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For Grants and Contracts

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The NIH Guide announces scientific
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NOTICES

Change in Receipt Date - RFA
Central Radiographic Laboratory, Bypass Angioplasty Revascularization
Investigation (BARI) - 86-HL-22-H 1
National Heart, Lung, and Blood Institute
Index: HEART, LUNG, AND BLOOD

DATED ANNOUNCEMENTS (RFPs and RFAs AVAILABLE)

RFP Available - RFP-NIH-NIDDK-86-13
Conference and Support Services for the National Kidney
and Urologic Diseases Advisory Board 1
This Acquisition is 100% Small Business Set-Aside
National Institute of Diabetes and Digestive and Kidney Diseases
Index: DIABETES AND DIGESTIVE AND KIDNEY DISEASES

RFP Available - RFP-NIH-NIAID-MIDP-87-8
Development of Additional Drugs for Treatment of Candidiasis 2
National Institute of Allergy and Infectious Diseases
Index: ALLERGY AND INFECTIOUS DISEASES

Availability of Request for Applications (RFA) - 86-HL-24
Studies of OMEGA-3 Polyunsaturated Fatty Acids in Thrombosis
and Cardiovascular Disease 2
National Heart, Lung, and Blood Institute
Index: HEART, LUNG, AND BLOOD INSTITUTE

ONGOING PROGRAM ANNOUNCEMENTS

Aging and the Cardiovascular System 3
National Institute on Aging
Index: AGING

Determination of the Therapeutic Usefulness of Maturation,
Differentiation and Anti-Growth Factor Substances in Cancer
Models 5
National Cancer Institute
Index: CANCER

Preclinical Studies of LAK Phenomenon 6
National Cancer Institute
Index: CANCER

Determination of the Therapeutic Usefulness of Purified
Cytokines in Cancer Models 7
National Cancer Institute
Index: CANCER

Use of Oncogene Related Products for Cancer Therapy 9
National Cancer Institute
Index: CANCER

NOTICES

CHANGE IN RECEIPT DATE - RFA

CENTRAL RADIOGRAPHIC LABORATORY, BYPASS ANGIOPLASTY REVASCLARIZATION INVESTIGATION (BARI) - 86-HL-22-H

P.T. 34; K.W. 0715040, 0785210, 0785190 0755015

The June 6 issue of the Guide included a notice of availability of a request for applications (RFA) on the above topic. Please note that the receipt date for cooperative agreement applications in response to this RFA should be September 12, 1986, instead of August 29. Questions and requests for the complete RFA may be addressed to:

Thomas L. Robertson, M.D.
Chief, Cardiac Diseases Branch
Federal Building - 3C06
7550 Wisconsin Avenue
Bethesda, Maryland 20892
Telephone: 301 - 496-1081

DATED ANNOUNCEMENTS (RFPs and RFAs AVAILABLE)

RFP AVAILABLE - RFP-NIH-NIDDK-86-13

CONFERENCE AND SUPPORT SERVICES FOR THE NATIONAL KIDNEY AND UROLOGIC DISEASES ADVISORY BOARD

P.T. 42; K.W. 0901026

THIS ACQUISITION IS 100% SMALL BUSINESS SET-ASIDE

NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), has a requirement to provide logistical and technical support for the National Kidney and Urologic Diseases Advisory Board in carrying out its mandated functions which include the establishment of subcommittees, the convening of workshops and conferences, the collection of data, and the preparation of its annual report for the Secretary, DHHS.

This acquisition is under a 100% Small Business Set-Aside. Organizations responding to this requirement shall be located within the Washington, D.C. Metropolitan area.

This is an announcement for a Request for Proposal (RFP). RFP No. NIH-NIDDK-86-13 will be issued on or about June 30, 1986 with a closing date tentatively set for August 18, 1986. It is expected that the contract will have a two-year period of performance.

To receive a copy of this RFP, please supply this office with two self-addressed mailing labels. Requests must cite the RFP number referenced above and will be honored if received within twenty calendar days after the solicitation issue date. Since a limited number of copies will be printed, requests shall be filled on first-come, first-served basis, until the supply is exhausted. Requests for copies of the RFP should be sent to the following address:

Shirley A. Shores
Contracts Management Branch
National Institute of Diabetes and Digestive and Kidney Diseases
Westwood Building, Room 602
Bethesda, Maryland 20892

This advertisement does not commit the Government to make an award.

