

# NIH GUIDE

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**U.S. DEPARTMENT OF HEALTH  
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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. 18, No. 19  
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DATED ANNOUNCEMENTS (RFPs AND RFAs)

SEER/SURVEILLANCE QUALITY CONTROL UNIT

RFP AVAILABLE: NCI-CN-95124-41

P.T. 34; K.W. 0715035, 0755018

National Cancer Institute

The National Cancer Institute will issue RFP No. NCI-CN-95124-41 upon request to the address shown below on or about June 5, 1989, and proposals will be due approximately July 20, 1989.

The National Cancer Institute, Division of Cancer Prevention and Control, Surveillance Program, is interested in soliciting proposals from organizations for maintaining a quality control unit (QCU) for the surveillance program. The purpose of the QCU is to assess and insure the completeness, accuracy and timeliness of data that are available to the NCI and are used to measure the progress of cancer control. A secondary purpose of the QCU is to reduce the variability in procedures and interpretations of data collection and abstraction conventions by individuals responsible for collecting and managing cancer surveillance information through education and communications. A third purpose of the QCU is to provide a research and evaluation component focused on assessment of the quality of surveillance data and the efficiency of existing surveillance systems to assure that they continue to serve the NCI program needs. Thus, the QCU makes a significant contribution to the National Cancer Program.

This RFP is for recompetition of an ongoing contract with the University of California at San Francisco. The National Cancer Institute expects to make one award.

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

Mrs. Susan K. Hoffman, Contract Specialist  
National Institutes of Health  
National Cancer Institute  
Research Contracts Branch, PCCS  
Executive Plaza South, Room 635  
9000 Rockville Pike  
Bethesda, Maryland 20892  
Telephone: (301) 496-8603

LARGE-SCALE AUTOMATED DNA SEQUENCING OF NEUROTRANSMITTER RECEPTOR GENES

RFP AVAILABLE: NIH-NINDS-89-10

P.T. 34; K.W. 0760050, 0760075, 0755045

National Institute of Neurological Disorders and Stroke

The National Institute of Neurological Disorders and Stroke has a new requirement which involves research to improve and provide large-scale DNA template production applicable to large-scale automated DNA sequence analysis.

The Contractor shall be required to work from established protocols to 1) provide single-stranded DNA templates to the Government and 2) improve upon the methods used to produce these templates. In most cases this shall include restriction endonuclease digest analysis of DNA fragments from lambda or cosmid clones and the use of the resulting information to subclone fragments of the cloned insert DNA into phagemid or plasmid vectors. The next step shall be the production of ordered, unidirectional deletions of DNA fragments from phagemids containing cloned DNA using exonuclease III and the analysis of these deleted subclones. The final step shall be the production of single-stranded DNA templates from phagemids or plasmids for use in automated DNA sequencing. The Contractor may be required to carry out alternate procedures which shall be either subsets of the above procedures or closely related procedures.

The Contractor shall be required to develop new procedures to accomplish the goals achieved by carrying out the procedures above or develop variations of the above procedures that allow more rapid sample preparation, greater number of samples to be processed simultaneously, and less variation in experimental results. An example of an improvement that the Contractor may perfect is the use of polymerase chain reaction to prepare single-stranded template DNA. To

accomplish these goals, offerors shall have expertise and experience in the areas of microbiology, molecular biology and nucleic acids biochemistry.

It is anticipated that one contract award will be made under this RFP, for a three-year period.

RFP No. NIH-NINDS-89-10 will be issued on or about June 1, 1989, with a tentative date for receipt of proposals set at August 1, 1989.

To receive a copy of the RFP, please submit a written request and two self-addressed mailing labels to the following address.

All responsible sources may submit a proposal which shall be considered by the Government.

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

Attn: RFP-NINDS-89-10

### DIABETES CENTERS

RFA AVAILABLE: 89-DK-09

P.T. 04; K.W. 0715075, 0785050, 0710030

National Institute of Diabetes and Digestive and Kidney Diseases

Application Receipt Date: November 20, 1989

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) invites applications for a Center grant to be awarded in Fiscal Year 1991. NIDDK anticipates the competitive award of one Diabetes Endocrinology Research Center (DERC) in Fiscal Year 1991.

### BACKGROUND

The NIDDK-supported DERCs are part of an integrated program of diabetes-related research support provided by NIDDK. These centers have provided a focus for increasing collaboration and cost effectiveness among groups of successful investigators at institutions with established comprehensive diabetes research bases.

