# NIH GUIDE for GRANTS and CONTRACTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Vol. 11, No. 4, March 26, 1982


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(Continued)

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*The GUIDE is published at irregular intervals to announce scientific initiatives and to provide policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in grants and contracts activities administered by the National Institutes of Health.*

*Two types of supplements are published by the respective awarding units. Those printed on yellow paper concern contracts: solicitations of sources and announcement of availability of requests for proposals. Those printed on blue paper concern invitations for grant applications in well-defined scientific areas to accomplish specific program purposes.*

## NOTICE

Change in Receipt Dates for RFA-NCI-DRCCA-CCB-82-6

An announcement in the January 29, 1982 Guide for Grants and Contracts (Vol. 11, No. 2, pages 15-18) summarized a Request for Proposals (RFA) for cancer control units for defined population studies. Receipt dates for letters of intent and application deadline for that RFA have been changed from March 31, 1982 to April 30, 1982 (letter of intent) and from July 15, 1982 to August 15, 1982 for submission of applications. Applications will be reviewed by the National Cancer Advisory Board at its May, 1983 meeting, with start dates around July, 1983. Additional information and copies of the RFA may be obtained from:

Carlos E. Caban, Ph.D.
Program Director
Division of Centers, Resources
and Community Activities
National Cancer Institute
National Institutes of Health
Blair Building, Room 716B
8300 Coleville Road
Silver Spring, Maryland 20910

## NOTICE

The Program Announcement "Experimental Research Related to Mammographic Screening for Human Breast Cancer" was published in the NIH Guide to Grants and Contracts, Vol. 9, No. 2, pp. 33-35, January 25, 1980. The Breast Cancer Program of the National Cancer Institute no longer considers it necessary to provide special encouragement for grant applications for animal and tissue culture studies that will provide new and relevant information on problems related to mammographic screening for human breast cancer. Cancellation of this Program Announcement does not prevent an investigator from submitting a grant related to this topic through the regular DRG mechanism.

## SPECIAL EMPHASIS RESEARCH CAREER AWARD IN LABORATORY ANIMAL SCIENCE (SERCA)

## ANIMAL RESOURCES PROGRAM

## DIVISION OF RESEARCH RESOURCES

### I. INTRODUCTION

The Division of Research Resources announces a new Special Emphasis Research Career Award in Laboratory Animal Science. This special award is made to develop multidisciplinary veterinary researchers who will direct their research toward refining the use of laboratory animals in biomedical research, the study of significant laboratory animal disease problems occurring in vivarial settings, and the development of new animal models useful in solving biomedical research problems.

This award emphasizes indepth experience for the laboratory animal specialist in various fundamental and clinical scientific disciplines. In the initial phase, the awardee is expected to develop capabilities in fundamental, applied, and/or clinical research. In the final phase, the awardee is expected to undertake a multidisciplinary research program aimed at a better understanding of a laboratory animal disease problem or development or utilization of an animal model in the solving of a biomedical research problem. This award is not intended for established investigators.

### II. BACKGROUND

Laboratory animals are used in approximately 55 percent of the research projects supported by the National Institutes of Health. The SERCA is meant to stimulate the development of research on laboratory animal disease problems and the further application of these phenomena to the solving of human health research problems. Some of the opportunities available are the development of new models, the utilization of the laboratory animal diagnostic laboratories supported by DRR, and other biomedical resources, in identifying new animal models, in further defining these models, and utilization of several species which have similar diseases to develop composite models which may be useful in solving health problems.

### III. OBJECTIVES OF THE AWARD

The SERCA provides opportunities for a biomedical researcher trained in laboratory animal science who wishes to develop research expertise in the broad fundamental and clinical disciplines essential for a multidisciplinary approach to research opportunities in laboratory animal science and to the utilization of laboratory animal health disorders, to the solution of human health problems.

This award is intended to:

- Encourage qualified individuals at early stages of their scientific careers to develop research interest and skill in disciplines such as laboratory animal medicine, pathology, microbiology, genetics, biochemistry, and behavioral sciences.

- Provide support for individuals to pursue a program of research in the various fundamental and clinical research disciplines related to laboratory animal sciences and animal health problems in laboratory animals, or models for human disease which may be identified by practitioners and bench scientists working with human health research problems.

- Create a pool of highly qualified laboratory animal investigators with experience and skills in the clinical and basic science disciplines necessary to develop a laboratory animal model. These investigators should possess indepth experience in their research disciplines and a breadth of knowledge in related fields of interest.

## IV. PROVISIONS OF THE AWARD

The SERCA provides 5 years of support for a multidisciplinary approach to research investigation and development. Awards will be made on an annual basis, and will be contingent upon the continued availability of funds.

During the first three years of SERCA support, the awardee is expected to develop capabilities in fundamental, applied and/or clinical research related to the basic and clinical science aspects of laboratory animal science. These activities should be oriented around the initiation of a specific research project(s). Exposure to multiple disciplines, such as physiology, biochemistry, genetics, immunology, pathology, microbiology, pharmacology, nutrition and epidemiology should be included in the candidate's plans presented in the original application. Investigators are encouraged to pursue these activities in more than a single laboratory at one institution. For this developmental phase, in addition to funds for salary and fringe benefits, up to $8,000 direct costs may be requested for research support (see section B.).

During the third year of SERCA support, an application must be submitted detailing plans for an extended research program for both years four and five of the award. The expanded research program, of the awardee's own design, must focus on the basic and clinical science aspect of laboratory animal science. In addition to plans for an expanded research program, this application should summarize progress made during the first 3 years of SERCA support and should include a detailed budget for research support not to exceed $15,000 per year direct costs (in addition to the awardee's salary and fringe benefits) for the fourth and fifth years of the award. The research support budget awarded for the last two years will be determined

following scientific review by DRR staff and Council. If the research support award is not favorably recommended, the continuation of salary support will be re-evaluated.

As detailed above, the SERCA grant is made annually to the awardee's parent institution for each budget period. Costs allowed may include:

A. Awardee's Salary

Up to a maximum of $30,000 from SERCA funds for salary support may be requested. In addition, fringe benefits will be provided and institutional supplementation is permitted.

B. Research Support (limited to $8,000/year for years 01 through 03 and $15,000 for years 04 and 05;

Equipment: Specialized research equipment essential to the proposed program may be requested. However, available facilities should include most of the necessary equipment;

Supplies: Consumable supplies essential to the proposed program may be requested;

Tuition for training courses: If essential to the awardee's individual training program, funds for tuition may be requested.

Other Costs: In addition, funds may also be requested for technical assistance, consultant costs, domestic travel, publication costs and other appropriate expenses which are essential to the proposed program.

C. Indirect Costs

Funds may be requested for the reimbursement of actual indirect costs at a rate of up to, but not to exceed, 8% of the total allowable direct costs of each award.

## V. CRITERIA FOR ELIGIBILITY

Candidates for a Special Emphasis Research Career Award in Laboratory Animal Science must:

1. Hold a D.V.M. degree.

2. Have a minimum of two years post-D.V.M. research experience which may include one year of clinical training in the sub-specialty of laboratory animal medicine or appropriate disciplinary training.

3. Be nominated by an institution on the basis of qualifications, interests, accomplishments, motivation and potential for a research career. Evidence of the commitment of the institution to the candidate's

research development must be provided. It is not essential for the applicant institution to commit itself in the application to eventual placement of the candidate on its permanent full-time faculty, but it is expected that institutions will choose the candidates with potential for appointment at that or similar institutions.

4. Plan, with an advisor who is a mature investigator in the field at the parent institution, a developmental and research program (which may involve travel to other institutions) in which the awardee will receive development and research experience in preparation for a future career of independent research. The candidate's proposed research projects during the first three years of the award must be described.

5. Agree to inform the DRR for a period of five years subsequent to completion of the award about academic status, publications, and grants or contracts relative to the focus of this award.

6. Candidates for an award must be citizens or noncitizen nationals of the United States or its possessions and territories or must have been lawfully admitted to the United States for permanent residence at the time of application.

## VI. APPLICATION

Applications must be submitted on form PHS-398, which is available at most grantee institutions, or may be obtained from the Division of Research Grants, NIH. Application receipt dates are June 1, October 1 and February 1.

Prospective applicants should contact the office listed below for supplemental instructions to be used in preparing the application, for information concerning peer review, and for inquiries related to applicant eligibility, appropriate areas of research emphasis, and SERCA program administration:

John E. Holman, D.V.M., Ph.D., Director
Laboratory Animal Sciences Program
Animal Resources Branch
Division of Research Resources
Building 31, Room 5B59
National Institutes of Health
Bethesda, Maryland 20205

Telephone: (301) 496-5175

## ANNOUNCEMENT

## SPECIAL EMPHASIS RESEARCH CAREER AWARD: DIABETES MELLITUS-OBSTETRICAL, PERINATAL, AND PEDIATRIC ASPECTS

**NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT**

**NATIONAL INSTITUTE OF ARTHRITIS, DIABETES, DIGESTIVE AND KIDNEY DISEASES**

Application Receipt Date: June 1 Annually

This is to announce the annual receipt date of June 1 for applications for the SERCA: Diabetes Mellitus - Obstetrical, Perinatal, and Pediatric Aspects. Applications received on or before June 1, 1982 should specify a project start date of July 1, 1983. The next receipt date will be June 1, 1983 for a possible start date of July 1, 1984.