RFP AVAILABLE - RFP-NIH-NIAID-MIDP-87-8

DEVELOPMENT OF ADDITIONAL DRUGS FOR TREATMENT OF CANDIDIASIS

P.T. 34; K.W. 0710080, 0740025, 0715125

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

The Bacteriology and Virology Branch of the Microbiology and Infectious Diseases Program

The National Institute of Allergy and Infectious Diseases has a requirement for the development of additional drugs for the treatment of candidiasis. The successful offeror must have capabilities and facilities to evaluate potential anti-candida drugs, to utilize in vivo models for initial evaluation of the antimicrobials, to utilize in vivo models for final evaluation of the active antimicrobials and to evaluate the results obtained from the in vivo models.

This is an announcement for an anticipated Request for Proposal RFP-NIH-NIAID-MIDP-87-8 will be issued on or about July 14, 1986 with responses due on September 3, 1986.

Requests for the RFP should be directed to the Chief, Contract Management Branch, NIAID, NIH, Westwood Building, Room 707, Bethesda, Maryland 20892. Please provide this office with two (2) self-addressed mailing labels.

All responsible sources may submit a proposal which will be considered by NIAID.

This advertisement does not commit the Government to award a contract.

AVAILABILITY OF REQUEST FOR APPLICATIONS (RFA) - 86-HL-24

STUDIES OF OMEGA-3 POLYUNSATURATED FATTY ACIDS IN THROMBOSIS AND CARDIOVASCULAR DISEASE

P.T. 34; K.W. 0715040, 0710095, 0765010, 0765025, 0705040, 1002004, 1002008, 1003001

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Division of Blood Diseases and Resources Division of Heart and Vascular Diseases

Application Receipt Date: December 1, 1986

The Blood Diseases Branch of the Division of Blood Diseases and Resources and the Lipid Metabolism-Atherogenesis Diseases Branch of the Division of Heart and Vascular Diseases, National Heart, Lung, and Blood Institute (NHLBI), announce the availability of a Request for Applications (RFA) on the above subject. Copies of the RFA are currently available from staff of the NHLBI.

The program will support basic and clinical research addressing the effect of omega-3 polyunsaturated fatty acids on processes that may be involved in thrombosis and cardiovascular disease. It is expected that the research projects will encompass a broad range of approaches and will require expertise from a variety of disciplines including molecular and cellular biology, biochemistry, hematology, metabolism, morphology and physiology.

Requests for copies of the RFA should be addressed to:

Carol H. Letendre, Ph.D.
Blood Diseases Branch
Division of Blood Diseases and Resources
National Institutes of Health
Federal Building, Room 5A12
Bethesda, MD 20892
Telephone: (301) 496-5911

Montaz Wassef, Ph.D.
Lipid Metabolism-Atherogenesis Branch
Division of Heart and Vascular Diseases
National Institutes of Health
Federal Building, Room 4A12
Bethesda, Maryland 20892
Telephone: (301) 496-1978

ONGOING PROGRAM ANNOUNCEMENTS

AGING AND THE CARDIOVASCULAR SYSTEM

P.T. 34; K.W. 0710010, 0715040, 0785055, 0760040, 1002034, 0745055

NATIONAL INSTITUTE ON AGING

BACKGROUND

Cardiovascular diseases are the most common cause of death among the elderly, and the percentage of deaths due to cardiovascular disease increases with age throughout the later years of life. Age-related changes in cardiac function, circulatory hemodynamics, blood pressure regulation, and lipid metabolism contribute importantly to morbidity and mortality in the elderly. Age-related changes in such other factors as cardiac muscle, the conduction system of the heart, arterial compliance, the microvasculature and the rheologic behavior of blood may have major effects on cardiovascular function, and may, in turn, affect functions of other organ systems. Changes with age in pulmonary function and kidney function are also integrally related to cardiovascular function. Improved understanding of the causes, rates of progression, and interactions among these variables may lead to preventive and therapeutic interventions designed to reduce the incidence of cardiovascular disease in the elderly. Because of the need for information on all the above topics, the National Institute on Aging (NIA) has a continuing interest in supporting research on relationships between aging processes and cardiovascular function and disease.

