NIH GUIDE for GRANTS and CONTRACTS

Department of Health and Human Services
Vol. 10, No. 11, October 9, 1981

IN THIS ISSUE:

(Continued)

HAVE YOU MOVED?

If your present address differs from that shown on the address label, please send your new address to: Grants and Contract Guide Distribution Center, National Institutes of Health, Room B3BN10, Building 31, Bethesda, Maryland 20205, and attach your address label to your letter. Prompt notice of your change of address will prevent your name from being removed from our mailing list.

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.

Index (Continued)

NOTICE

CHANGE IN PUBLICATION DATE

The July 1981 issue of NIH Public Advisory Groups: Authority, Structure, Functions, Members will not be published this year. The January 1982 issue will be published as usual.

NOTICE

NEW RESEARCH AND RESEARCH TRAINING PROGRAM ANNOUNCEMENTS

NOW AVAILABLE

ALCOHOL, DRUG ABUSE, AND MENTAL HEALTH ADMINISTRATION

These program announcements provide current information about areas in which support is available from the ADAMHA Institutes.

Potential applicants for research grants and for National Research Service Awards may obtain these updated program announcements:

1. Mental Health Research Support Programs
2. Alcohol Research Grants
3. Alcohol Research Centers Grants
4. Drug Abuse Research Grants
5. ADAMHA National Research Service Awards for individual Fellows
6. ADAMHA National Research Service Awards for Institutional Grants

Contact the following offices at agency headquarters, Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA), 5600 Fishers Lane, Rockville, Maryland 20857:

NATIONAL INSTITUTE OF MENTAL HEALTH
Public Inquiries Section
Room 11A-21

NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM
Office of Public Affairs
Room 16-95

NATIONAL INSTITUTE ON DRUG ABUSE
Office of Communications and Public Affairs
Room 10A-56

NOTICE

CORRECTION

INDIVIDUAL NRSA FELLOWSHIP APPLICATIONS

A program announcement for National Research Service Awards for "Clinical Studies of Chemosensory Disorders" (Vol. 10, No. 10, September 4, 1981, pp. 26-28) instructed prospective applicants to use PHS Forms 416-1, 416-2, and 416-3 for Individual Postdoctoral Fellowship applications. Please be advised that Form 416-2 ("Facilities and Commitment Statement") was incorporated.

NOTICE

CANCER THERAPY EVALUATION PROGRAM

TITLE: RESEARCH CLINICAL TRIALS PROGRAM

NATIONAL CANCER INSTITUTE

The Division of Cancer Treatment of the National Cancer Institute announces that its research clinical trials program (phases II, III, and IV), currently funded by R10 grants and contracts, will in the future be entirely supported by cooperative agreements. The Institute is taking this step following a thorough review of the research clinical trials program in the light of recent legislation governing the selection of Federal funding instruments (the Federal Grant and Cooperative Agreement Act, P.L. 95-224). That legislation specifies that support or stimulation of an activity authorized by Federal statute is to be funded by an assistance mechanism (i.e., grant or cooperative agreement), and further provides that the cooperative agreement is to be used when substantial involvement on the part of the funding agency is anticipated during the performance of the activity.

The DGT research clinical trials are assistance relationships entailing substantial and defined involvement with NCI staff. Specifically a designated NCI staff person will assist in coordinating the activities of the group and will be responsible for monitoring the group's progress. The precise details of this collaboration will be spelled out in a "terms of award statement" which will form the basis for the cooperative agreement and will be appended to each notice of award. Prospective applicants may contact NCI for information regarding specific features of these awards.

NCI anticipates converting all current R10 grants and research clinical trials contracts to Cooperative Agreements. Future applications for any new cooperative clinical trials efforts will be funded under this mechanism; applications for new R10 grants will no longer be accepted. The funding and length of each award application will be developed from the recommendations of the technical peer review committee and the National Cancer Advisory Board.

The terms and conditions of the award will be governed by Federal regulations, Title 45, Part 74 (Administration of Grants). The Public Health Service Grants Policy Statement will apply to awards made under this program. Work under this program will be monitored by government program directors. They will receive all required progress reports and determine whether satisfactory progress is, in fact, being made

ANNOUNCEMENT

RESEARCH FELLOWSHIPS TO SWEDEN, SWITZERLAND AND FRANCE

FOGARTY INTERNATIONAL CENTER

The Fogarty International Center, National Institutes of Health, has been requested to announce that the Swedish Medical Research Council, the Swiss National Science Foundation, and the French National Institute of Health and Medical Research (INSERM) will each make available in 1982 several research fellowships to qualified U.S. biomedical scientists. These fellowships will provide postdoctoral training in basic or clinical areas of medical research.