The award is intended to:

- o encourage qualified individuals in the early stages of their post-graduate medical and scientific careers to develop research interests and skills in the obstetrical, perinatal, and pediatric aspects of diabetes mellitus;
- o provide support for individuals to pursue a program of research in various fundamental and clinical research disciplines related to diabetes mellitus during pregnancy and its associated neonatal morbidity and mortality; and
- o create a pool of highly qualified investigators with experience and skills in the obstetrical, perinatal, and pediatric aspects of diabetes mellitus for a future role in research, teaching, and clinical care.

The Special Emphasis Research Career Award provides the opportunity for an obstetrician or pediatrician with developing research interests to acquire experience and skill in the broad fundamental and clinical scientific disciplines essential for a multidisciplinary approach to the endocrinologic and metabolic aspects of diabetes mellitus in obstetrical, perinatal, and/or pediatric contexts. This SERCA emphasizes in-depth experience in several fundamental and clinical scientific disciplines which are not dependent upon a single laboratory or institution.

PROVISIONS OF THE AWARD

This nonrenewable award provides support for a five-year period of full-time research and related activities. The latter may include research development activities as well as involvement in patient care to the extent that it will strengthen research skills. The SERCA grant made to the awardee's parent institution provides up to $30,000 per year for full-time salary support plus fringe benefits. A maximum of $8,000 per year during the first three years and up to $20,000 per year during the last two years will be provided for necessary research costs including technical assistance, equipment, supplies, consultant costs, domestic travel, patient care cost, publication, and other costs.

Working closely with an advisor, the candidate is expected to develop capabilities in fundamental, applied, or clinical research in the metabolic and endocrinologic aspects of diabetes in gestational, perinatal, or pediatric contexts. These activities should be

design. Exposure to multiple disciplines, such as physiology, biochemistry, biophysics, pharmacology, nutrition and epidemiology should be included in the candidate's plans. Investigators are encouraged to pursue these activities in more than a single laboratory. At the completion of this five-year award, the individual should be in a position to compete in regular NIH research grant award programs.

ELIGIBILITY REQUIREMENTS

Candidates for the SERCA Award must: (1) hold an M.D. or equivalent professional degree (e.g., D.D.S., D.O., D.V.M., etc.); (2) have a minimum of three years post-M.D. experience, including one year of clinical training in obstetrics, pediatrics or endocrinology-metabolism, or two years post-M.D./Ph.D. experience or equivalent. M.D./Ph.D. applicants should possess significant experience in metabolism, endocrinology, obstetrics, pediatrics, physiology, biochemistry, pharmacology, or other relevant areas of interest, such as epidemiology; (3) be citizens or noncitizen nationals of the United States or its possessions or territories or must have been lawfully admitted to the U.S. for permanent residence at the time of application; (4) meet certain other eligibility requirements specified in the SERCA Program Guidelines (See "For Additional Information").

DEADLINE FOR RECEIPT OF APPLICATIONS

SERCA applications will be received once a year according to the following schedule:

| Application Date | Council Review | Start Date |
|---|---|---|
| June 1 | Jan/Feb* | July 1* |

* of the year following application receipt.

FOR ADDITIONAL INFORMATION

Prospective applicants are encouraged to review the SERCA Guidelines which detail eligibility requirements and application procedures. In addition, prior to preparing an application, individuals are strongly encouraged to discuss their potential eligibility as well as their areas of research interest with the Program Director listed below. Requests for copies of the SERCA Guidelines as well as questions related to eligibility, etc., should be directed to:

Maureen Harris, Ph.D., M.P.H.
Acting Director, Career Development Program
National Institute of Arthritis, Diabetes,
Digestive and Kidney Diseases, NIH
Westwood Building, Room 607
Bethesda, Maryland 20205

Telephone: (301) 496-7595

## ANNOUNCEMENT

## SPECIAL EMPHASIS RESEARCH CAREER AWARD: DIABETES MELLITUS - CARDIOVASCULAR, METABOLIC, AND ENDOCRINOLOGIC ASPECTS

**NATIONAL HEART, LUNG, AND BLOOD INSTITUTE**

**NATIONAL INSTITUTE OF ARTHRITIS, DIABETES, DIGESTIVE AND KIDNEY DISEASES**

Application Receipt Date: June 1 annually

This is to announce the regular annual receipt date of June 1 for applications for the SERCA: Diabetes Mellitus - Cardiovascular, Metabolic, and Endocrinologic Aspects. Applications received on or before June 1, 1982 should specify a project start date of July 1, 1983. The next receipt date will be June 1, 1983 for a possible start date of July 1, 1984.

The award is intended to:

- o encourage qualified individuals in the early stages of their post-graduate medical and scientific careers to develop research interests and skills in the metabolic, endocrinologic, and cardiovascular aspects of diabetes mellitus;

- o provide support for individuals to pursue a program of research in various fundamental and clinical research disciplines related to diabetes mellitus and its sequelae, at one or more domestic institutions which offer superior opportunities in these areas; and

- o create a pool of highly qualified investigators with experience and skills in the cardiovascular, metabolic, and endocrinologic aspects of diabetes mellitus for future roles in related areas of research.

The Special Emphasis Research Career Award (SERCA) provides the opportunity for an individual with developing research interests to acquire experience and skill in the broad fundamental and clinical scientific disciplines essential for a multidisciplinary approach to the study of the metabolic, endocrinologic, and cardiovascular aspects of diabetes mellitus. This award emphasizes in-depth experience in several fundamental and clinical scientific disciplines which are not necessarily dependent upon a single laboratory institution.

PROVISIONS OF THE AWARD

This non-renewable award provides support for a five-year period of full-time research and related activities. The latter may include research development activities as well as involvement in patient care to the extent that it will strengthen research skills. The SERCA grant made to the awardee's parent institution provides up to $30,000 per year full-time salary support plus fringe benefits. A maximum of $8,000 per year during the first three years and $20,000 per year during the last two years will be provided for necessary research costs including technical assistance, equipment, supplies, consultant costs, domestic travel, patient care costs, publication, and other costs.

While working closely with an advisor, the awardee is expected to develop capabilities in fundamental, applied, and/or clinical research in the cardiovascular, metabolic, and endocrinologic aspects of diabetes. This should include exposure to multiple disciplines, such as physiology, biochemistry, biophysics, pharmacology, nutrition, and/or epidemiology. Investigators are encouraged to pursue these activities in several laboratories, and if appropriate, at more than one institution. In addition, an applicant must propose a research project of his/her own design which focuses on the cardiovascular, endocrinologic, and metabolic aspects of diabetes and which is of such scope that, within three years, evidence of independent investigative capability will be present. At the completion of this five-year award, the individual should be in a position to compete in regular NIH research grant award programs.

ELIGIBILITY REQUIREMENTS

Candidates for the SERCA Award must (1) hold an M.D. or equivalent professional degree (e.g., D.D.S., D.O., D.V.M., etc.); (2) have a minimum of three years post-M.D. experience, including one year of clinical training in the sub-specialties of either cardiovascular disease or endocrinology-metabolism, or two years post-M.D./Ph.D. experience or equivalent. M.D./Ph.D. applicants should possess significant experience in metabolic, endocrine, or related areas, cardiovascular physiology, biochemistry, pharmacology, or other relevant areas of interest, such as epidemiology; (3) be citizens or noncitizen nationals of the United States or its possessions or territories or must have been lawfully admitted to the U.S. for permanent residence at the time of application; (4) meet certain other eligibility requirements specified in the SERCA Program Guidelines.

FOR ADDITIONAL INFORMATION

Prospective applicants are encouraged to review the SERCA Guidelines which detail eligibility requirements and application procedures. In addition, prior to preparing an application, individuals are strongly encouraged to discuss their potential eligibility as well as their areas of research interest with the Program Director listed below. Requests for copies of the SERCA Guidelines as well as questions related to eligibility, etc., should be directed to:

Maureen Harris, Ph.D., M.P.H.
Acting Director, Career Development Program
National Institute of Arthritis, Diabetes,
Digestive and Kidney Diseases, NIH
Westwood Building, Room 607
Bethesda, Maryland 20205

Telephone: (301) 496-7595

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA NIH-NCI-DRCCA-82-2

# THE ROLE OF NATURAL INHIBITORS IN THE PREVENTION OF CANCER

## NATIONAL CANCER INSTITUTE

Application Receipt Date: June 15, 1982
Letter of Intent Receipt Date: April 30, 1982

The Division of Resources, Centers, and Community Activities, National Cancer Institute, is interested in supporting studies which are directed at examining the role of several natural inhibitors in the prevention of cancer.