RESEARCH GOALS AND SCOPE

The NIA encourages research on the causes of age-related cardiovascular changes (and changes in risk factors for cardiovascular disease) and on the role of cardiovascular factors in age-related physiologic and pathologic changes. Epidemiologic, clinical, and experimental studies involving humans and animals or in vitro systems are needed. Examples of research topics include:

- o Factors affecting the rate of change in diastolic and systolic blood pressure with age.
- o Factors regulating the changes with age in plasma lipids and lipoproteins.
- o Causes of orthostatic hypotension in older persons.
- o Causes of the rapid rise in cardiovascular mortality in the eighth and *ninth decades of life,*
- o Changes with age in structure and function of arteries and veins.
- o Causes of diminished arterial compliance and its effects on blood pressure and cardiac function.
- o Causes and effects of age-related changes in proliferative response of vascular smooth muscle cells.
- o Age-related changes in the rheologic behavior of blood.
- o Age-related changes in the microcirculation.
- o Causes and effects of age-related declines in cardiac sensitivity to catecholamines.
- o Age-related changes in the structure and function of the conduction system of the heart.
- o Relation of myocardial hypertrophy to aging.
- o Age-related changes in circulatory hemodynamics.
- o Relationship of blood pressure to changes in cognitive function in late life.
- o Changes with age in platelet adhesiveness, coagulation, and thrombolysis.

The research areas listed above are not intended to limit applications in any research area related to aging and the cardiovascular system. The NIA encourages innovative research in the epidemiology, prevention, and treatment of cardiovascular disease in the elderly, as well as mechanisms of age-related changes in the cardiovascular, renal, and pulmonary systems.

MECHANISMS OF SUPPORT

Applications may be submitted for any of the conventional NIH grant support mechanisms, including the individual research project grant, program project, Clinical Investigator, First Independent Research Support and Transition (FIRST) Research Career Development, and Physician Scientist Awards, and individual and institutional postdoctoral Research Service Awards (NRSAs). The above list is not exhaustive; potential applicants are encouraged to communicate with the NIA staff contact listed at the end of this announcement regarding funding mechanisms and project design. Potential applicants for program project awards should contact NIA staff very early in the planning stages.

APPLICATION AND REVIEW PROCEDURES

Applications should be submitted on PHS Form 398 (research grants), PHS Form 6025 (institutional NRSA), or PHS Forms 416-1, 416-2, and 415-3 (individual NRSA).

Applicants may obtain information and the appropriate application kits from their institution's grants office or by writing or calling:

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

Applicants should enter the phrase "NIA Program Announcement: Aging and the Cardiovascular System" in response to item 2 (Response to a Specific Program Announcement) on the first (face) page of their application.

Applicants are encouraged to notify the NIA staff listed at the conclusion of this announcement at least 30 days before sending the completed application to the Division of Research Grants (address below).

Applications should be submitted according to the deadlines for the appropriate review schedule and mailed to:

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

Applications will be reviewed for scientific merit in accordance with NIH policy and procedure involving peer review. Awards will be made on a competitive basis with all applications competing for NIA funding.

APPLICATION RECEIPT DATES

For institutional and individual NRSAs, and senior fellowships awards, the deadline dates are January 10, May 10, and September 10.

For all other awards, the deadline dates for new applications are February 1, June 1, and October 1. The deadlines for competing renewals of Research Project (R01) grants are March 1, July 1, and November 1. The deadlines for competing renewals of Program Projects are February 1, June 1, and October 1.