These programs are administered by the Fogarty International Center (FIC).

ELIGIBILITY

Applicants must meet the following requirements:

Be a U.S. citizen or permanent U.S. resident.

Hold a doctorate degree in one of the biomedical sciences or related fields.

Have had professional experience in the health or biomedical sciences of at least two of the last four years.

Have had less than 10 years of postdoctoral experience.

SUPPORT

Under the agreements with each country, the awarding country's institution will provide for all international transportation costs to the place of assignment and will pay the awardee's stipend.

DURATION OF PARTICIPATION

The starting date of the fellowship is usually set by mutual agreement of the applicant and the institution. Fellowships are normally for 12 months, but exceptions may be considered.

APPLICATION AND SELECTION

Specific application information and material are available from the Fogarty International Center. In addition to biographical information, the applicant must provide evidence of acceptance by a training institution and preceptor under whom he will train. A research plan should be developed with the preceptor and presented clearly and explicitly in the application.

After an initial review by the Division of Research Grants, the applications will be sent for final selection and awarding to the appropriate country. Applicants will be notified by the appropriate country of the selection decision.

The deadline for receipt of application is December 1, 1981. All correspondence concerning these fellowships must be clearly marked as "Swedish Medical Research Council," "Swiss National Science Foundation," or "INSERM."

INQUIRIES AND APPLICATION MATERIALS

International Research and Awards Branch
Fogarty International Center
National Institutes of Health
Bethesda, Maryland 20205

Telephone: (301) 496-1653

ANNOUNCEMENT

EXTRAMURAL ASSOCIATES PROGRAM

NATIONAL INSTITUTES OF HEALTH

Application receipt date: January 31, 1982

The National Institutes of Health (NIH) invites nominations for the 1982-83 Extramural Associates Program to promote the entry and participation of ethnic minorities and women in NIH-supported research.

Temporary appointments of employees between Federal executive agencies, state and local governments, institutions of higher education, and Indian tribal governments, can be effected under the Intergovernmental Personnel Act (IPA) of 1970 (Public Law 91-648). In recent years, significant numbers of personnel from academic institutions have used the IPA mechanism to gain thorough knowledge of research concerns of the NIH, the support through which this research is being accomplished, and the policies and procedures which govern the awarding of grants and contracts. Yet institutions which traditionally contribute to the basic preparation of minorities and women for biomedical science are not utilizing this opportunity to an equal extent. While not excluding any individuals or institutions from the available options under the IPA, the NIH Extramural Associates Program was specially established to redress a noticeable imbalance in the current use of an available opportunity.

The NIH will invite two groups of up to eight key science administrators from schools which contribute significantly to the pool of minorities and women in science, to spend five months in residence in the Washington, D.C. area. Salary and related expenses will be reimbursed by the NIH to the limit allowed under the IPA. In addition, a per diem allowance will be provided to cover the normal cost of living while in Washington, D.C.

While in the Program, the Associates will work in rotating assignments with senior staff members at the NIH and other Federal agencies. They will attend seminars, committee meetings, workshops, site visits and will have the opportunity to gain information concerning legislative, budgetary and other Federal health-related programs associated with grant and contract activities.

The NIH expects that such information will primarily benefit the institutions from which the Associates come, in that they will be the lead resource administrators from whom faculty and students can obtain information about health research programs funded by the NIH. In addition, the NIH expects immediate benefits from the special contributions to be made by these experienced administrators while at the NIH.

Nominations of a candidate will be accepted from the president or an equivalent official of an eligible institution. In addition to the general requirements of the IPA, emphasis for selection of Associates will be on the demonstrated contribution of an institution to the advancement of ethnic minorities and women; on its plan to utilize the Associate's newly gained knowledge; and on the qualifications, experience and interest of the nominee.

All Associates will be required to participate in the program for five months beginning on or about August 1, 1982 or February 1, 1983. **Nominations and completed applications are due by January 31, 1982;** selections will be announced by April 30, 1982.