### OBJECTIVES AND SCOPE

The objectives of the DERCs are to bring together investigators from relevant disciplines in a manner which will enhance and extend the effectiveness of research related to diabetes and its complications. A diabetes center must be an identifiable unit within a single university medical center or a consortium of cooperating institutions, including an affiliated university. The overall goal of the DERC is to bring together on a cooperative basis, clinical and basic science investigators in a manner which will enrich the effectiveness of diabetes research. An existing program of excellence in biomedical research in the area of diabetes and related metabolic and endocrine disorders is required. This research should be in the form of NIH-funded research projects, program projects, or other peer-reviewed research that is in existence at the time of submission of a center application. Close cooperation, communication, and collaboration among all involved personnel of all professional disciplines are ultimate objectives. Applicants should consult with NIDDK staff concerning plans for the development of the center.

The DERCs are based on the core concept. Cores are defined as shared resources that enhance productivity or in other ways benefit a group of investigators working in diabetes or diabetes-related areas to accomplish the stated goals of the center. Two other types of activities may also be supported with center funding - a pilot and feasibility program and an enrichment program. The pilot and feasibility program provides modest support for new initiatives or feasibility research studies. This program is directed at new or established investigators in other research disciplines where their expertise may be applied to diabetes research. The center grant may also include limited funds for program enrichment such as seminars, visiting scientists, consultants, workshops, etc.

## MECHANISM OF SUPPORT

NIDDK expects to award one DERC Grant in Fiscal Year 1991 on a competitive basis. The receipt of one competitive continuation application is anticipated, which will compete for the award along with other applications received in response to this announcement. Foreign institutions are not eligible to apply. The anticipated award will be for five years and is contingent upon the availability of appropriated funds. The RFA (general description and Guidelines for the DERC) and consultation may be obtained from:

Dr. Sanford A. Garfield  
Diabetes Centers Program Director  
Division of Diabetes, Endocrinology, and Metabolic Diseases  
Westwood Building, Room 626  
National Institute of Diabetes and Digestive and Kidney Diseases  
Bethesda, Maryland 20892  
Telephone: (301) 496-7418

## REVIEW PROCEDURES

Applications for a DERC grant will be evaluated in national competition by the NIH grant peer review process. Applications will be reviewed initially by a special review committee convened by the NIDDK and subsequently by the National Diabetes and Digestive and Kidney Diseases Advisory Council.

## METHOD OF APPLYING

Potential applicants are urged to submit a letter of intent regarding their application. The letter of intent is nonbinding and is not a precondition for an award. The letter of intent should include the name(s) of the principal investigator and principal collaborators, descriptive titles of the core facilities and pilot/feasibility projects, and the organization(s) involved.

Applications must be submitted using PHS Form 398 (Rev. 10/88). The RFA label contained in the application kit must be affixed to the bottom of the face page of the original copy of the application. Failure to use this label could result in delayed processing and review of your application.

Mail the completed application (original and four copies) to:

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

Simultaneously submit two copies to Dr. Sanford A. Garfield at the address noted above.

The special single receipt date for submissions in response to this announcement is November 20, 1989, with earliest funding December 1, 1991.

## MINORITY-BASED COMMUNITY CLINICAL ONCOLOGY PROGRAM

RFA AVAILABLE: 89-CA-06

P.T. 34, FF; K.W. 0785140, 0785035, 0404004, 0795003

National Cancer Institute

Letter of Intent Receipt Date: July 14, 1989  
Application Receipt Date: October 13, 1989

The Division of Cancer Prevention and Control (DCPC), National Cancer Institute (NCI), is interested in establishing a cancer control effort, which is designed to link physicians involved in the care of minority cancer patients to the NCI clinical trials program, and to provide minority cancer patients/subjects with state-of-the-art treatment and cancer control research opportunities. DCPC invites applications from domestic institutions with greater than 50 percent of new cancer patients from minority populations for cooperative agreements in response to this Minority-Based Community Clinical Oncology Program (Minority-Based CCOP) Request for Applications (RFA).

## BACKGROUND INFORMATION

Overall, survival rates from cancer in minority populations are less than in whites. For example, data from the Surveillance, Epidemiology, and End Results (SEER) Program, NCI, show that the five-year relative survival rate (1975-1984) for all cancer sites in blacks is 39.6 percent compared to 51.3 percent for whites. Site-specific survival rates of black patients with breast, rectal, corpus uteri, and bladder cancers are lower than those for whites by 12, 12, 30, and 22 percents, respectively. In addition to poorer survival outcomes, cancer incidence and mortality rates for selected cancer sites in minority populations are higher compared to whites.