INQUIRIES AND CORRESPONDENCE

Correspondence, including requests for information and advice, should be directed to:

Lot B. Page, M.D.
National Institute on Aging
National Institutes of Health
Building 31, Room 5C-21
Bethesda, Maryland 20892
Telephone: (301) 496-1033

These programs are described in the Catalog of Federal Domestic Assistance No. 13.866, Aging Research. NRSAs will be supported under the authority of the Public Health Service Act, Section 472, 42 USC 2891-1, and administered under PHS grants policy and Federal Regulation 42 CFR Part 66. Other awards will be funded 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 the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

DETERMINATION OF THE THERAPEUTIC USEFULNESS OF MATURATION, DIFFERENTIATION AND ANTI-GROWTH FACTOR SUBSTANCES IN CANCER MODELS

P.T. 34; K.W. 0415000, 0740015, 0760020, 0755020, 0780015

NATIONAL CANCER INSTITUTE

The Biological Response Modifiers Program (BRMP), Division of Cancer Treatment (DCT), National Cancer Institute (NCI) invites grant applications from interested investigators for basic and applied studies concerned with the determination of the therapeutic usefulness of maturation, differentiation and anti-growth factor substance in cancer models. In making this program announcement it is not the intent of the NCI to make or imply any delimitation related to biological response modifiers research, but rather to stimulate investigator-initiated research in biological response modifiers related to cancer therapy.

BACKGROUND

This Program Announcement addresses maturation, differentiation and anti-growth factor substances. The area of developmental biology holds enormous potential for regulation of abnormal growth. For example, there are experiments that strongly suggest that normal embryonic products may permanently alter the phenotype of malignant cells. Terato-carcinoma cells introduced into a blastocyst are induced to differentiate into normal structures by factors acting locally in the embryo. Mullerian inhibition factor, the well-characterized protein responsible for determination of sex, appears active in vitro against human ovarian carcinoma. With the increasing evidence that oncogene products may play a role in normal differentiation, learning how the embryo regulates their sequential expression may be very useful to reestablish regulation in the human tumors in which disordered oncogene expression may be pathogenetic. The continuing progress being made in clarifying the mechanisms of regulation of bone marrow differentiation and the recognition of the existence of stem cell-like cells in the tumor directs attention to the possibility that tumor cell differentiation may be achieved through therapeutic means. In other words, the possibility exists that some factors exist which will not kill the tumor cells but will actually cause their further differentiation away from the malignant state. Peptide growth factors and certain other substances, have, for example, been shown to induce maturation (terminal differentiation) of tumor cells in vitro. Animal tumor models are needed to assess these substances as potential anticancer agents. Another area of possible application to therapy involves compounds directed against low molecular weight peptide growth factors. These factors which promote cell division and anchorage-independent growth of normal and transformed human cells in vitro and may be required for tumor growth in vivo have been recently identified and characterized. Suitable animal models need to be developed to assess the potential therapeutic efficacy of agents which specifically block these growth factors.

OBJECTIVES AND SCOPE

Studies are encouraged to develop transplanted or spontaneous animal tumor models to determine the therapeutic efficacy of anticancer agents which act by specifically blocking the actions of specific peptide growth factors. These factors might include both normal and tumor cell products. Of particular interest are animal tumors shown to be responsive in vitro to a peptide growth factor (for example epidermal growth factor) and agents shown to specifically block this same factor. In similar fashion an animal tumor model may be developed which can demonstrate the anticancer activity of maturation and differentiation factors which are capable of inducing terminal differentiation of various transformed cell lines in vitro. Examples of cell lines previously shown to be responsive to such agents include PC-12 pheochromocytoma cells and HL-60, Kg-1, and K 562 myeloid leukemia cells. Transplantable tumors of these, similar or newly developed cell lines might form the basis of a suitable animal tumor model focusing on therapeutic application.

STAFF CONTACT

For further information, investigators are encouraged to contact:

Dr. Carl M. Pinsky, Chief
Biological Resources Branch
Biological Response Modifiers Program
Division of Cancer Treatment
National Cancer Institute
Frederick Cancer Research Facility
Building 426 - Room 1
Frederick, MD 21701-1013
Telephone: (301) 698-1098

METHOD OF APPLYING

Non-profit organizations and institutions, governments and their agencies, for profit organizations, and individuals are eligible to apply. Applications should be submitted on form PHS 398, which is available in the grants and contracts business office at most academic and research institutions or from the Office of Grants Inquiries, Division of Research Grants (DRG), NIH. In space #2 on the first page of this form, indicate the title of the Program Announcement.