Additional information concerning the program or the application process may be obtained by writing or calling:

Mrs. Jean G. Oliver, Director
Extramural Associates Program
National Institutes of Health
Building 31, Room 1B59
9000 Rockville Pike
Bethesda, Maryland 20205

Telephone: (301) 496-9728

ANNOUNCEMENT

BIOMEDICAL RESEARCH SUPPORT GRANT APPLICATIONS FOR FISCAL YEAR 1982

DIVISION OF RESEARCH RESOURCES

Application receipt date: January 1, 1982

BACKGROUND INFORMATION

The Biomedical Research Support Grant (BRSG) Program is specifically designed to provide funds on a continuing basis to eligible institutions heavily engaged in health-related research to strengthen their programs by allowing flexibility available to the institutions to meet emerging opportunities in research; to explore new and unorthodox ideas; and to use these research funds in ways and purposes which they (the institutions), in their judgment feel would contribute effectively to the furtherance of their research program.

ELIGIBILITY

Awards are made to non-profit institutions not directly to individual investigators. Health professional schools, other academic institutions, hospitals, state and municipal health agencies, and research organizations may apply if the institution received a minimum of three allowable PHS biomedical or health-related behavioral research grants, totaling $200,000 (including direct and indirect costs), awarded during FY 1981 (October 1, 1980 through September 30, 1981). Federal institutions and institution
s located in a foreign country are not eligible.

NOTE: Other academic includes, as a single eligible component, all other schools, departments and free-standing institutes of the institution except the health professional schools.

AWARD CONDITIONS

The BRSG award is for one year and must be renewed annually. The start date is April 1. It is estimated that approximately 500 BRSG awards will be made in FY 1982.

The amount of each BRSG award is based upon a formula that is applied to the total of direct and indirect costs awarded for allowable PHS research grants.

The BRSG program is described in the Catalog of Federal Domestic Assistance, Number 13.337, Biomedical Research Support. 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 45 CFR Part 74 and the Biomedical Research Support Grant Information Statement and Administrative Guidelines. This program is not subject to A-95 Clearinghouse or Health Systems Agency Review.

METHOD OF APPLYING

BRSG application kits (Form NIH-147-1) will be mailed on or about November 27 to all current BRSG grantees.

Completed BRSG applications must be received by January 1, 1982.

If an institution believes that it has become eligible to apply for the BRSG program, please write or call:

Biomedical Research Support Program
Division of Research Resources
Office of Grants and Contracts Management
National Institutes of Health
Bethesda, Maryland 20205

Attention: Mrs. Gilda Polletto
Grants Management Specialist

Telephone: (301) 496-5131

REQUEST FOR RESEARCH GRANT APPLICATION: RFA

NHLBI-DLD-82G-A

IMMUNE RESPONSES IN THE LUNG UNDERLYING INTERSTITIAL PULMONARY FIBROSIS

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: January 15, 1982

I. BACKGROUND INFORMATION

Inhalation of organic or inorganic agents or microorganisms can be the initiating event in the development of fibrotic lung disease. It is probably no coincidence that such exposure can also result in a variety of immunologic reactions within the lung. In hypersensitivity pneumonitis (an example of which is farmer's lung disease), the production of antibody against the offending inhaled agent is known to be an important element in the development of the disease. In other fibrotic lung diseases, an immunologic component is strongly suspected, but evidence of direct immunologic involvement is missing. For example, in silicosis and asbestosis, direct evidence for implication of immune cells or cell products in the lesion is absent, although autoantibodies (including antinuclear antibody and rheumatoid factor) have been observed in the serum of many of the patients with these diseases. Despite the apparent close association between immunologic activities within the lung and fibrotic lung disease, relatively little research is being carried out to understand the basic immune responses of the lung or their relationship to pulmonary fibrosis.

There is evidence that the lung functions at least to some degree as an independent "lymphoid organ" although interactions with systemic immunologic organs are also evident. The lung can express its immunologic capabilities in numerous ways, such as through the development of locally produced antibodies, activated phagocytic cells, or sensitized lymphocytes, the last being capable of mediating immunologic activities either directly or through mediator molecules. Although a number of studies have examined immune mechanisms in the lung including local responses, attendant macrophage-lymphocyte interactions, and the types of lymphocytes present in the lung in various pulmonary disease states, these processes are still poorly understood. In addition, it is not known whether animal species used in these studies develop immunity in the lung by the same mechanisms as in man. A better understanding of the underlying immunologic processes, including precise elucidation of early initiating as well as resultant (effector) immune events and pathways in the lung and the relationship of these processes to pulmonary fibrosis, is required in order to better diagnose, treat, and prevent these diseases.