One way to develop and implement effective treatment and cancer control strategies in minority populations, and thereby reduce disparities in cancer incidence, morbidity, and survival rates between whites and minority populations, is to provide broader access to clinical research and greater involvement of minority populations in the clinical trials process. In general, there is limited participation in clinical trials research by black, Hispanic, Asian-American, Native-American and other minority cancer patients. A major factor influencing participation in clinical research by minority patients is access to the clinical trials process.

The Community Clinical Oncology Program (CCOP), which was first initiated in 1983, has proven to be a successful model for bringing the benefits of clinical research to cancer patients in their communities by providing support for community physicians to enter patients on treatment and cancer control research protocols. During the first phase of CCOP, a patient log record-keeping system on all new cancer patients seen by a participating physician, and for whom protocols were available, showed that 7 percent of CCOP patients were minorities. This compares to 13 percent minority representation in SEER and 20 percent in the general U.S. population. A similar ethnic profile of minority patient participation in clinical trials is seen during the second phase of the CCOP. Through the Minority-Based CCOP, DCPC aims to meet a need of minority cancer patients and individuals at risk for cancer by establishing a system of oncology programs for participation in clinical research trials through the NCI network.

## RESEARCH GOALS AND SCOPE

The Minority-Based CCOP initiative is designed to:

- o Bring the advantages of state-of-the-art treatment and cancer control research to minority individuals in their own communities by having practicing physicians and their patients/subjects participate in clinical treatment and cancer control research protocols;
- o provide a basis for involving a wider segment of the community in clinical research by increasing the involvement of primary health care providers and other specialists in treatment and cancer control research;
- o provide an operational base for extending cancer control, and reducing cancer incidence, morbidity, and mortality in minority populations by accelerating the transfer of newly developed cancer prevention, detection, treatment, and continuing care technology to widespread community application;
- o facilitate wider community participation in future treatment and cancer control research approved by NCI; and
- o examine selected issues in Minority-Based CCOP performance and evaluate its impact in the community.

## MECHANISM OF SUPPORT

Awards will be made as Cooperative Agreements. The Cooperative Agreement is an assistance mechanism involving cooperation by NCI staff as described in the RFA. Depending on individual costs and available funds, NCI anticipates making up to eight (8) awards under this RFA with total funding not expected to exceed \$1.2 million per year. Awards will be for three (3) years as described in the RFA.

**STAFF CONTACT**

Additional information and copies of the RFA may be obtained from:

Carrie P. Hunter, M.D.  
Program Director, CCOP, CORB, DCPC, NCI  
Executive Plaza North, Room 300-G  
Bethesda, Maryland 20892  
Telephone: (301) 496-8541

**NATIONAL COOPERATIVE VACCINE DEVELOPMENT GROUPS FOR THE ACQUIRED IMMUNODEFICIENCY SYNDROME**

RFA AVAILABLE: 89-AI-16

P.T. 34; K.W. 0715008, 0740075, 1002045, 0760080, 1002008, 0710030

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: June 19, 1989  
Application Receipt Date: August 10, 1989

The National Institute of Allergy and Infectious Diseases (NIAID) announces the availability of an RFA for the funding of National Cooperative Vaccine Development Groups for the Acquired Immunodeficiency Syndrome (NCVDG). The RFA (available on request) invites applications aimed at the development of effective vaccines for the prevention of AIDS. Scientific approaches to the development of effective AIDS vaccines appropriate to the RFA may range from research on whole virus vaccines, through the production of preparations with recombinant DNA techniques and synthetic approaches, to the use of viral vectors to deliver antigenic materials. Applications directed towards vaccine development for AIDS-associated opportunistic infections are not invited. Otherwise, scientific approaches to the development of effective vaccines appropriate to the RFA are broad and limited only by the creativity and ability of the applying group to exploit leads from basic studies in virology, molecular biology, and immunology.

Each NCVDG will be assembled by the Principal Investigator to form a multidisciplinary consortium representing the various skills needed to successfully design and evaluate vaccine entities and strategies for the prevention of AIDS. Inasmuch as it is unlikely that all of the outstanding talents required to exploit fundamental leads from various scientific disciplines will be found in a single institution, each Group is envisioned as being multi-institutional as well. Thus each NCVDG will be assembled by the Principal Investigator and may consist of a number of Laboratory Projects representing the scientific disciplines required to attain the Group's goal and objectives. The various Laboratory Projects, including that of the Principal Investigator, may be mobilized from academic or research institutions, and industry. It is expected that the rationale for design of potential vaccines, the synthesis or production of specific candidates, and the models for evaluation will originate within the Group and be based on leads from their own and others' fundamental research.