The original and six copies of the application should be sent or delivered to:

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

In order to alert the DCT to the submission of applications with primary thrust directed to biological response modifiers research, applicants are encouraged to send a brief letter of intent to Dr. Pinsky. Applications in response to this announcement will be reviewed in accordance with the usual National Institutes of Health (NIH) peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants. Following this initial review, the application will be evaluated for program relevance by an appropriate National Advisory Council/ Board. The review criteria customarily employed by the NIH for regular research grant applications will prevail. All PHS and NIH grant policies governing regular research project grants apply to applications received in response to this program announcement.

DEADLINE

Applications will be accepted in accordance with the usual NIH receipt dates for new applications. Deadline dates are: October 1, February 1, July 1.

This program is described in the Catalog of Federal Domestic Assistance No. 13.395, Cancer Treatment Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

PRECLINICAL STUDIES OF LAK PHENOMENON

P.T. 34; K.W. 0740015, 0415000, 1002015

NATIONAL CANCER INSTITUTE

The Biological Response Modifiers Program (BRMP), Division of Cancer Treatment (DCT) of the National Cancer Institute (NCI) invites grant applications from interested investigators for basic and applied studies concerned with preclinical studies of LAK phenomenon. In making this program announcement it is not the intent of the NCI to make or imply any delimitation related to biological response modifiers research, but rather to stimulate investigator-initiated research in biological response modifiers related to cancer therapy.

BACKGROUND

Recently, systemic administration of a biological response modifying (BRM) therapy to patients with cancer has resulted in consistent and reproducible antitumor effects. The preliminary results from the NCI's Surgery Branch using lymphokine activated killer (LAK) cell therapy has led to the development of a comprehensive plan in the Division of Cancer Treatment (DCT), including plans for both intramural and extramural clinical trials. In addition, considerable intramural work is underway preclinically. Some preclinical extramural research is underway, but in order to bring this approach to more rapid clinical application, additional research should be encouraged.

OBJECTIVES AND SCOPE

This Program Announcement is intended to encourage new extramural, investigator-initiated preclinical research in the lymphokine activated killer cell (LAK) phenomenon. The following is a list of areas felt to be potentially fruitful for new investigation: (1) therapeutic studies in additional experimental animal tumor systems, (2) combinations of LAK cells, IL-2 and standard therapy in established experimental animal tumor systems, (3) identification of the target on tumor cells that is recognized by LAK cells, and the receptor on the LAK cells which

recognizes the target, (4) studies to optimize LAK cell generation in experimental animals in vivo, after administration of IL-2, or other BRMs, (5) studies on human or experimental animal cells to optimize the ex vivo generation of LAK cells, (6) identification and purification of the LAK cell cytotoxic effector molecule, and (7) further study of the process by which LAK precursors are rendered cytotoxic. These are only a sampling of the areas in which research efforts may prove fruitful. The aim of this program announcement will be to encourage highly innovative research initiatives evaluating these, or other, promising leads. Eventually, concepts arising from these studies will be tested in clinical trials.

STAFF CONTACT

For further information, investigators are encouraged to contact:

Dr. Carl M. Pinsky, Chief
Biological Resources Branch
Biological Response Modifiers Program
Division of Cancer Treatment
National Cancer Institute
Frederick Cancer Research Facility
Building 426 - Room 1
Frederick, MD 21701-1013
Telephone: (301) 695-1098

METHOD OF APPLYING

Non-profit organizations and institutions, governments and their agencies, for profit organizations, and individuals are eligible to apply. Applications should be submitted on form PHS 398, which is available in the grants and contracts business office at most academic and research institutions or from the office of Grants Inquiries, Division of Research Grants (DRG), NIH. In space 2 on the first page of this form, indicate the title of the Program Announcement.

The original and six copies of the application should be sent or delivered to:

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

In order to alert the DCT to submission of applications with primary thrust directed to biological response modifiers research, applicants are encouraged to send a brief letter of intent to Dr. Pinsky.

Applications in response to this announcement will be reviewed in accordance with the usual National Institutes of Health (NIH) peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants. Following this initial review, the application will be evaluated for program relevance by an appropriate National Advisory Council/Board. The review criteria customarily employed by the NIH for regular research grant applications will prevail. All PHS and NIH grant policies governing regular research project grants apply to applications received in response to this program announcement.

