaglandins may have a mediating role, as may the renin-angiotensin system, but the precise signals to which erythropoietin-producing cells of the kidney respond are unknown.

Structure/function relationships of erythropoietin in interacting with target cell surface receptors are not known, nor are the identity and nature of these receptors, the processes following erythropoietin interaction with the receptor, and the nature of the subsequent intracellular changes. The interaction of hormone with receptor causes the increased production of globin as well as expression of other erythropoietin-sensitive genes. The study of the regulation of erythropoietin-sensitive genes, including trans-acting factors stimulated by the erythropoietin-receptor complex, is important.

Several classes of erythroid progenitor cells respond to erythropoietin, but the primary target appears to be the colony-forming unit-erythroid (CFU-E), the most mature of the erythroid progenitor cells. The biochemical response mechanisms are unknown. Erythropoietin's effect on target cells other than erythroid progenitor cells is an important topic also, and deserves study. Examples include blood vasculature, renal cells and bone.

The effects of growth factors on individual cells eventually are modulated and finally are turned off. There are a number of ways this may happen biochemically, including competition for the receptor by inactive hormone fragments and
modification of the receptor. The mechanisms of natural limitation of the growth promoting effects of erythropoietin need study.

APPLICATION AND REVIEW PROCEDURES

Applications in response to this RFA will be reviewed for scientific and technical merit by an initial review group which will be convened by the Division of Extramural Activities, NIDDK, solely to review these applications. Upon receipt, applications will be evaluated for their responsiveness to the objectives of this RFA. If an application is judged unresponsive at this stage, the applicant will be contacted and given an opportunity to withdraw the application or to have it considered for the regular research grant program of the NIH. Should the proposal submitted in response to the RFA be substantially similar to a research application already under consideration by the NIH, the applicant will be asked to withdraw either application. Simultaneous submission of identical applications will not be allowed.

Funding decisions will be based on Initial Review Group and the National Diabetes and Digestive and Kidney Diseases Advisory Council recommendations and relevance to the Objectives and Scope of the RFA. Applicants should request a start date of September 30, 1987.

Awards will be made as research project grants. Contingent on availability of funds, the NIDDK plans to make available $1.2 million for the total (direct and indirect) costs of this program in fiscal year 1987. It is anticipated that six to eight grants will be awarded, for up to five years of support.

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

David G. Badman, Ph.D.
Hematology Program Director
Division of Kidney, Urologic, and Hematologic Diseases, NIDDK
Westwood Building, Room 621
Bethesda, Maryland 20892
Telephone: (301) 496-7458

PROSPECTIVE RANDOMIZED STUDIES CORRELATING CURRENT TREATMENT PROCEDURES WITH PAIN REDUCTION IN PANCREATIC CANCER PATIENTS

RFA AVAILABLE: 87-CA-03
P.T. 34; K.W. 0715035, 0715150, 0745005
National Cancer Institute
Application Receipt Date: April 9, 1987

The Division of Cancer Prevention and Control, through the Organ Systems Program, invites research grant applications from organizations capable and interested in participating in a network of collaborating research groups charged with carrying out studies in the reduction of pain in pancreatic cancer patients.

OBJECTIVE AND SCOPE

This RFA will be utilized to initiate prospective, randomized studies, which will be implemented through a collaboration among the successful applicant organizations. The NCI proposes to encourage up to five existing pain research groups to assemble the expertise and patients needed to evaluate pancreatic cancer pain. The main goal is to determine which of the currently used, single or combined, procedures for treating pancreatic cancer patients are correlated with measurable and significant pain relief.

BACKGROUND

Since there are no treatments for pancreatic cancer which increase survival significantly, and there is no known way to prevent the disease, a special research emphasis to identify the best current methods to reduce pain and thus improve the quality of life deserves high priority.