Awards will be made as Cooperative Agreements. Assistance via a Cooperative Agreement differs from the research grant in that the Government component (in this instance, the NIAID) awarding the Cooperative Agreement anticipates substantial involvement during performance. The nature of NIAID staff participation is described in the RFA. However, the applying Group must define its objectives in accord with its own interests and perceptions of approaches to vaccines for AIDS prevention.

It is anticipated that 5 to 7 awards will be made, each averaging \$500,000 to \$750,000 in direct costs.

The proposed applicant institution will be responsible for the Group's application. Awards will be made to the applicant institution on behalf of the group as a whole and not to individual Laboratory Projects within the Group. The applicant institution will provide a Central Operations Office for the Group. The applicant institution will be responsible for the performance of the entire Group and will be accountable for the funds awarded. The participation of the Government through the NIAID extramural staff is aimed at facilitating a concerted effort by the Group. The interaction of academic and non-profit research institutions with commercial organizations and Government is expected to favor efficient development of AIDS vaccines and will facilitate their subsequent refinement and evaluation in clinical trials.

The RFA is available from:

Dr. Dale R. Spriggs  
NIAID, AIDS Program  
Vaccine Research and Development Branch  
6003 Executive Blvd., Room 234P  
Rockville, Maryland 20892  
Telephone: (301) 496-8200

MURINE IMMUNODEFICIENCY LENTIVIRUS MODEL FOR AIDS

RFA AVAILABLE: 89-AI-17

P.T. 34; K.W. 0715008, 0755020, 1002045, 0765033

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: July 14, 1989

Application Receipt Date: August 25, 1989

The National Institute of Allergy and Infectious Diseases (NIAID) announces the availability of an RFA for the development of a murine immunodeficiency lentivirus model for the acquired immunodeficiency syndrome (AIDS). The RFA (available on request) invites applications to develop a murine immunodeficiency lentivirus model for AIDS which would expedite studies of pathogenesis, and evaluation of potential therapies and vaccines. Applicants are encouraged to propose novel strategies for obtaining such a model with a rational approach for the identification, isolation, and molecular and biological characterization of naturally occurring murine lentiviruses. It will be important to address multiple alternatives since there will be no way to guarantee success of a single search strategy. Scientific and technical merit of the zoology/ecology collaborators or contractors will be critical in the evaluation of the applications.

Mouse strains and viruses developed in this research must be made available to the AIDS Research and Reference Reagent Program for world-wide distribution to qualified researchers.

Awards will be made as individual research (R01) grants.

Investigators from any institution, foreign or domestic, are eligible to apply for this funding.

This RFA is available from:

Dr. Linda M. Muul  
Pathogenesis Branch  
NIAID, AIDS Program  
6003 Executive Blvd., Room 214N  
Rockville, Maryland 20892  
Telephone: (301) 496-8378

ONGOING PROGRAM ANNOUNCEMENTS

MOLECULAR MECHANISMS OF CELL DEATH DURING AGING

P.T. 34; K.W. 0710010, 1002004, 0765010, 0765033, 0790005, 0705055

National Institute on Aging

INTRODUCTION

Cell death in multicellular organisms takes place in a variety of circumstances. For example, the death of certain cells may occur as part of a developmental program; in connection with organ involution or regression as in the adult thymus; during cell renewal processes where specialized, differentiated, non-dividing effete cells such as granulocytes and erythrocytes are replaced by newly-formed cells; as a consequence of toxic or harmful environmental conditions; when potentially harmful cells such as neoplastic or virus-infected cells are targeted for destruction by surveillance systems; or because of senescence of the cells themselves or the host organism. In an entity as complex as the cell there are processes such as nucleic acid and protein synthesis, transport of ions, nutrients and other metabolites across membranes, and structures such as membranes and cytoskeleton whose function and integrity must be faithfully maintained

because they are essential for cell viability. Defense mechanisms such as DNA repair and heat shock proteins have evolved which allow the cell to repair, or prevent injury to vital molecules when faced with stressful or potentially harmful environmental conditions.