DEADLINE

Applications will be accepted in accordance with the usual NIH receipt dates for new applications. Deadline dates are: October 1, February 1, June 1.

This program is described in the Catalog of Federal Domestic Assistance No. 13.395, Cancer Treatment Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

DETERMINATION OF THE THERAPEUTIC USEFULNESS OF PURIFIED CYTOKINES IN CANCER MODELS

P.T. 34; K.W. 0740015, 0755020, 0415000

NATIONAL CANCER INSTITUTE

The Biological Response Modifiers Program (BRMP), Division of Cancer Treatment (DCT), National Cancer Institute (NCI) invites grant applications from interested investigators for basic and applied studies concerned with the determination of the

therapeutic usefulness of purified cytokines in cancer models. In making this program announcement it is not the intent of the NCI to make or imply any delimitation related to biological response modifiers research, but rather to stimulate investigator-initiated research in biological response modifiers related to cancer therapy.

BACKGROUND

This Program Announcement addresses Cytokines. These factors are proteins and glycoproteins in the 5,000 to 100,000 molecular weight range. The cytokines obtained from lymphoid tissues or supernatants of mononuclear cell cultures are called lymphokines. Some have been shown to have direct cytotoxic or antiproliferative activity, some modulate and exert selective regulatory effects on various components of immune responses and others affect bone marrow proliferation, or ossification or vessel proliferation. Production and purification of cytokines have been a problem in the past. More recently, means have been developed to obtain cytokines from lymphoid lines in culture and use of genetic engineering technology to trans-pose genes into microbial organisms, thus, helping to resolve the problem. Administration of cytokines that can selectively activate or suppress certain components of the immune system may produce a beneficial anti-tumor effect in vivo.

OBJECTIVES AND SCOPE

Studies to be proposed should evaluate the therapeutic value of defined cytokines in anti-tumor immunity. Currently available cytokines, purified to near homogeneity, may be used in both in vivo and in vitro studies to evaluate and monitor specific effects on the various cellular components of the anti-tumor response. A further stage of analysis could involve testing the therapeutic efficacy of various cytokine preparations in transplantable and spontaneous animal tumor models. Investigators may restrict their study to a single cytokine or may wish to perform comparative studies on various cytokines. A goal of the studies should be to provide information relevant to the choice of a Cytokine(s) for preliminary clinical testing and the type(s) of tumor host relationship most amenable to effective biological modification using cytokines.

STAFF CONTACT

For further information, investigators are encouraged to contact:

Dr. Carl M. Pinsky, Chief
Biological Resources Branch
Biological Response Modifiers Program
Division of Cancer Treatment
National Cancer Institute
Frederick Cancer Research Facility
Building 426 - Room 1
Frederick, MD 21701-1013
Telephone: (301) 695-1098

METHOD OF APPLYING

Non-profit organizations and institutions, governments and their agencies, for profit organizations, and individuals are eligible to apply. Applications should be submitted on form PHS 398, which is available in the grants and contracts business office at most academic and research institutions or from the Office of Grants Inquiries, Division of Research Grants (DRG), NIH. In space 2 on the first page of this form, indicate the title of the Program Announcement.

The original and six copies of the application should be sent or delivered to:

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

In order to alert the DCT to the submission of applications with primary thrust directed to biological response modifiers research, applicants are encouraged to send a brief letter of intent to Dr. Pinsky.

Applications in response to this announcement will be reviewed in accordance with the usual National Institutes of Health (NIH) peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants. Following this initial review, the application will be evaluated for program relevance by an appropriate National

Advisory Council/Board. The review criteria customarily employed by the NIH for regular research grant applications will prevail. All PHS and NIH grant policies governing regular research project grants apply to applications received in response to this program announcement.

DEADLINE

Applications will be accepted in accordance with the usual NIH receipt dates for new applications. Deadline dates are: October 1, February 1, and July 1.