This program is described in the Catalog of Federal Domestic Assistance, No. 13.838, Lung Diseases. 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.

In characterizing immune responses in the lung, many studies in the past have used agents (e.g., sheep red blood cells) or doses which one would not ordinarily expect to encounter, particularly in a disease situation. It is anticipated that applications submitted in response to this announcment will address these considerations.

II. GOALS AND SCOPE

The specific goal of this program is to encourage the submission of research grant applications which will contribute to the elucidation of the processes by which the lungs initiate and develop immune reactions prior to or during pulmonary fibrosis. Proposed research should include studies designed to increase understanding of initiating events during the response of the lung to potentially pathogenetic substances. It is also important that interactions among the pulmonary and extrapulmonary lymphoid elements be elucidated since such interactions are probably an integral part of the response. In animal studies, it is important that consideration be given to the species of animal, noting differences from man. For example, the amount of bronchus-associated lymphoid tissue is high in some animals (rats and rabbits) but low in others (dogs); it is also low in man. Such differences must be considered in making the extrapolation from animal studies to human disease states. A general approach might include one or more of the following topics:

A. Origin of immune cells found in the lung and interactions between pulmonary and extrapulmonary lymphoid tissue

Because of the apparent relationship between the immunologic activities within the lung and interstitial fibrosis, the basic mechanisms by which immunity is produced in the lung parenchyma need to be clearly understood. There are suggestions that the lung can respond independently of the rest of the body to immunologic stimuli, and this compartmentalization needs to be further defined, for example, by studying the regional response to a highly localized stimulus using known pathogenetic agents. Experimental approaches are encouraged which address the full array of local responses as well as the interaction between local (pulmonary) and systemic, humoral and cellular responses to these agents in order to define the interrelationships between these anatomic entities. One approach might be to determine what role, if any, the bronchus-associated lymphoid tissue plays in the production of immune cells and antibody in the lung parenchyma after antigenic stimulation during the disease process. Research is also needed to clarify the sources of lymphoid cells in the parenchyma, routes taken by these cells in reaching the parenchyma, and the mechanisms by which they are attracted to the area. Studies are needed which would investigate the immunologic responses which take place following well-defined, local instillation of agents known or thought to be pathogenetic.

B. Entrance, processing, and clearance of pathogenetic agents in the lung

It is important to establish the defense mechanisms by which the lung attempts to deal with agents which may cause interstitial lung disease. Clearance of these agents is undoubtedly linked with immune responses as well as with pathologic processes and therefore warrants further study. It is likely that clearance mechanisms within the lung will vary widely depending on the physical and chemical properties of the agent, and studies should examine a spectrum of agents in order to establish the variety of possible mechanisms. The role of various components on the air side of the alveolus including, but not limited to, macrophages, alveolar fluids, and solutes within the fluids (e.g., immunoglobulins), needs to be investigated. In addition, it would be important to establish the form in which substances reach the lower airways and the interstitium as well as the "processing" prior to or after reaching those locations.

C. The alveolar macrophage as a regulatory cell in pulmonary immune responses

The alveolar macrophage may be an important participant in the development of mineral dust pneumoconioses as well as other forms of interstitial lung disease. While it is clear that this cell is involved in the clearance of inhaled particles and very likely produces damage to the lung parenchyma through release of lysosomal enzymes, its importance in various immunologic sequences after exposure to pathogenetic agents remains to be defined. Both immunologic suppressor and helper functions have been ascribed to the alveolar macrophage, suggesting a role for this cell in the development of lung immunity. Therefore, studies are needed to clarify the activities of the macrophage and to relate such findings to the etiology and pathogeneses of interstitial lung disease.