The proposed studies should seek to (1) elucidate further the protective effect of several natural inhibitors in reducing the incidence of various site specific cancers, and (2) lead to a greater understanding of the extent, or action, of several natural inhibitors in the possible cancer prevention processes in humans. Clinical and epidemiological studies are being requested to develop basic information which may be helpful at a later date in decision making with regard to the application of the compounds in clinical trials for chemoprevention.

Grants may be awarded to profit and nonprofit organizations and institutions, governments and their agencies, and occasionally to individuals. This type of grant solicitation (the RFA) is utilized when it is desired to encourage investigator-initiated research projects in areas of special importance to the National Cancer Program. Applicants funded under the RFA are supported through the customary NIH grant-in-aid, in accordance with PHS policies applicable to Research Project Grants, including cost sharing. However, the RFA solicitation represents a single competition, with a specified deadline for receipt of applications. All applications received in response to the RFA will be reviewed by the same National Institutes of Health (NIH) Initial Review Group.

The present RFA announcement is for a single competition with a specified deadline of June 15, 1982 for receipt of applications. Applications should be prepared and submitted in accordance with the aims and requirements described in the following sections:

I. BACKGROUND

Chemoprevention refers to the intake or use of chemical agents to interrupt a sequence of events leading to malignancy, or that follow the exposure of an individual to carcinogenic agents which may result in the development of malignancy. A number of natural inhibitors including vitamin C, beta carotene, vitamin A or its analogs, selenium and alpha tocopherol have been associated, in animals or test systems, with the inhibition of carcinogenesis or have been

This program is described in the Catalog of Federal Domestic Assistance number 13.393, Cancer Cause and Prevention Research. Awards are under authorization of the Public Health Service Act, Section 301(c) and Section 402 (Public Law 78-410, as amended; 42 USC 241; 42 USC 282) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

associated with reduced cancer incidence, in epidemiological investigations. A number of mechanisms have been postulated including increased detoxification of the carcinogen, alteration of metabolism by decreased activation, scavenging of the active molecular species, prevention of the carcinogenic agent from reaching the critical target in the cell, altering permeability or transport, and competitive inhibition.

Because of the numerous reports concerning the effectiveness of these compounds in interfering with carcinogenesis in animals and the many epidemiological studies suggesting a possible negative association of them with cancer incidence, especially in dietary factors and nutrition studies, this RFA is announced.

II. OBJECTIVES AND SCOPE

The purpose of this RFA is to solicit applications from qualified investigators interested in furthering the understanding of the role of beta carotene, vitamin A or analogs, vitamin C, selenium and alpha tocopherol in the prevention of cancer.

The studies envisioned include, but are not necessarily limited to, the following approaches:

(1) a. Case Control Studies - utilizing cancer patients and suitable matched controls to study the possible relationship of the designated inhibitors with cancer incidence. Measurement of inhibitor intake or levels should be as direct as possible; indices not specific for these inhibitors will not be considered for the RFA. These studies may also include investigation of appropriate biological indicators such as serum markers, enzyme levels, etc.

b. Alternate approaches would involve the study of existing data bases with accurate intake information on the designated compounds and the subsequent prospective study of the development of cancer in a defined population.

(2) Cohort Studies - involving a population which has consumed varying levels of the designated inhibitors. The investigator would subsequently determine the relative risks of cancer incidence through follow-up of the population over a number of years. Examination of appropriate biological indicators of intake are also desired.

(3) Safety and Adverse Health Effects Studies - Human studies examining the long-term consequence of chronic intake of various compounds to monitor for possible adverse health effects. These studies would be initiated in defined populations identified as having high intake levels of the inhibitors. Approaches might be either case control or cohort studies. Wherever possible, collection and assessment of these data should be incorporated into the studies listed in (1) or (2). Understandings gained through these investigations would also be valuable in examining the feasibility of conducting clinical trials.

(4) Risk Reduction Clinical Trials - A fourth category of interest involves populations known to be at very high risk but free of neoplasia, or high risk with identified precursory or pre-cancerous lesions. These studies would require the administration of the designated natural inhibitors in a

randomized study with follow-up to determine the effect of the compound. Proposals involving studies of populations already having neoplastic lesions are not acceptable within the scope of this RFA, but may be submitted in accordance with appropriate grant guidelines and may be of interest to other components of the NCI; such proposals would not be responsive to this RFA, however, and would be handled through the usual grant-review process.

Several items with regard to the proposal itself are provided as follows:

(1) The applicant is encouraged, where germane, to focus attention on a specific target group, or to identify a source of data, and to address the methodological, organizational, and theoretical issues in a detailed manner.

(2) The applicant should provide a description of the target or population group chosen and should justify the selection of this group. The group should be specified, where appropriate, by age, sex, race, socio-economic status, dietary customs, education, location, occupational or life style risk factors, and relevancy to a specific cancer problem and to its possible prevention by the designated inhibitors.

(3) The applicant should specify the source of data and should document its availability and any required cooperation. If possible, the applicant is encouraged to draw upon existing data rather than collection of extensive original data.

(4) Successful grant awardees under this RFA will be required to cooperate with the National Cancer Institute in the evaluation of the role of these designated inhibitors in cancer prevention. A program meeting of one or two days' duration will be held in Bethesda each year of the program in order to review and assess overall progress. Proposals should contain a statement that awardees will participate in this aspect of the program and proposals should include sufficient travel funds within the budget to accommodate expenses for one or two participants at this annual project meeting.

## III. MECHANISM OF SUPPORT

This RFA will use the traditional National Institutes of Health grant-in-aid. Responsibility for the planning, direction and execution of the proposed research will be solely that of the applicant. The total project period for applications submitted in response to the present RFA should not exceed three years. The intent is to fund at least six projects, with total costs amounting to approximately $2.0 million for the first year. This level of activity is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the National Cancer Institute, the award of grants pursuant to this RFA is also contingent upon the continuing availability of funds for this purpose.

## IV. REVIEW PROCEDURES AND CRITERIA

### A. Review Method

Each application submitted in response to the RFA will be reviewed by: (1) an appropriate review panel of the National Institutes of Health, and (2) the National Cancer Advisory Board at one of its scheduled quarterly meetings. All applications will be evaluated on a competitive basis.

B. Review Criteria

Applications must be responsive to this RFA, in the sense of being directed towards the attainment of the stated programmatic goals and fall within one or more of the specified research categories (see II. OBJECTIVES AND SCOPE). If the application is judged by the National Cancer Institute to be not responsive, the applicant will have the opportunity of having the application considered along with other unsolicited proposals received by the National Institutes of Health in the review cycle which is current at that time.

The factors considered in evaluating each response to this RFA will be:

1. Scientific merit of the research approach, design, and methodology.

2. Scientific, technical, or medical significance and originality of the proposed research.

3. Research experience and/or competence of the Principal Investigator and staff to conduct the proposed studies.

4. Adequacy of time (effort) which the Principal Investigator and staff would devote to the proposed studies.

5. Relevancy and appropriateness of the specific target population along with assurance as to their accessibility.

6. Identity of sources of data, tissues, fluids, etc., procedures for their analysis and assurances as to their accessibility.

7. A willingness to work cooperatively with other projects of a similar nature and with the NCI on the project.

8. Reasonableness of the proposed budget and duration.

V. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are asked to submit a one-page letter of intent which includes a very brief synopsis of proposed areas of research and identification of any other participating institutions. This letter should be sent to Dr. Malone at the address located under VI.

The Institute requests such letters only to provide an indication of the number and the scope of applications to be received. The letter of intent is not binding; it will not enter into the review of any proposal subsequently submitted nor is it a necessary requirement for application.

B. Format of Application

Applications must be submitted on Form PHS 398, the application form for research project grants. Application kits are available at most institutional business offices, or may be obtained from the Division of Research Grants,

NIH. The conventional presentation format and details applicable to regular research grant applications should be followed, and the requirements specified under Review Criteria (IV.B.) must be fulfilled. The words "PROPOSAL IN RESPONSE TO RFA NIH-NCI-DRCCA-82-2, STUDIES TO EXAMINE THE ROLE OF NATURAL INHIBITORS IN THE PREVENTION OF CANCER," must be typed in bold letters across the top of the face page of the application.

C. Application Procedures

The completed original application and six (6) copies should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

To ensure their review, applications should be received by June 15, 1982. Applications received after that date will not be considered under this RFA, but the applicant will have the opportunity of having them considered in the next regular grant review cycle. Also, the Division of Research Grants (DRG) will not accept any application in response to this announcement, that is the same as one currently being considered by any other NIH awarding unit. A copy of the application should also be sent to Dr. Malone at the address shown below.

VI. INQUIRIES

Inquiries may be directed to:

Winfred F. Malone, Ph.D., M.P.H.
Preventive Medicine Branch
Blair Building - Room 624
National Cancer Institute
Bethesda, Maryland 20205

Telephone: (301) 427-8648

## REQUEST FOR RESEARCH GRANT APPLICATION: RFA

## NIH-NIAID 82-6

## PROGRAM PROJECTS IN TRANSPLANTATION IMMUNOLOGY

## NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Application Receipt Date: August 2, 1982

The National Institute of Allergy and Infectious Diseases (NIAID) invites applications for program project grants, to be initiated during FY 1983, to conduct investigations of the immune system in human recipients of allografts.