In some cases, the molecular events that lead to cell death are reasonably well known. For example, in complement-mediated lysis the membrane attack complex causes the formation of channels in the target cell's membrane, which therefore becomes leaky and no longer functions as a permeability barrier. In other cases, however, the critical event(s) in cell death is not known; nor is it known which molecular lesions are irreversible and which can be repaired or prevented by the cell's protective mechanisms. Questions such as why and how senescent cells die are relevant to understanding the aging process in complex organisms. Furthermore, the role of cell death in age-related diseases and degenerative conditions is unknown. This question is particularly important in neural tissue, where cell regeneration is either non-existent or at best quite limited.

#### SPECIFIC OBJECTIVES

The National Institute on Aging (NIA) wishes to encourage applications for research projects investigating the molecular events that may lead to, or accompany, cell death during aging. While the study of cell death in any circumstance may be appropriate under this program, its relevance to the aging process must be explicit. The following questions illustrate the type of research that this program announcement intends to foster.

#### BASIC MECHANISMS OF CELL DEATH

- o What intracellular conditions predispose the cells to irreversible damage, e.g., elevation of calcium ion concentration, oxidizing agents, etc.? By what mechanisms?
- o What are the critical sites or molecules which, when damaged, result in cell death if not repaired?
- o Which potentially lethal lesions can be repaired by the cell, and which lesions are irreversible?
- o What are the cellular mechanisms that prevent or reverse potentially lethal lesions, and how do they work? Are these defense mechanisms impaired in senescence?
- o Do senescent cells die because they are programmed to die, do they die because of damage resulting from the accumulation of damage inflicted by a hostile environment, or both?
- o What tissues are most sensitive to loss of function due to cell death?
- o Although cells may die for a variety of reasons, are there common steps in the pathways leading to cell death?
- o What naturally-occurring molecules are toxic to cells leading to cell death, and how do they function?

#### CELL DEATH IN AGE-ASSOCIATED DISEASES AND DEGENERATIVE CONDITIONS

The role of cell death in the pathogenesis of several age-related diseases and degenerative conditions is an intriguing and largely unexplored possibility. Explorations of this possibility are limited by technical difficulties in determining the extent of cell death in many tissues. Important avenues for research thus include the following:

- o Testing new techniques to determine the rate and extent of in vivo cell loss and/or cell death in tissues susceptible to age-related diseases (e.g. articular cartilage, bone, cardiac muscle, vascular endothelium; cell loss in the CNS is discussed in the next section).
- o Studies to determine the possible role of cell loss and/or cell death in specific age-associated diseases and conditions. Examples include the possible role of chondrocyte loss in osteoarthritis, loss of osteoblasts or osteoblast progenitor cells in osteoporosis, loss of striated muscle fibers in age-associated degenerative muscular conditions, loss of parietal cells in atrophic gastritis, cell loss associated with disorders of gait and balance, and cell loss in the sinoatrial node in age-associated arrhythmias.

- o Studies to determine the role of cell in age-associated changes in renal, pulmonary, muscular, and other physiologic functions.

#### CELL DEATH IN THE AGING NERVOUS SYSTEM

One of the most critical issues in the neurobiology of aging concerns the specific mechanisms of selective cell loss in the brain. Neuronal death is especially critical due to the non-replicative nature of most cells in the central nervous system; CNS structural change and/or loss of neurons is the hallmark of many of the age-associated disorders of the brain such as Alzheimer's disease. The inability of the CNS to replace lost neurons and the complex structure of the brain raise a number of unique research questions.

- o Is there significant cell loss associated with normal healthy aging of the brain as there is during early development or is it only as a result of incipient disease?
- o Do the mechanisms of cell loss associated with normal brain aging differ from those associated with diseases of the CNS?
- o What accounts for the selective vulnerability of specific neurons in various diseases?
- o What is the role of trophic factors in the survival and death of neurons in the aging CNS?
- o Is there increased vulnerability to endogenous and environmental toxins in the aging CNS and if so what is the nature of this vulnerability?
- o Under what conditions do excitatory amino acid neurotransmitters become excitotoxic?
- o What are the molecular mechanisms by which toxins trigger cell death in the aging CNS?
- o What role does neuronal connectivity and activity play in the survival or death of neurons in the adult and aging CNS?
- o What is the role of altered gene expression in neuronal cell death?
- o How does the aging CNS compensate for cell loss?
- o What roles do vascular and glial elements play in neuronal survival and death; are changes in the transport mechanisms for glucose, oxygen and other essential elements involved?
- o Are the quantitative methods used for estimating cell loss in the aging nervous system accurate or are new methods needed?
- o What role do changes in neuroendocrine and immune factors play in neuronal cell death in the aging nervous system?
- o What is the role of stress and glucocorticoids in neuronal cell death?
- o Are intracellular metabolic changes such as modifications in mitochondrial oxidative metabolism primary or secondary causes of neuronal cell death?
- o How do membrane changes affect inter- and intracellular signal transduction during normal aging and diseases of aging?
- o How do changes in homeostatic mechanisms that regulate cytosol calcium concentration lead to cell death?