The research topics presented above are provided only to indicate the scope of research that would meet the goals of this program. Investigators are not restricted to these approaches nor do they have to include all of them in a single proposal. Investigators are encouraged to consider other approaches. The emphasis of the proposal, however, must be specifically directed toward elucidating the immune responses in the lung to agents known or thought to produce fibrotic lung disease in man, when administered in doses which realistically mimic natural exposure. Studies of local production of secretary immunoglobulin, IgA, will not be acceptable since pulmonary production of this antibody appears to be limited to the airways, and there is no evidence to suggest an etiologic role for IgA in interstitial lung disease. The other immunmoglobulin classes, however, particularly IgG and IgE, are appropriate for study. This program will support only studies of immune responses in the lung or interactions between pulmonary and generalized immune systems. Proposals to study only systemic reponses to substances, even if delivered by a pulmonary route, will not be considered responsive to this RFA.

III. MECHANISM OF SUPPORT

The support mechanism for this program will be the NIH grant-in-aid; successful applicants will plan and execute their own research program. Upon initiation of the program, the Division of Lung Diseases will sponsor periodic workshops to encourage exchange of information among investigators who participate in this program. Prospective grantees should include in their grant applications a statement indicating their willingness to participate in such information exchange activities.

Although this program is included and provided for in the financial plans for Fiscal 1982, award of grants pursuant to this request for grant applications is contingent upon receipt of appropriate funds for this purpose. It is anticipated that four to six proposals will be aches would represent valid responses to this announcement, it is anticipated that there will be a range of costs among individual grants awarded. However, it is not the intent of this request to solicit proposals for large multidisciplinary studies encompassing a variety of essentially independent research project. Applicants are requested to furnish their own estimates of the time required to achieve the objectives of the proposed research project; however, the award for this proposal must not exceed 5 years. At the end of the initial award period, renewal proposals may be submitted for further competitive review. It is anticipated that support will begin on July 1, 1982.

The current policies and requirements which govern the research grant programs of the National Institutes of Health will prevail, including the requirement for cost sharing.

IV. REVIEW PROCEDURES AND CRITERIA

Upon receipt, applications will be reviewed for their responsiveness to the specific objectives described in this announcement. If an application is judged unresponsive, the applicant will be contacted and given an opportunity to withdraw the application or to submit it for consideration in the regular review cycle of the NIH. Initial technical merit review will be arranged by the Division of Research Grants (DRG). Secondary review will be undertaken by the National Heart, Lung, and Blood Advisory Council in May 1982.

Because the underlying theme of this RFA is also of interest to the National Institute of Allergy and Infectious Diseases (NIAID), it is possible that secondary assignment of applications received in reponse to this RFA may be made to that institute by the DRG.

If a proposal submitted in response to this RFA is identical to a research grant application already submitted to the NIH for review, the applicant will be asked to withdraw the pending application before the new one is accepted. Simultaneous submission of identical applications will not be allowed.

The factors to be considered in the scientific merit evaluation of each application will be identical to those used in traditional NIH research grant application evaluation, including an assessment of the importance of the proposed research problem; the novelty and originality of the approach; the training, experience, and research competence or promise of the investigator(s); the adequacy of the experimental design; the suitability of the facilities; and the appropriateness of the requested budget relative to the work proposed.

V. METHOD OF APPLYING

1. Letter of Intent

Prospective applicants are asked to submit a brief letter of intent which would include a synopsis of the proposed research as well as the names of other institutions which might collaborate on the project. The Institute requests such letters only to obtain an indication of the number and scope of applications to be received. A letter of intent is not a requirement for application, nor is it binding, and information provided in the letter will not enter into the review of any application subsequently submitted.

To be useful to the Institute, the letter of intent should be sent by December 1, 1981, and should be addressed to Dr. Hugh B. Stamper, Jr., Division of Lung Diseases, National Institutes of Health, Westwood Building, Room 6A05, Bethesda, Maryland 20205.

2. Format for Applications

Applications should be submitted on the standard research grant application form, PHS-398 (Revised 5/80), which may be obtained at the applicant's institution business or research office. If form PHS-398 is not available at the institution, it may be obtained by contacting the Division of Research Grants, Office of Grants Inquiries, Room 449, Westwood Building, Bethesda, Maryland 20205, phone (301) 496-7591. The conventional presentation in format and detail for regular research grant applications should be utilized.

3. Application procedure

The completed 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 must be received by January 15, 1982.