BACKGROUND INFORMATION

The Genetics and Transplantation Biology Branch of the Immunology, Allergic and Immunologic Diseases Program of the NIAID sponsors basic and applied research in immunogenetics and transplantation immunology through grants and contracts, and by providing cells and reagents for histocompatibility testing. This request for applications (RFA) is intended to stimulate the formulation of collaborative, coordinated approaches, involving transplant clinicians and basic immunologists, to the clarification and manipulation of the immune processes that determine acceptance or rejection of allografts.

The practice of transplantation has evolved to the point that the technical aspects of the surgery are not limiting. The major remaining hazards are associated with rejection and with the immunosuppressive therapy employed to prevent or control it. In immunology, momentous advances in technical procedures and in the understanding of molecular and cellular processes have been made very recently. The major new tools available to immunologists include cell culture and propagation techniques, monoclonal antibodies of exquisite specificity produced by cell hybridization, and techniques of genetic analysis and manipulation at the molecular level. The major conceptual advances are centered on the clarification of the complex regulatory mechanisms involving soluble factors and interactions among specialized cell populations. Transplant recipients subjected to manipulation of their immune system both by means of the immunosuppressive therapy and by the graft itself constitute a unique resource in which a large range of procedures is already accepted practice. They, therefore, offer a superb opportunity to basic immunologists for the investigation of the human immune system subjected to deliberate disturbances. In turn, the guidance to the clinician that will result from the understanding of the immunological events that transpire in connection with transplantation and its treatment and from the elucidation of the mechanisms that connect and control these events should prove invaluable.

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This program is described in the Catalog of Federal Domestic Assistance No. 13.855, Immunology, Allergic and Immunologic Diseases Research. Awards will be made under the authroity 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 Regulation 42 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

RESEARCH GOALS AND SCOPE

1. The program project grant is awarded to an institution on behalf of a program project director for the support of a broadly based but highly integrated long-term research program. It is anticipated that ultimately several awards will be made for work focused on organ and tissue transplantation. The beginning date of the awards is expected to be April 1, 1983 and their terms are up to five years.

2. Support, under the program project grant, will be available for the acquisition of resources necessary for the conduct of the scientific studies (salaries, equipment, supplies, etc.) and for such development of research procedures as will render them useful in a clinical setting. Support will not be provided for other non-research activities such as routine patient care or continuing medical education.

3. Applications should heavily emphasize collaboration in research between transplant clinicians and immunologists, and the application of the most up-to-date concepts and techniques of immunology to the evaluation of the immune system of the recipients in all circumstances attendant to the transplantation.

   The application should be a multidisciplinary research program that has a well defined central research focus or objective. As with other program projects, the individual projects of which they consist should be interrelated, all contributing to the program objective.

4. The objectives of the research should be (a) the clarification of the status of the immune system, specifically of the immunoregulatory balance (1) prior to transplantation in its relatively normal state or, if the transplant is occasioned by a disturbance of the immune state, in the causative disordered state, (2) in the course of preparation for the transplant whose objective is the reduction of responsiveness (immunosuppression) or the induction of tolerance, (3) postoperatively during maintenance immunosuppression as the graft becomes established, (4) during rejection episodes, and (5) during treatment of rejection, and (B) the modulation of immunological activity on the basis of the information so obtained.

5. Appropriate approaches may include but are not restricted to investigations of:

   (a) cellular regulatory interactions among the lymphocyte subpopulations

   (b) modulation of immune activity by soluble factors, including antibodies specific for lymphocyte subsets and antiidiotype antibodies

   (c) effects of chemical and physical agents used for immunosuppression of the metabolic processes and, overall, on the physiological functions of the lymphocytes of patients

(d) cell cloning and molecular genetic manipulations of lymphocytes whose objective is the production of cells with properties of use in therapeutic procedures

6. The investigations should center on human subjects and may deal with cells of the immune system maintained and/or propagated in vitro. Such studies on animal models may be undertaken as will provide direct guidance for the planning and conduct of the clinical investigations.

7. Designation of the Program Project Director should be based upon accomplishment, experience as a senior scientist, and ability to assume leadership of the investigative group and responsibility for scientific, professional and administrative functions. A substantial commitment of time is expected. Leaders of individual projects should have demonstrated a substantial record of accomplishment in transplantation and/or immunology.

MECHANISM OF SUPPORT

In FY 83 NIAID plans to award at least one Program Project in Transplantation Immunology, contingent upon the availability of funds. Support of the Program project(s) will be limited to a maximum of five years. Funding beyond the first year will be contingent on satisfactory progress and availability of funds. Consideration of renewal will be subject to reissuance of this RFA.

The receipt date for applications will be August 2, 1982. They will undergo initial review in November 1982 by the Transplantation Biology and Immunology Subcommittee of the Allergy, Immunology and Transplantation Committee and secondary review by the NIAID Advisory Council in January, 1983. April 1, 1983 will be the earliest starting date for successful applications.

Grant funds may be utilized to support the reserch activities of scientific and professional personnel, administration, consultation services, central support services, equipment, supplies, travel, and publication costs. Support for research-related costs of patient involvement may be authorized. Since the program cannot provide funds for new construction, adequate physical facilities must be available for the primary needs of the project. However, moderate alterations or renovations to enhance clinical or laboratory facilities may be allowed if they are necessary to meet objectives of the proposed program.

PROCEDURES AND CRITERIA

Applications assigned to the NIAID will be reviewed initially by the Transplantation Biology and Immunology Subcommittee of the Allergy, Immunology and Transplantation Research Committee, managed by the Program and Project Review Branch, Extramural Activities Program, NIAID.

The steps in the review process may, but need not, include a project site visit to evaluate the overall merit of the application.

Review Criteria:

Review criteria include evaluation of the following, not necessarily in order of importance:

- The scientific merit and significance of the overall program goals and the development of a well-defined central research focus.
- The cohesiveness and multidisciplinary or multifaceted scope of the program.
- The leadership, scientific ability, and administrative competence of the Program Project Director and his or her commitment and ability to devote substantial time and effort to the program.
- The qualifications, experience, and commitment of the collaborating investigators responsible for the various aspects of the program including their ability to devote adequate time and effort to the program.
- The academic and physical environment in which the research will be conducted, including the availability of space, equipment, patients, and the potential for interaction with active scientists from other departments and/or institutions.
- A sound administrative and organizational structure that facilitates attainment of the objective(s) of the program.
- Arrangements for internal quality control of on-going research, allocation of funds, day-to-day management, internal communications and cooperation among the investigators involved in the program, contractual agreements, and replacement of the Program Project Director, if required, on an interim of permanent basis.
- The institutional strength, stability, and commitment to research and to the program, including fiscal responsibility and management capability to assist the Program Project Director and staff in following NIH/PHS policy.
- The appropriateness of the period of support and budget requested in relation to the proposed program.

Review by the National Allergy and Infectious Diseases Advisory Council:

The final review will be conducted by the National Allergy and Infectious Diseases Advisory Council. Factors that will be considered in this review include:

- Results of the initial scientific and technical merit review.
- Significance to NIAID program goals.
- National needs and program balance.
- Policy and budgetary considerations.

LETTER OF INTENT

Prospective program directors are encouraged to submit a "Letter of Intent" for preliminary screening by NIAID staff.

Letter of Intent should cover the following points:

1. A brief description of each of the individual projects and a brief discussion of how these projects will be interrelated.

2. A description of available laboratory facilities.

3. Ongoing basic and clinical research relating to transplantation and immunology, identifying existing projects and sources of support.

4. Past research by members of the proposed investigative group in transplantation and immunology.

5. A description of all clinical facilities available for use by the proposed project.

6. Specific information on the institution's present relevant patient load and projections for patient involvement in clinical investigation.

7. The academic positions and major research interests of the program director and his professional staff who will be involved in the work of the program project.

Letters of intent are due no later than April 30, 1982, and upon receipt will be screened by NIAID staff to determine the eligibility and suitability of the projected proposals.

Inquiries and letters should be directed to:

Henry Krakauer, M.D., Ph.D.
Chief, Genetics and Transplantation
Biology Branch
Immunology Allergic and Immunologic
Diseases Program
National Institute of Allergy and
Infectious Diseases
Westwood Building, Room 752
5333 Westbard Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-7551

CONSEQUENCES OF LACK OF RESPONSIVENESS TO THE RFA OR LATE SUBMISSION

Based upon the Letter of Intent, potential applicants will be promptly advised whether or not their proposal is found to be within the research goals and scope of the program as defined in this RFA. Applicants will then have an opportunity to correct deficiencies or weaknesses and to restructure their submissions accordingly. Formal applications that are not responsive to the RFA or are not received by August 2, 1982 will not be accepted for review and will be returned to the applicant.