Qualified scientists who plan to investigate these issues, or other issues of similar nature, are invited to apply for research grants under this program.

#### APPLICATION AND REVIEW PROCEDURES

The primary mechanisms for support of this program are:

- o Research grant (R01)
- o Program Project Award (P01)

- o First Independent Research Support and Transition (FIRST) Award (R29)
- o Career grants, which include:  
     Research career development award (K04)  
     Clinical investigator award (K08)
- o Training grants (T32)
- o Fellowships (F32, F33)

Research project grant (R01 and R29) applications, fellowships (F32, F33) and research career development awards (K04) will be reviewed for scientific and technical merit by an appropriate study section in the Division of Research Grants. All other applications will be reviewed by an appropriate peer review group. Secondary review will be by an appropriate National Advisory Council.

There are no set-aside funds for these applications. Applications compete on the basis of scientific merit with all other applications. The review criteria are the traditional ones underlying scientific merit.

Researchers who are considering making an application in response to this announcement are welcome to discuss their project, and the range of grant mechanisms available, with NIA staff in advance of formal submission. This can be done either through a telephone conversation or a brief letter giving the descriptive title of the proposed project and identifying the principal investigator and, when known, other key participants. Applications related to the health of women and minorities are particularly encouraged.

Applicants should use the regular research project and program project grant application form 398 (Rev. 9/86) for R01, R29, P01, T32, K04 and K08 applications, and form 416-1 (revised 7/88) for F32 and F33 applications. These are available at the applicant's institution or from:

Office of Grants Inquiries  
 Division of Research Grants  
 Westwood Building, Room 449  
 National Institutes of Health  
 Bethesda, Maryland 20892  
 Telephone: (301) 496-7441

To expedite the application's routing within NIH, please check "Yes" on item 2 of the face sheet of the application indicating that your proposal is in response to this announcement and print "Mechanisms of Cell Death." In assigning applications to NIA or other Institutes, accepted referral guidelines will be followed.

Mail the completed application (with 6 copies) to:

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

Receipt dates for Research Grant, Program Project Grant, Research Career Development Award and First Award applications are February 1, June 1, and October 1; those for Institutional Training Grant and Fellowship applications are January 10, May 10, and September 10.

Depending on your particular research interests, correspondence and inquiries should be directed to:

Basic mechanisms of cell death

Huber Warner, Ph.D.  
 Molecular Biology Program Administrator  
 Biomedical Research and Clinical Medicine  
 Building 31, Room 5C21  
 National Institute on Aging  
 Bethesda, Maryland 20892  
 Telephone: (301) 496-6402

## Role of cell death in age-associated diseases

Evan Hadley, M.D.  
Chief, Geriatrics Branch  
Biomedical Research and Clinical Medicine  
Building 31, Room 5C27  
Bethesda, Maryland 20892  
Telephone: (301) 496-6761

## Cell death in the aging nervous system

Creighton Phelps, Ph.D.  
Neuroplasticity Program Administrator  
Neuroscience and Neuropsychology of Aging  
Building 31, Room 5C32  
National Institute on Aging  
Bethesda, Maryland 20892  
Telephone: (301) 496-9350

## THE AGING OF RETARDED ADULTS

P.T. 34; K.W. 0710010, 0715130

National Institute on Aging

### INTRODUCTION

The National Institute on Aging (NIA) seeks research applications focused on retarded adults as they grow old. This announcement responds to U.S. Senate Appropriations Report language (Rpt. 100-399) for Fiscal Year 1989 that the NIA should consider conducting studies in the area of social gerontological aspects of aging and mental retardation, as well as the biological and psychological aspects of the aging process among individuals with mental retardation and related conditions.

The announcement is part of the broad program of the Institute which was established by law for the "conduct and support of biomedical, social, and behavioral research and training related to the aging process and the diseases and other special problems and needs of the aged." It supplements NIA's broad announcement on HEALTH AND EFFECTIVE FUNCTIONING IN THE MIDDLE AND LATER YEARS. (See NIH GUIDE FOR GRANTS AND CONTRACTS, VOL. 12, NO. 6, JUNE 17, 1983.) It is issued by the Behavioral and Social Research Program in collaboration with the other NIA programs on Neuroscience and Neuropsychology of Aging and on Biomedical Research and Clinical Medicine.