The NCI recognizes that research on pain in pancreatic cancer is technically difficult to conduct. The relatively low incidence of the disease combined with a brief survival results in few study subjects becoming available at an institution at any specific time. Furthermore, the complexity of the disease course elevates the numbers of patients which would be required for testing hypotheses adequately. An inter-organizational networking effort might overcome these difficulties and make possible the accrual of sufficient patients to answer definitive questions.
ELIGIBILITY

Organizations with established pain research facilities are encouraged to take the leadership in response to this RFA. Such organizations before applying are required to have the capacity for establishing liaison with investigators involved in clinical research in cancer, including specific expertise in the treatment of pancreatic cancer. The applicant organization or its affiliate should be involved in treating pancreatic cancer patients. At the time of submission, the required qualified investigators, technical expertise, patient populations, and facilities should exist in the applicant organization and its proposed affiliates.

APPLICATION SUBMISSION AND REVIEW

A potential applicant organization is encouraged, but is not required, to submit a letter of intent, and is encouraged to consult with NCI staff before submitting. Letters of intent are requested by January 16, 1987. The letter of intent will not enter into the review of an application submitted in response to this RFA.

Applications responsive to this RFA will be reviewed for scientific merit by an appropriate peer review group composed primarily of non-Federal experts and set up by the Division of Extramural Activities, National Cancer Institute. Reviewers will consider each application in terms of its projected research plans, and of the proposed means for implementing collaborative network activities. Applications will be reviewed in competition with each other on a nationwide basis. This RFA solicitation is a single competition and has one specific deadline for receipt of applications.

MECHANISM OF SUPPORT

The support mechanism for this program will be the NIH investigator-initiated research grant (R01). Awards may be made to domestic non-profit and profit organizations. An applicant organization may apply for a period of support of up to three years. Funds, if awarded, would support research related to the protocols developed by the collaborative network. The awards would also support travel, planning, communications and data management connected with the network effort. Contingent upon the availability of funds and dependent upon the receipt of a sufficient number of applications of high scientific merit, it is anticipated that five awards will be made at an annual total cost of approximately $400,000. Before the end of the three-year period of funding, the Pancreatic Cancer Pain Network will be evaluated by the NCI and a means for possible continued or expanded support determined.

INQUIRIES

Requests for copies of the RFA in its expanded form should be addressed to:

William E. Straile, Ph.D.
Cancer Centers Branch
Division of Cancer Prevention and Control
National Cancer Institute
Blair Building, Room 727
Bethesda, Maryland 20892-4200
Telephone: (301) 427-8818

ONGOING PROGRAM ANNOUNCEMENTS

PHYSICIANS' ROLE IN LOWERING ELEVATED LIPIDS BY DIET

P.T. 34; K.W. 0710095, 0715020, 0745055, 0760040, 0765025

National Heart, Lung, and Blood Institute

The National Heart, Lung, and Blood Institute (NHLBI) has supported laboratory, epidemiological and clinical studies which demonstrated that elevated blood cholesterol is an important risk factor for coronary heart disease and that blood cholesterol levels can be lowered both by diet and drugs. The Lipid Research Clinics Coronary Primary Prevention Trial (CPPT) reported that by lowering elevated blood cholesterol levels the risk of coronary heart disease is reduced. Following the publication of these results, the National Institutes of Health held a consensus development conference in December 1984 to review the current scientific evidence and make appropriate practice recommendations for blood cholesterol reduction.

The Consensus Development Conference Statement contains several observations and recommendations, including a number which were specifically directed to practicing physicians. Their recommendations included the following:
Adults with high-risk blood cholesterol levels (values greater than the 90th percentile) should be treated intensively by dietary means under the guidance of a physician, dietitian or other health professional; if response to diet is inadequate, appropriate drugs should be added to the treatment regimen.

Adults with moderate-risk blood cholesterol levels (values between the 75th and 90th percentiles) should be treated intensively by dietary means, especially if additional risk factors are present.

These two recommendations define a large population (25 percent of all adult Americans) for dietary intervention. The potential impact on clinical practice is considerable. Thus there is a pressing need to develop and refine processes through which health professionals can begin to implement these recommendations.

Medical school curricula in the past have included little emphasis on nutrition. Some efforts at a limited number of schools are overcoming this problem, but the majority of physicians who participated in the 1983 NHLBI Survey expressed considerable reservation about their ability to achieve and maintain changes in food habits by patients and families.