METHOD OF APPLYING

Before preparing an application, the prospective applicant should request a copy of the NIAID Information Brochure on Program Projects from:

Dr. Nirmal Das
Executive Secretary
Allergy, Immunology and Transplantation
Research Committee
National Institute of Allergy and
Infectious Diseases
National Institutes of Health
Westwood Building, Room 706
5333 Westbard Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-7966

In order to assure adequate review it is important to follow instructions in the Information Brochure, which contains details on the format and requirements for multidisciplinary grant applications.

Use the standard research grant appliction form PHS 398 (Rev. 5/80), available in most institutional business offices or from the Division of Research Grants, NIH. In addition to following accompanying format instruction for the development of the application, include expanded material listed above under the eight points for the "Letter of Intent" and other additional information as outlined in the Information Brochure. For purposes of identification and processing, the YES box in item 2 of the face page of the application should be marked and the words Program Project in Transplantation Immunology should be typed. A brief covering letter should be attached indicating submission is in response to this NIAID announcement.

Forward to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, Maryland 20205

Please forward a copy (not the original) of the cover letter and the application to: (1) Dr. Henry Krakauer in order to alert NIAID to the submission of the proposal, and (2) the Chief, Program and Project Review Branch, NIAID, Room 703, Westwood Building, National Institutes of Health, Bethesda, Maryland 20205.

## ANNOUNCEMENT

## CLINICAL INVESTIGATOR AWARD

## NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: August 2, 1982
(August 1 annually thereafter)

### PURPOSE

The National Heart, Lung, and Blood Institute (NHLBI) announces the availability of Clinical Investigator Awards. The clinical investigator award program is intended to:

- o encourage newly trained clinicians to develop clinical and basic research interests and skills in the areas of cardiovascular, pulmonary, or blood diseases and the blood banking sciences;

- o increase the pool of physician investigators in the areas of cardiovascular, pulmonary, or blood diseases and the blood banking sciences.

These awards provide the opportunity for clinically trained physicians with a commitment to research to develop into independent biomedical research investigators.

The award will enable candidates to undertake up to five years of special study and supervised experience tailored to individual needs with a sponsor (or sponsors) competent to provide research guidance. This award is intended to cover the transition between postdoctoral experience and a career in independent investigation. The clinical investigator award differs from the NIH Research Career Development Award (RCDA) in that it seeks to develop research ability in individuals with a clinical background early in the candidate's career rather than to promote the further development of research skills of individuals already demonstrating significant research achievement.

### BACKGROUND

Despite a recent decline in the death rate from coronary heart disease, cardiovascular disease continues to be the number one cause of death in the United States. Arteriosclerosis and hypertension account for almost one million deaths annually. An estimated 40 million Americans have diseases of the heart and blood vessels, resulting in a large burden of acute and chronic illness and disability. Heart and blood vessel diseases cost the economy more than $50 billion per year in wages, lost productivity, and expenses for medical care.

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This program is described in the Catalog of Federal Domestic Assistance Nos. 13.837, 13.838, and 13.839. 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 A-95 Clearinghouse or Health Systems Agency review.

Diseases of the lung constitute a major national health problem. An estimated 10 million Americans, both young and old, are currently affected by these diseases with an annual estimated cost to the nation of over $17 billion. In the newborn, the most common cause of death is neonatal respiratory distress syndrome. Neonatal RDS is implicated in the development of adult respiratory diseases as well. Fibrotic and immunologic lung diseases are major causes of lung problems in the young adult and may cause chronic obstructive pulmonary diseases. Of the adult respiratory diseases, emphysema and chronic bronchitis are the major causes of death.

Asthma, emphysema and chronic bronchitis represent particularly pressing health problems, since the death rate and prevalence of these conditions have increased at an alarming rate over the past 15 years. As a disabling disease, emphysema is the third leading cause of worker retirement on Social Security disability payments.

Diseases of the blood underlie, or are critical contributors to, many disorders affecting mankind. As a consequence, they are major causes of death and disability in the United States. Nevertheless no valid estimate of their adverse economic impact can be realistically made since disorders of the blood not only affect the blood itself, but all the organs and tissues through which it flows. Platelet and clotting disorders affect large numbers of individuals suffering from hemorrhagic or thrombotic episodes. Significant segments of the population have sickle cell disease, Cooley's anemia, or other hemolytic disorders. Anemias due to other mechanisms affect smaller numbers of patients. Furthermore, it is difficult to estimate the economic consequences of an inadequate blood banking and blood resource system, since the supply and management of blood and blood products underlie much routine and emergency medical practice.

The clinical investigator award program is designed to encourage recently trained physicians to develop their clinical and basic resource interests and research capabilities in heart, lung, or blood disease* areas. To help support the transition from clinical training status to that of a productive research investigator, the clinical investigator award will provide early support for clinicians with potential for developing into independent researchers.

IMPLEMENTATION

Beginning in Fiscal Year 1980, under the authorizations in Public Health Service Act, Section 301(c) and Section 413(a), the National Heart, Lung, and Blood Institute has funded clinical investigator awards. Each grant has a duration of five years and is non-renewable. Funding beyond the first year of the grant is contingent on satisfactory progress during the preceding year.

The status of the clinical investigator award program will be reviewed four years from the date of the first awards to determine whether the program should be continued. In addition, to assess the effectiveness of the program in fulfilling its objectives, the Institute intends, after completion of each grant, to follow the progress of the recipient for a period of five years to determine: (1) the investigator's professional affiliation(s),

* The term "blood diseases" covers research into many aspects of bone marrow function and disorders of the red cell, megakaryocyte, platelet, and coagulation systems. Research on disorders of white cells, including the leukemias and other blood malignancies, and basic immunology related to the lymphoid system are the responsibility of other Institutes of the NIH and therefore cannot be supported through this mechanism.

\. ,ier record of subsequent grant or contract support, and (3) his/her record of sc ,tific publications. It is anticipated that the experience and results achieved by the awardee from this special grant program, in the majority of cases, will provide the basis for successful competition in the regular research support programs of the Institute. The receipt date for applications will be **August 2, 1982** and on August 1 each year thereafter. They will be evaluated by an initial review group and by the National Heart, Lung, and Blood Advisory Council. The earliest start date for successful applications will be July 1, 1983.

PROVISIONS OF THE AWARD

The clinical investigator awardee will be supported for a maximum of five years. All funds must be used to support the original awardee. Support is based on a full-time, twelve-month appointment. The awardee will be provided salary support of up to $25,000 in the first year with subsequent years up to a ceiling of $30,000, plus fringe benefits. The actual salary must be consistent with the established salary structure of the institution for persons of equivalent qualifications, experience, and rank.

Up to a total of $10,000 annually may be provided for supplies, equipment, travel, etc., which are necessary for pursuit of the awardee's research program. An appropriate sponsor must assume responsibility and provide guidance for the development of the candidate's research program.

Institutions may apply for awards on behalf of named individuals meeting the criteria for this award. Evidence of the commitment of the institution and sponsors to the candidate's research and career development is to be included in the application.

The grant will be made annually to the awardee's parent institution for each of the five annual budget periods. Costs allowed may include:

1. Awardee's Salary

   Up to a maximum of $25,000 in the first year with subsequent years up to a ceiling of $30,000 for full-ime support; in addition, fringe benefits will be provided. Institutional supplementation is permitted.

2. Research Support

   Up to a maximum of $10,000 per year.

   - o Equipment: specialized research equipment essential to the proposed program. The available facilities should include most of the necessary equipmnent;
   - o Supplies: consumable supplies essential to the proposed program;
   - o Travel: domestic travel essential to the proposed program;
   - o Tuition for training courses: if essential to the awardee's individual research development program; and
   - o Other: publication costs, patient costs, etc., necessary for the research program.

3. Indirect Costs

Funds will be provided for the reimbursement of actual indirect costs at a rate up to, but not exceeding, 8 percent of the total direct costs of each award, exclusive of tuition, fees, and expenditures for equipment.

ELIGIBILITY

1. The award is designed to provide intensive, supervised research experience for clinicians. Thus, candidates are restricted to those holding health-professional degrees in the clinical sciences (M.D., D.O., or equivalent). Candidates ordinarily will have completed their clinical experience by the time the award can be made. Ordinarily a candidate in the following categories will not qualify:

   a) with more than 6 years of postdoctoral experience at the time of award;

   b) with previous independent NIH research support or its equivalent;

   c) with less than three years total postdoctoral clinical experience at the time of the award.

   In exceptional circumstances, individuals in one or more of the above categories may qualify for the award. However, the applicant must provide sufficient justification for such an exception.

   Candidates should have broad clinical training, should demonstrate individual competence in clinical activities, and should show research potential in the chosen area of interest. Candidates must provide evidence of a serious intent for research and academic careers.

2. Applicants for a Clinical Investigator Award may not submit a concurrent applicaion for an NIH Research Career Development Award, Academic Award, or for a New Investigator Research Award. A Clinical Investigator Awardee may subsequently apply for a research project grant.