### BACKGROUND

Little is known about retarded adults as they grow older. The problem has become acute as the size of the older retarded population has increased, in part as a result of improved intervention and care. In future years the problem will become still more severe as the aging of the baby boom cohort increases the number of retarded adults whose parents, or other primary caretakers, are themselves old. Research on these adults and their caretakers is incomplete in several ways. It has been hampered by changing definitions of retardation. Moreover, it has relied too heavily on cross-sectional research, a strategy that provides useful data but that compounds the interpretative difficulties brought on by the different definitions of retardation and different medical and social conditions prevailing at different time periods. Useful background reading can be found in Janicki, M.P. & Wisniewski, H.M. (Eds.) (1985). *Aging and Developmental Disabilities*. Baltimore, Paul H. Brookes, and in Seltzer, M.M. & Krauss, M.W. (1987). *Aging and Mental Retardation: Extending the Continuum*. Washington: American Association on Mental Retardation.

### SPECIFIC OBJECTIVES

Applications are sought that examine the nature and needs of the middle-aged and older retarded population. Sample topics are described below. However, applications on other related topics are also encouraged.

#### 1. Demographic and Epidemiological Research

Data on the characteristics of this population have been plagued by problems created by the changing definition of retardation and by the suspected existence of many retarded adults, living with the help of family members, who are unknown to service agencies. These problems make forecasting the size and future composition of this population hazardous. New analyses of existing

data bases are needed; in addition, new data are needed that use a consistent definition of retardation and that incorporate effective procedures for sampling retarded adults unknown to service agencies.

Illustrative research topics include:

- o analyses of chronic diseases and co-morbidities
- o research that yields projections of life expectancy for retarded adults, with and without surviving parents
- o adaptations of such instruments as Activities of Daily Living and Instrumental Activities of Daily Living questionnaires; assessments of projections of functional ability based on these measures
- o demography of surviving older people with developmental disabilities other than retardation

## 2. Adaptive Functioning in Older Retarded Adults

Existing standardized tests of intellectual functioning often are inadequate to assess people who are retarded. The nature of particular syndromes, experience, and the existence of informal support networks allow considerable independence of function for which these tests cannot compensate. Such tests are also unlikely to capture changes in competence as people age, as they cope with illness, or as informal supports change. Approaches are needed, therefore, that test older retarded adults in everyday tasks and relate their competence to psychomotor and to cognitive abilities, as well as to existing social and physical aids. For mildly retarded adults who live independently, little is known about how job history, friendships, and social activities alter adaptive functioning as these adults age. Research is needed to track such patterns of activity and to understand how changes in activities affect these retarded adults.

Some illustrative topics include:

- o To what extent do differences in functioning among different-aged older retarded adults reflect the effects of experience and of setting versus the effects of age?
- o What accounts for the wide variation in adaptive functioning achieved by adults with similar degrees of retardation? Do these individual differences remain stable in the later adult years?
- o Do older retarded men and women differ substantially in patterns of development and decline?

## 3. Social Interactions and Family Support

Little is known about how the aging of parents and other caregivers of retarded adults affects both the parents themselves and also the retarded adult. Among the likely events in a middle-aged and older retarded individual's life are: transition from parent as caregiver to some other source of care; death of a parent; and change in residence with resulting change in social support and social relations. Research is needed to explore the effects of such changes on these adults and their caregivers. Among mildly retarded individuals, the impact of such life events as death of a spouse or retirement needs particular study. Do the effects of these transitions on mildly retarded adults mirror their effects on the general population?

Examples of research include:

- o What are the factors that predict an orderly and smooth transition from parental care to some other support system?
- o Do changes in the characteristics of the family support system predict more accurately the need for social services in later adulthood than do changes in the characteristics of the retarded adult?
- o How do retarded adults' feelings of control, perceptions of changes in competence, and overall assessment of quality of life change as they incur transitions in later life?
- o What is the role of siblings in providing care and social support for older retarded adults?

- o What beliefs do other adults hold about older retarded people? How do these beliefs affect, or how are they affected by, interactions with older retarded adults?