Medical school curricula in the past have included little emphasis on nutrition. Some efforts at a limited number of schools are overcoming this problem, but the majority of physicians who participated in the 1983 NHLBI Survey expressed considerable reservation about their ability to achieve and maintain changes in food habits by patients and families.

Research is needed to determine effective ways in which physicians can play an active role in improving nutrition counseling for patients. The purpose of this Announcement is to stimulate and encourage the cooperative effort of medical, nutritional and behavioral science investigators in submitting research grant applications to develop and evaluate innovative methods for the incorporation of effective nutrition counseling in physicians' practices.

A wide diversity of experimental designs of intervention strategies would be appropriate. Quantitative evaluation of a patient's blood cholesterol level change which is clearly attributable to application of an independent variable by physicians and/or others in practice settings, might be an outcome measure common to several designs.

Representative practice situations and patients are desirable so that results can be generalized to other physicians and other patient populations. Although cholesterol control in some patients requires pharmacologic intervention, the focus of the present Announcement is on dietary treatment as the means of reducing elevated blood cholesterol.

Examples of interventions might include training of physicians to participate in nutrition counseling efforts, training of practice site personnel for nutrition counseling, influencing third party payers to incorporate cholesterol-reducing nutrition counseling as part of their reimbursable charges, and innovative strategies for referral of patients to other health professionals or appropriate health care organizations for counseling individually or in groups. These strategies are meant to be exemplary and are not all-inclusive. Investigator innovation is strongly encouraged.

It is suggested that applicants address the following areas in their grant application: significance of the proposed research to cardiovascular health; scientific basis for the proposed research design and strategy; the specific hypotheses to be tested; research design to be implemented; sample size calculations needed for statistical significance; procedures for sample selection; a detailed description of the independent variable to be applied; detail concerning the measurement of blood cholesterol and any other dependent variables to be utilized; and the approaches for data management and data analysis.

It is anticipated that successful respondents to this announcement may be invited to meet annually to discuss protocols and to compare results with the intent of enhancing the prospects of finding effective means through which physicians in a practice setting can reduce elevated blood cholesterol levels of their patients. Budgets should include an annual meeting in Bethesda for 1 or 2 persons.

The above topics are intended to provide examples only and do not preclude the submission of applications involving other research approaches to the issues under consideration.

Application Submission and Review

Application receipt dates for new applications are the regular application receipt dates of February 1, June 1, and October 1. The earliest possible award date is
approximately ten months after the receipt date. Applicants should use the regular research grant application PHS Form 398, which is available at most institutional business offices or from the Division of Research Grants (DRG), NIH.

To identify responses to this announcement, check "yes" and put "Physicians' Role in Lowering Elevated Lipids by Diet" under item 2 of page 1 of those grant applications relating to the topics identified herein. The completed application should be mailed to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20892

The DRG will assign applications for review according to the NIH process for regular research grant applications. Additional information may be obtained by contacting:

Albert W. Sparrow, M.D., M.P.H.
Marilyn Farrand, R.D.
Prevention and Demonstration Research Branch
Division of Epidemiology and Clinical Applications
National Heart, Lung, and Blood Institute
National Institutes of Health
Federal Building, Room 6C05
7550 Wisconsin Avenue
Bethesda, Maryland 20892
Telephone: (301) 496-2465

This program is described in the Catalog of Federal Domestic Assistance No. 13.837, Heart and Vascular Disease Research. Awards will be made 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 42 CFR Part 52 and 45 CFR part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372, or to Health Systems Agency Review.

ERRATUM

SMALL GRANTS ON SOMATIC CELL TRANSFER OF GENES ASSOCIATED WITH SPECIFIC METABOLIC AND ENDOCRINE DISEASES

P.T. 34; K.W. 0715135, 1002008, 1002019, 1002027, 1003002, 0755040, 0760015

National Institute of Diabetes and Digestive and Kidney Diseases

Application Receipt Date: March 2, 1987

The Program Announcement, Vol. 15, No. 28 December 5, 1986 issue of the NIH Guide for Grants and Contracts is incorrect. The correct title should be "Small Grants on Somatic Cell Transfer of Genes Associated with Specific Metabolic and Endocrine Diseases."