3. The grantee institution must be a domestic university, medical school, or comparable institution with strong, well-established research and training programs, adequate numbers of highly trained faculty in clinical and basic science departments, and commitment and capability to provide guidance to clinically oriented individuals in the development of independent research careers.

   Candidates must be nominated by an institution on the basis of qualifications, interests, accomplishments, motivation, and potential for a research career. Evidence of the commitment of the institution to the candidate's research and development must be provided.

4. Candidates must have one or more sponsors or advisors who are recognized as accomplished investigators in the research proposed at the applicant's institution. The sponsor must provide: a) his/her concept of a development

and research plan for the awardee; b) his/her curriculum vitae (updated) with complete bibliography and research support; and c) a letter indicating his/her evaluation of the proposed awardee and his/her willingness to provide guidance and support.

5. Candidates must provide a description of the proposed research and career development plan for the five-year period of the award. The candidate must be prepared to commit full-time effort to the objectives of this award. It is required that a minimum of 75 percent effort be devoted to the research program. The balance of effort can be devoted to other clinical and teaching pursuits only if they are consonant with the program goals, i.e., the awardee's development into an independent biomedical research investigator.

6. Awardees and their sponsors will be required to submit a special, detailed progress report at the end of the third year of support. This report is to contain specific information concerning progress and accomplishments and, in particular, an appropriately detailed research plan and protocol.

7. Candidates must agree to inform the National Heart, Lung, and Blood Institute annually for a period of five years subsequent to completion of the award about academic status, publications, and research grants or contracts received.

8. Candidates for an award must be citizens or non-citizen nationals of the United States or its possessions and territories or must have been lawfully admitted to the United States for permanent residence at the time of application.

APPLICATION

Applications must be submitted on form PHS 398 which is available at the grantee institution. The original and six (6) copies of the application should be clearly labeled "NHLBI CLINICAL INVESTIGATOR AWARD PROGRAM."

The chairperson of the department sponsoring the candidate should submit, a signed statement, as part of the application, detailing the department's commitment to the candidate.

Completed grant applications should be mailed to the following address:

Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20205

Upon receipt of each application at NIH, a postal card acknowledging receipt will be mailed to the applicant.

The applicant should ask three present or former supervisors or preceptor to send a letter to the Review Branch, Division of Extramural Affairs, NHLBI, attesting to his/her potential for conducting independent research. The applicant is responsible for making necessary arrangements to ensure that the reference letters are mailed by the supervisors/preceptors directly to the Review Branch.

Applications for this award are due **August 2, 1982.** The earliest start date for awards is July 1, 1983.

Subsequent competitions will occur on a once-a-year basis and the receipt dates will be August 1 of each year.

REVIEW CRITERIA

Applications for clinical investigator awards will undergo initial merit review in the Review Branch, Division of Extramural Affairs, NHLBI. Secondary review will be by the National Heart, Lung, and Blood Advisory Council. Criteria for review include:

- The candidate's potential for a career in independent research;
- The candidate's commitment to a research career;
- The eligibility of the candidate as defined in the program announcement;
- The overall merit of the candidate's five-year plan for research and the development of research skills;
- The quality of the candidate's clinical training and experience;
- The institution's ability to provide quality facilities, resources, and opportunities necessary to the candidate's research development;
- Presence of highly trained faculty in clinical and basic science departments relative to the area of study; and
- The ability and plans of the sponsor (or sponsors) who will provide the candidate with the guidance necessary for career development in research.

NHLBI STAFF CONTACTS

Inquiries about the program should be directed to:

Research Training and Development Officer
DIVISION OF BLOOD DISEASES AND RESOURCES
National Heart, Lung, and Blood Institute
Federal Building, Room 514A
Bethesda, Maryland 20205

Telehone: (301) 496-1817

Research Training and Development Officer
DIVISION OF HEART AND VASCULAR DISEASES
National Heart, Lung, and Blood Institute
Federal Building, Room 3A-08
Bethesda, Maryland 20205

Telephone: (301) 496-1724

Research Training and Development Officer
DIVISION OF LUNG DISEASES
National Heart, Lung, and Blood Institute
Westwood Building, Room 6A-05
Bethesda, Maryland 20205

Telephone: (301) 496-7668

Letters of reference and inquiries regarding review procedures should be directed to:

Dr. Carol Letendre, Executive Secretary
Research Manpower Review Committee
National Heart, Lung, and Blood Institute
Westwood Building, Room 548
5333 Westbard Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-7363

## ANNOUNCEMENT

## CANCER CONTROL SCIENCE PROGRAM

## NATIONAL CANCER INSTITUTE

### I. BACKGROUND AND GOALS

The Cancer Control Program of the National Cancer Institute (NCI) is located within the Division of Resources, Centers and Community Activities (DRCCA). DRCCA has recently described the new Cancer Control Program directions, emphasizing more cancer control research, in a "Statement on Cancer Control" which was adopted in January 1981.

The Division of Resources, Centers and Community Activities, NCI, invites grant applications from interested investigators for the support of Cancer Control Science Programs. These programs will provide a scientific focus within which investigators can conduct a variety of cancer control research studies.

This "Cancer Control Science Program," together with the "Cancer Control Research Units for Defined Population Studies" program, replace the Outreach Program described in the June 1976 "Grant Guidelines to Cancer Centers for Community Outreach Programs," and the "Cancer Control Developmental and Support Grants" described therein. (The availability of a Request for Applications for a single competition for Cancer Control Research Units for Defined Population Studies was announced in the January 29, 1982 issue of the Guide. Copies of RFA-NCI-DRCCA-CCB-82-6 may be obtained from the staff contact listed at the end of this announcement.)

### II. CANCER CONTROL RESEARCH

Cancer control research includes both prevention (primary and secondary) and management (diagnosis, pre-treatment evaluation, treatment, rehabilitation, and continuing care). It builds on the research and knowledge bases of epidemiological, biomedical, clinical, behavioral and other sciences. It requires carefully designed investigations, often including both study and control groups and/or defined denominator populations.

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This program is described in the Catalog of Federal Domestic Assistance No. 13.399, Cancer Control. Awards will be made under the authority of the Public Health Service Act, Title IV, Section 403 (Public Law 78-410, as amended; 42 USC 284) and administered under PHS grant policies and Federal regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse of Health Systems Agency review.

The "Statement on Cancer Control," which sets forth the general scope and definition of cancer control research, states, in part:

> "The goal of a cancer control program is to reduce cancer incidence, morbidity, and/or mortality by:
>
> 1) identifying approaches that might accomplish this and performing research in defined populations to determine which are effective,
>
> 2) selective promotion and evaluation of these approaches, and
>
> 3) selective education and information dissemination for health professionals and/or the public.

The scope of cancer control includes prevention, screening, diagnosis, pretreatment evaluation, treatment, rehabilitation, and continuing care activities.

The national cancer effort includes both research into and application of control methods. These are complementary and not antagonistic activities and are part of an ordered sequence, as indicated in the following statement adapted by the Board of Scientific Counselors from the report of the President's Biomedical Research Panel.

> 'The continuum from the discovery of new knowledge to the application of such knowledge in health care includes a number of steps:
>
> 1. discovery, through research, of new knowledge and the relating of new knowledge to the existing base;
>
> 2. translation of new knowledge, through applied research, into new technology and strategy for movement of discovery into health care;
>
> 3. validation of new technology through clinical trials in defined populations, and in other ways;
>
> 4. determination of the safety and efficacy of new technology for wide-spread dissemination through demonstration projects;
>
> 5. education of the professional community in proper use of the new technology and of the lay community on the nature of these developments; and
>
> 6. skillful and balanced application of the new developments to the populations.'

Cancer control includes 2 through 5, although different relative emphasis may be placed on each of those points depending on the specific cancer and whether prevention or treatment efforts are involved.

Control and research must be mutually reinforcing and only the coordinated planning and implementation of research and control strategies will assure maximum yield from the dollars invested, maximum quality for the activities supported, and maximum, probability that the research effort will continue to provide advance suitable for future application in the control of cancer.

Cancer control should support three types of activities in defined populations:

1. research to determine how, whether and to what extent, actions proposed for a particular cancer are effective;

2. research to determine the optimal strategies for promoting actions proved efficacious for particular cancers; and

3. selective implementation of those promotional strategies proven efficacious for particular cancers.

Cancer control efforts should give highest priority to cancers meeting more than one of the following criteria:

1. cancers causing the greatest mortality/morbidity in the United States;

2. cancers for which substantial risk of cancer has been associated with common exposures...(added for this CCSP announcement);

3. cancers for which apparently effective actions are available.

The development of an effective national program for cancer control requires qualified personnel, particularly with training and experience in the disciplines of epidemiology, biostatistics, and disease control administration, and the placement of these individuals in responsible positions."

## III. PHASES OF CANCER CONTROL RESEARCH

The Division of Resources, Center, and Community Activities is testing the idea of categorizing cancer control research studies into phases. Applicants are asked to classify each research project as Phase I, II, III, IV, or V as noted in the table below, and also as prevention (primary and secondary) or management (diagnosis, pretreatment evaluation, treatment, rehabilitation and continuing care). If a study does not fit this classification, the reasons it does not fit should be described.