#### 4. Intervention Strategies

Research is needed on interventions to increase the skills mastered by older retarded adults, to foster maintenance of skills, and to decrease dependence on institutional or organizational support. Behavioral interventions (such as training) and environmental interventions (such as altering the accessibility of staff support) might be evaluated for their ability to improve functioning. Technological interventions (e.g., equipment to aid performance or to improve health) and pharmacological interventions can also be investigated to determine whether they improve independent functioning and the quality of life of both older retarded adults and their caretakers.

Sample topics include:

- o Can older retarded adults who live at home learn to manage some of the tasks once assumed by aging parents?
- o Can the competencies displayed by institutionalized retarded adults be enhanced by changes in setting or by changes in patterns of structured interaction?
- o How can the burden of care of aging parents of retarded adults be reduced by technological interventions?
- o How do older and younger retarded adults with the same etiology vary in responsiveness to particular pharmacological and behavioral interventions?

#### 5. Service and Care Research

Research is needed on, for example, the problems of matching service and care to aging retarded adults; or, the economics of different service and care solutions. Both the kinds of care necessary (e.g., respite care for aging caretakers, part-time institutional care) and the quality of care, as assessed by its effect on retarded adults and older familial caretakers, need to be addressed.

Research is also needed on what services older retarded adults have used in the past. Such research can identify the most frequent causes of service use in early and later adulthood and can identify consequences of the use of services on particular individuals.

Some possible research questions include:

- o What are the advantages and disadvantages of age integrated versus age separated, and ability integrated versus ability separated facilities?
- o How does respite care affect the quality of relations between older retarded adults and their family caretakers?
- o How do the economics of different care solutions (e.g., institutional, home support) vary with changing numbers and geographical distribution of the aging retarded population?
- o What factors predict successful entry of older retarded adults into recreation programs designed for seniors?

#### METHODOLOGY

The topics covered by this announcement are diverse and require varied methodological approaches. Nevertheless, research with a cohort-longitudinal component is especially sought. Most current research on older retarded adults is cross-sectional. Adults born in one time period (with particular definitional criteria and institutional practices) are compared against other adults born at other times with very different practices. Studies could trace different cohorts of retarded adults for an extended time. Only by such investigation can intra-individual changes in functioning be differentiated from differences between people of different ages that might reflect cultural change rather than true age-related change.

NIA also urges applicants to give added attention to the inclusion of women, as well as men, and minorities in study populations. Investigators are

reminded that merely including quotas of such participants in a given study is insufficient to guarantee generalization of results.

#### APPLICATION AND REVIEW PROCEDURES

Research project grant (R01, R29) applications, individual fellowships (F32, F33), and research career development awards (K04) will be reviewed for scientific and technical merit by an appropriate study section in the Division of Research Grants. Other applications will be reviewed by an appropriate institute review group. Secondary review will be by the National Advisory Council of the relevant Institute.

Applications assigned to NIA compete on the basis of scientific merit with all other applications assigned to the Institute. The review criteria are the traditional considerations underlying scientific merit. Researchers considering an application in response to this announcement are encouraged to discuss their project, and the range of grant mechanisms available, with NIA staff prior to formal submission.

Applicants should use the regular research project grant application form (PHS 398 Rev. 10/88) for R01, R29, P01, T32 and K04 applications, and the PHS 416-1 (Rev. 7/88) form for F32 and F33 applications. These forms are available at the applicant's institutional Application Control Office or from the Office of Grants Inquiries, Division of Research grants, NIH (see address below). In order to expedite the application form's routing within NIH, please check "yes" on item number 2 on the face sheet of the application indicating that your proposal is in response to this announcement and print THE AGING OF RETARDED ADULTS.

Mail the completed application (with 6 copies) to:

Division of Research Grants  
National Institutes of Health  
Westwood Building, Room 240  
Bethesda, Maryland 20892\*\*  
Telephone: (301) 496-7441

Receipt dates for the Research Project Grant, the Research Program Project Grant, Research Career Development Awards, and the First Independent Research Support and Transition Award applications are February 1, June 1, and October 1; those for the National Research Service Awards applications are January 10, May 10, and September 10.

Correspondence and inquiries (please indicate Aging of Retarded Adults in your inquiry) should be directed to staff at:

Dr. Robyn Barr  
Behavioral and Social Research  
National Institute on Aging  
Building 31C, Room 5C32  
Bethesda, Maryland 20892  
Telephone: (301) 496-3136

This program is described in the Catalog of Federal Domestic Assistance No. 13.866, Aging Research. 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 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to Health Systems Agency review.

\*\*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