This program is described in the Catalog of Federal Domestic Assistance No. 23.395, Cancer Treatment Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 73-410, 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 the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

USE OF ONCOGENE RELATED PRODUCTS FOR CANCER THERAPY

P.T. 34; K.W. 0740015, 0415000, 0760045, 1002015

NATIONAL CANCER INSTITUTE

The Biological Response Modifiers Program (BRMP), Division of Cancer Treatment (DCT) of the National Cancer Institute (NCI) invites grant applications from interested investigators for basic and applied studies concerned with the use of oncogene related products for cancer therapy. In making this program announcement it is not the intent of the NCI to make or imply any delimitation related to biological response modifiers research, but rather to stimulate investigator-initiated research in biological response modifiers related to cancer therapy.

BACKGROUND

This Program Announcement addresses use of oncogene and oncogene-related products for cancer therapy in animal models. A number of cellular genes collectively called "proto" oncogenes have been identified which are involved in the control of cellular proliferation and differentiation and have been shown to be direct mediators of cell transformation. Activation of these cellular genes as oncogenes appears to play an important role in both initiation and maintenance of oncogenesis. Several "proto" oncogenes have been identified in the human genome and a number of these have been found to be expressed in the activated form in various human tumors. In tissue culture, inhibition of oncogene activity appears to be associated, in several instances, with reversion of the transformed state. Where functional products of oncogenes have been described, they have been localized to the cell membrane, cytoskeletal elements, or the nucleus. These all represent areas where alterations might be expected to lead to the expression of a malignant phenotype, such as lack of contact inhibition and uncontrolled cell division. Expansion of knowledge of how biological response modifiers and oncogenes interact through investigator-initiated research could provide useful information for the future understanding of how oncogenesis is initiated and maintained and how immunity may be enhanced towards specific oncogene induced malignancies.

OBJECTIVES AND SCOPE

This Program Announcement is intended to stimulate research that will develop and utilize oncogene products or reagents made against these products for therapy in animal model systems. Development of oncogene or oncogene-related products for therapeutic evaluation may involve use of tumor-associated membrane antigens for monoclonal antibody production and development of vaccines, use of monoclonal antibodies directed against growth factors or growth factor receptors controlled by or encoded by oncogenes or analysis of factors that inhibit the action of oncogene products that control cell division. Other reasonable approaches directed toward cancer therapy employing oncogene or oncogene-related products or related reagents with antitumor potential may be proposed. Studies may involve the isolation and characterization of these products for the purpose of evaluating their ability to modify or alter tumor initiation, growth and/or metastases as well as stimulating cytotoxicity in vivo or in vitro through activation of macrophages, cytotoxic T cells or natural killer cells. Additional proposals involving studies on how oncogene or oncogene-related products may interfere with specific immune functions will also be considered. Therapeutic potential may be evaluated in the treatment of transplanted, induced or spontaneous animal tumors or human tumor xenografts in nude athymic mice or rats.

STAFF CONTACT

For further information, investigators are encouraged to contact:

Dr. Carl M. Pinsky, Chief
Biological Resources Branch
Biological Response Modifiers Program
Division of Cancer Treatment
National Cancer Institute
Frederick Cancer Research Facility
Building 426 - Room 1
Frederick, MD 21701-1013
Telephone: (301) 695-1098

METHOD OF APPLYING

Non-profit organizations and institutions, governments and their agencies, for profit organizations, and individuals are eligible to apply. Applications should be submitted on form PHS 398, which is available in the grants and contracts business office at most academic and research institutions or from the Office of Grants Inquiries, Division of Research Grants (DRG), NIH. In space #2 on the first page of this form, indicate the title of the Program Announcement.

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Westwood Building, Room 240
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In order to alert the DCT to the submission of applications with primary thrust directed to biological response modifiers research, applicants are encouraged to send a brief letter of intent to Dr. Pinsky.

Applications in response to this announcement will be reviewed in accordance with the usual National Institutes of Health (NIH) peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants. Following this initial review, the application will be evaluated for program relevance by an appropriate National Advisory Council/Board. The review criteria customarily employed by the NIH for regular research grant applications will prevail. All PHS and NIH grant policies governing regular research project grants apply to applications received in response to this program announcement.

DEADLINE

Applications will be accepted in accordance with the usual NIH receipt dates for new applications. Deadline dates are: October 1, February 1, June 1.

This program is described in the Catalog of Federal Domestic Assistance No. 13.395, Cancer Treatment Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.