TYPE OF CANCER CONTROL STUDY

| Phase | Phase Title/Description | Prevention | Management |
|---|---|---|---|
| Phase I | Hypothesis Development | | |
| Phase II | Research on Study Components or Methods Needed to Test the Hypothesis | | |
| Phase III | Case-Control Studies and Other Controlled Studies Which Are Not Defined Population Studies | | |
| Phase IV | Defined Population Studies | | |
| Phase V | Demonstration and Implementation Studies | | |

Definitions

Phase I.
Hypothesis Development

Development of cancer control hypotheses of which control measures, approaches, or interventions should be tested to determine whether they can reduce cancer incidence, morbidity and/or mortality. These hypotheses often will come from basic laboratory, clinical, or epidemiological research which provides evidence for etiological associations or clinical advances for a specific cancer; the basic research itself will not be considered part of cancer control research.

Phase II.
Research on Study Components or Methods Needed to Test the Hypothesis

Methodological research is included here, such as development and testing of questionnaires, studies of compliance, development and testing of screening procedures, pilot tests of the control measures identified in the hypotheses, or testing of methods from other diseases or disciplines on cancer problems.

Phase III.
Case Control Studies and Other Controlled Studies Which Are Not Defined Population Studies

These are research efforts aimed at testing a hypothesis. While the populations may not necessarily be representative of any larger population, the cancer control idea should receive a careful scientific assessment. Certain cohort or cross-sectional studies might be

## VIII. INQUIRIES AND CORRESPONDENCE

Carlos E. Caban, Ph.D.
Program Director
Division of Resources, Centers and
Community Activities
National Cancer Institute
Blair Building, Room 716B
8300 Colesville Road
Silver Spring, Maryland 20910

Telephone: (301) 427-8663

## ANNOUNCEMENT

## MINORITY HYPERTENSION RESEARCH DEVELOPMENT SUMMER PROGRAM

## NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
## DIVISION OF HEART AND VASCULAR DISEASES

Application Receipt Date: September 15, 1982

The Division of Heart and Vascular Diseases of the National Heart, Lung, and Blood Institute is accepting competing and renewal applications for Institutional National Research Service Awards for research training under the Minority Hypertension Research Development Summer Program.

The Minority Hypertension Research Development Summer Program is intended to (1) encourage the recruitment and development of minority investigators in specialized areas of research, prevention, control and education related to hypertension and (2) stimulate hypertension research, prevention, control and education by offering minority school faculty members and graduate students the opportunity to enhance their research capabilities in these areas.

Training will be offered through HYPERTENSION TRAINING CENTERS which have well-established hypertension research and training programs and are within 100 miles of (a) minority school(s) or provide satisfactory alternative arrangements for communication and exchange. The centers will collaborate with minority schools to work out plans for the identification, selection and development of participating minority school faculty members or graduate students.

Minority schools are those in which a majority or significant proportion of its enrollment is comprised of students of minority ethnic groups-including, but not limited to, Blacks, Spanish-speaking Americans, Native Americans, Pacific Islanders and Asian Americans-and has a demonstrated commitment to the special encouragement of minority faculty, students, and investigators. The Minority School must commit itself to encouraging appropriate faculty members or graduate students to participate in this program, to continue the faculty members or graduate students in status after the summer session(s) and guarantee at least limited resources for his or her hypertension research and teaching activities.

Participating faculty members or graduate students must be nominated by the Minority School, be accepted by the Training Center, and agree to report annually for six years after training on his or her academic status, publications, grants or contracts and teaching activities related to hypertension.

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This program is described in the Catalog of Federal Domestic Assistance No. 13.837, Heart and Vascular Diseases Research. Awards will be made under the authority of the Public Health Service Act, Section 472, 42 USC 2891-1, and administered under PHS grants policy and Federal Regulations 42 CFR Part 66. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

Applications may request funds to provide stipends for the duration of a summer program of $1,115-$1,565 per month for minority school faculty member participants and $420 per month for minority school graduate student participants. In addition, funds may be requested for trainee travel; tuition and fees essential to the training; health insurance coverage for participants during the summer session; and up to $1,250 per faculty member and $750 per graduate student for institutional allowances which includes personnel, supplies, equipment essential to the program and consultant costs when specifically justified. Indirect cost allowances will be limited to 8 percent of the total allowable direct costs or the actual rate, whichever is lower. These budget items are subject to administrative revision.

The present announcement is for a single competition with a September 15, 1982 receipt date for applications. These applications will be reviewed at the February 1983 meeting of the National Heart, Lung, and Blood Advisory Council. The meritorious ones will be awarded beginning May 1, 1983. Applications not received by September 15, 1982, will be returned to the applicant. Guidelines for the development of the application may be obtained by contacting Dr. George A. Hayden at (301) 496-1724.

LETTER OF INTENT

Prospective Training Center applicants should submit a letter of intent not later than May 15, 1982 to:

Dr. George A. Hayden
Research Training and Development Branch
Division of Heart and Vascular Diseases
National Heart, Lung, and Blood Institute
Federal Building, Room 3A-08
Bethesda, Maryland 20205

The Institute requests such letters to obtain an indication of the number and the scope of applications which will require merit review. A letter of intent is not binding and will not enter into the review of any proposal subsequently submitted. The letter should briefly describe the composition of the Hypertension Training Center, participating Minority Institutions, the overall approach, and areas of interest for the Minority Hypertension Research Development Summer Program.

## ANNOUNCEMENT

## SMALL VESSEL PROSTHESES

## NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

The National Heart, Lung, and Blood Institute encourages interested investigators to submit research grant applications which will lead to the development and clinical application of small caliber (5 mm or less) vascular grafts. Applications received in response to this Program Announcement will be assigned by the Division of Research Grants to study sections for review according to the NIH process for regular research grant applications. Funding for this activity is in competition with all regular competing grant applications. The purpose of this Program Announcement is to inform the scientific community of the need for additional work in this area. The long-range goal of this program is to develop natural or synthetic graft materials and the clinical protocols for implantation of small caliber vascular prostheses in humans. The development of successful small vessel prostheses may involve contributions from materials science, surface chemistry, rheology, pharmacology, hematology, vascular surgery and veterinary medicine.

The National Heart, Lung, and Blood Institute has a specific interest in supporting research which will lead to an understanding of the basic mechanisms of graft failure and/or lead to potential solutions to problems with current small vessel prostheses. In current surgical practice, autologous vascular tissue is used whenever possible for repair or replacement procedures involving small caliber vessels because these tissues maintain patency better than commercially available prostheses. There is a clinical need for small caliber grafts which will remain patent when used in coronary bypass, in vascular repair in the pediatric patient, in peripheral vascular surgery, and in vascular access for renal dialysis or chemotherapy. Grafts with poor runoff are particularly prone to failure. Intimal proliferation in the graft itself or in the distal vascular bed is a frequent cause of failure. Furthermore, the vascular beds proximal and distal to the graft may become compromised by progression of atherosclerosis, thereby reducing flow and leading to failure. A number of failure mechanisms have been hypothesized but appropriate means to prevent or correct such failures have not been identified.

The recommendations of the Workshop on Vascular Prostheses (NIH Publication No. 82-1215) identified a number of research areas which could lead to development of improved grafts. These areas include better understanding of the role of surface chemistry, physical chemistry and bulk engineering properties of graft materials in success or failure, including the mechanism of failure at the suture line; role of fluid dynamics; understanding of mechanisms which would promote human endothelial cells to populate the graft intima; and development of an appropriate animal model which will accurately predict clinical performance.

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This program is described in the Catalog of Federal Domestic Assistance number 13.837, Heart and Vascular Diseases Research. Grants will be awarded under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grant policies and Federal Regulations, most specifically at 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

Applicants submitting responses to this announcement are encouraged to have a clearly focused hypothesis regarding the failure mechanism of currently available materials when used as grafts of this small size in humans. Any one of a number of approaches could be appropriate, including research plans which propose a direct demonstration of the importance of this failure mechanism, or which seek new ways to prevent failure. Some applicants may prefer to test grafts or grafting procedures while others examine relevant discrete components of the problem. As with any research grant application, the choice of a well-controlled experimental design could be an important consideration, since graft failure may be the result of complex interactions.

Potential studies might involve investigation and demonstration of failure mechanisms at low flow using model systems and/or through analysis of retrieved implants, development of new materials with appropriate characterization and validation, identification of pharmacologic regimens to prevent failure, or development and validation of animal models for specified applications; other topic areas may also be appropriate. Research may involve currently available or new materials; studies may be conducted in animals, or in adults or children with due regard for all relevant ethical considerations.

Careful delineation of the methods to be used to characterize the experimental system is encouraged, particularly with regard to physical and chemical properties of graft materials, verification of flow rates, surgical techniques, numbers of animal or data points in a group, and frequency of collection of data points. A clear definition of the experimental end point could be helpful to the reviewers, as well as the criteria to be used to determine whether the hypothesis has been confirmed. Since a proposed hypothesis may already have been discussed within the community or may already be accepted as fact, an explanation of the new information to be gained from the proposed work, its need, and its relative importance may be appropriate.

Support for this research is available through investigator initiated research grants. Application receipt dates are July 1, November 1, and March 1. Applications should be submitted on form PHS 398; these forms are available in the business or grants and contracts office at most academic and research institutions or from the Division of Research Grants, NIH. In order to identify the application as a response to this program announcement, check "yes" on Item 2 of the application face page with the title SMALL VESSEL PROSTHESES. The original and six copies should be submitted to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, Maryland 20205

An additional copy of the application should be mailed to:

Dr. Frances A. Pitlick
Devices and Technology Branch
National Heart, Lung, and Blood Institute
Federal Building, Room 312
7550 Wisconsin Avenue
Bethesda, Maryland 20205

Requests for additional information or questions regarding this program may be directed to Dr. Pitlick at (301) 496-1586.

## RESEARCH GRANTS IN NEURAL REGENERATION, NEURAL PLASTICITY AND RELATED DEVELOPMENTAL BIOLOGY

## NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE

Injury to the nervous system entails exceptional physical, financial and emotional hardship on persons directly affected and on their closest associates, as well as on the community at large. The Stroke and Trauma Program (STP) of the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) encourages the submission of applications for research grants in neural regeneration, neural plasticity and in the developmental biology related to these processes. While the ultimate aim is complete restitution of nervous system function in humans, the STP recognizes that basic as well as clinical studies at all levels are required in order to achieve these goals.

Studies related to neural regeneration and plasticity in the brain, spinal cord and peripheral nervous system are, by their nature, complex and require employment of state-of-the-art biochemical, biophysical, physiological, morphological, behavioral, pathological, pharmacological, immunological and other approaches, either individually or in collaborative settings. Investigators should submit carefully designed, well integrated, and adequately documented research applications.

New insights are sought with respect to factors that may inhibit or facilitate optimal healing as evidenced by return of function in the nervous system to pre-injury levels. Areas of research interest in neural regeneration and plasticity include, but are not limited to, the following examples:

- intracellular and extracellular processes concerned with removal of neural tissue debris;
- post-traumatic neural tissue status including glial and vascular responses to injury;
- trophic and growth factors;
- specifying agents and guidance cues;
- hormonal and enzymatic influences;
- intra- and intercellular signalling;
- molecular or ionic fluxes and cellular constituents, cell membranes and the extracellular milieu;
- synthesis and assimilation of proteins, lipids and carbohydrates associated with regeneration;
- cellular and molecular mechanisms of axoplasmic transport;
- membrane incorporation and membrane properties;
- collateral sprouting and neurite extension;
- regional and cellular metabolism (locally and at a distance) prior to and shortly after injury, as well as during reparative stages;

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This program is described in the Cataloge of Federal Domestic Assistance, number 13.853, Stroke and Trauma Research. Grants will be awarded 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 A-95 Clearinghouse or Health Systems agency review.

- involvement of other supportive elements such as connective and vascular tissues;
- the neurotransmitter, neuroreceptor and neurochemical environment in which regenerative activities occur;
- identification of the tissues, cells and substrates critical to the regeneration process;
- re-establishment of neural connectivity;
- the mechanisms responsible for activation and expression of the genetic features regulating the relevant cellular and extracellular elements (since the ability to regenerate neural and other components is species and tissue related);
- neuronal and supportive cell genetic expression in the developmental and regenerative mode of the nervous sytem;
- neural transplants as an approach to the remediation of specific neurologic deficits and the further definition of the nervous system and its effector organs;
- materials science research (e.g., in the development of substrate prosthetic devices to facilitate regrowth of axons in the injured nervous sytem) suggesting additional approaches to understanding the molecular complexities and interactions associated with outgrowing neurites and their substrates;
- latent synapses, remodelled circuitry, and rehabilitative training following injury;
- behavioral, chemical, functional and structural correlates of restored or revised neural circuits.

Applicants are encouraged to develop and use those new and refined methodologies, instrumentation, and surgical procedures which will permit more detailed determination of features involved in neural regeneration. This includes development and use of pertinent in vivo or in vitro models that may serve to demonstrate factors involved in neural regenerative processes.

Investigators should consider submitting well-focused applications addressing one or more compelling questions related to neural regeneration and/or plasticity. Where sufficient baseline data are available, an approach should be entertained that will help test hypotheses that are pivotal to future studies along specific avenues of research. Proposed mechanisms responsible for observations to date would be of obvious interest to other investigators working in the same or related areas. The application must convey the investigators' ability to employ the methodologies described, e.g., listing relevant publications or the inclusion of preliminary data when available. Methodological as well as experimental controls should be described, especially when non-standard or controversial techniques are proposed. Other important elements may include the sequence and timing of proposed studies, potential difficulties and their resolution, quantitation and management of data where appropriate, and adequate justifications of all budgetary requests.

Applications should be prepared on form PHS 398 following instructions contained in the application kit. These kits are available at most institutional business offices or from the Division of Reserch Grants, NIH. The applications will be judged on scientific merit in accord with NIH policy and procedures involving peer review. Initial review will be by an appropriate study section of the DRG. Final review will be by the National Advisory Neurological and Communicative Disorders and Stroke Council. Applications judged more responsive to program interests of other Institutes at the NIH will be assigned accordingly.

Deadline dates for the receipt of new applications are March 1, July 1, and November 1.

The phrase NEURAL REGENERATION AND PLASTICITY should be typed in item 2, of the first (face) page of the application. The original and six copies of the application should be mailed to the following address:

Division of Research Grants
National Institutes of Health
Room 240, Westwood Building
Bethesda, Maryland 20205

One copy of the application is to be sent to the address below. For additional information applicants are encouraged to contact:

Stroke and Trauma Program
National Institute of Neurological and
Communicative Disorders and Stroke
Room 8A13, Federal Building
Bethesda, Maryland 20205

Telephone: (301) 496-4226

## ANNOUNCEMENT

## EPIDEMIOLOGY OF ORAL DISEASES IN MINORITIES

## NATIONAL INSTITUTE OF DENTAL RESEARCH

The National Institute of Dental Research (NIDR) invites applications for support of epidemiological research related to the oral health problems of racial and ethnic minority groups. Research proposed should go beyond descriptions of the nature and extent of the oral health problems experienced by minorities and should offer hypotheses to be tested that would shed light on the relevant factors and conditions that contribute to the problems.

Research proposed may be directed at one or more of the areas noted below and may be confined to a particular minority group. Applicants are encouraged to offer creative proposals which would help improve the understanding of the oral health problems of minorities and provide insight as to how the oral health status of such groups might be improved.

Identified as particularly appropriate for support by the NIDR are epidemiological studies directed toward the identification of the patterns of occurrence of the oral diseases and conditions noted below, and the factors and conditions, including behavioral factors, responsible for, or contributing to these oral health problems:

- Dental Caries, including the prevalence of both coronal and root caries in different age groups;

- Periodontal Diseases, studies using new methodologies for objective measurement of disease activity;

- Congenital Craniofacial Anomalies (including cleft palate), Dentofacial Malrelations, and Acquired Craniofacial Defects;

- Oral Malignancies, Other Oral Soft Tissue Diseases, and Nutritional Deficiencies with Oral Manifestations.

The deadlines for the receipt of research grant applications by the Division of Research Grants are March 1, July 1, and November 1. Review and award of such applications will be through the usual NIH procedures governing research project grants. The award of grants pursuant to this announcement is contingent upon the receipt of responsive proposals of high scientific merit and the availability of appropriated funds.

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This program is described in the Catalog of Federal Domestic Assistance Numbers 13.840, 13.841, 13.842, 13.844, and 13.878. 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 A-95 Clearinghouse or Health Systems Agency review.

Applications should be submitted on Form PHS 398, which is available in the business or grants office at most academic or research institutions. If not, application forms may be obtained from:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Room 448, Westwood Building
Bethesda, Maryland 20205

Inquiries regarding this announcement may be directed to one or more of the individuals noted below according to the particular area of concern that the applicant wishes to address:

Dr. John D. Townsley
Caries Research Grants and Contracts Branch
Telephone: (301) 496-7884

Dr. Samuel Kakehashi or
Dr. Paul F. Parakkal
Periodontal Diseases Program Branch
Telephone: (301) 496-7784

Dr. Jerry D. Niswander or
Dr. John D. Suomi
Craniofacial Anomalies Program Branch
Telephone: (301) 496-7807

Dr. Paul D. Frazier or
Dr. David A. Wolff
Soft Tissue Stomatology and Nutrition
Program Branch
Telephone: (301) 496-7807

Dr. Aaron Ganz or
Dr. Patricia S. Bryant
Pain Control and Behavioral Studies
Program Branch
Telephone: (301) 496-7491

The mailing address of the above individuals is:

National Institutes of Dental Research
National Institutes of Health
Westwood Building
Bethesda, Maryland 20205