The face page of the application must be labeled to indicate that it is submitted in response to this program announcement: RFA-NHLBI-DLD-82G-A, "Immune Responses in the Lung Underlying Interstitial Pulmonary Fibrosis."

VI. INQUIRIES

Inquiries may be directed to Dr. Hugh B. Stamper, Jr., Division of Lung Diseases, National Institutes of Health, Westwood Building, Room 6A05, Bethesda, Maryland 20205. Telephone: (301) 496-7034.

Applicants may also wish to alert the NIAID of the submission of applications of possible interest to that institute by contacting Dr. Robert A. Goldstein, Immunologic, Allergic and Infectious Diseases Program, National Institutes of Health, Westwood Building, Room 752, Bethesda, Maryland 20205.

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NIH-NCI-DCT-BRMP-81-5

MONOCLONAL ANTIBODY IN CANCER THERAPY

NATIONAL CANCER INSTITUTE

Application receipt date: December 15, 1981

The Division of Cancer Treatment of the National Cancer Institute (NCI) invites grant applications from interested investigators for basic and applied studies to evaluate the therapeutic effectiveness of monoclonal antibody administration in man.

Grants are awarded only to 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 National Institutes of Health (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 NIH Initial Review Group.

The present RFA announcement is for a single competition with a specified deadline of December 15, 1981, for receipt of applications. Applications should be prepared and submitted in accordance with the aims and requirements described in the following sections:

I. BACKGROUND INFORMATION

Biological response modifiers refers to agents or approaches that alter the relationship between tumor and host by modifying the host's biological response to tumor cells, with a resultant therapeutic benefit. The application of these agents with a primary intent of therapy is the major focus of the Biological Response Modifiers Program.

This program is described in the Catalog of Federal Domestic Assistance number 13-395, Cancer Treatment 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.

The components of the BRM program include immunoaugmenting agents, immunomodulating treatments, immunorestorative agents, interferon inducers; interferon and cytokine factors; thymic hormones and factors; tumor antigens and cell surface modifiers, anti-tumor antibodies, antitumor immune cells; maturation and differentiation factors.

This RFA addresses the component anti-tumor antibodies and specifically hybridoma derived monoclonal antibodies. Experimental studies have been carried out on the therapeutic effects of anti-tumor antibodies in animal models and, to a lesser extent, in man. Such studies have been hampered in animals by the lack of potent antibody and in man by the lack of solid evidence for the presence of tumor specific antigens and therefore for the anti-tumor specificity of the antibody employed. The recent utilization of hybridomas for the production of monoclonal antibodies should help in identifying human tumor antigens. It may also provide large quantities of highly specific high-titered antitumor antibody for possible therapeutic testing. Monoclonal antibodies provide a chemically and immunologically homogeneous reagent of defined specificity. They can be obtained in quantities necessary for therapeutic evaluation in man either as a means of selectively eliminating tumor populations directly or indirectly by eliminating or inactivating suppressor cellular components of the immune system.

II. OBJECTIVES AND SCOPE

Studies to be proposed should evaluate the therapeutic effectiveness of monoclonal antibody administration in man. Monoclonal antibodies directed against specific antigens expressed on human tumor cells or on lymphoid cells suppressing an effective anti-tumor immune response may be evaluated alone or coupled with drugs, toxins, or radioisotopes to determine the pharmacokinetics, clinical toxicity, potential efficacy as anti-cancer agents and maximum tolerated dose that can be administered parenterally. Parameters to be monitored following administration of monoclonal antibody preparations as therapeutic agents could include degree and specificity of binding to target cells, fate of antibody bound tumor cells, modulation of target antigen and alterations in circulating tumor cells and tumor antigen.

III. MECHANISM OF SUPPORT

This RFA will use the 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 several projects, with total costs amounting to approximately $1.323 million for the first year. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. Also, although this program is provided for in the financial plans of the National Cancer Institute, the award of grants pursuant to this RFA is contingent upon the 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 Division of Research Grants, National Institutes of Health, and (2) the National Cancer Advisory Board. All applications will be evaluated by a single review group in competition with each other.

Future renewal applications will not compete for earmarked funds. Instead, all renewal applications will be considered as unsolicited grant applications which will compete with all other unsolicited applications received by NIH.

B. Review Criteria

Applications must be responsive to this RFA, in the sense of being directed towards the attainment of the stated programmatic goals (see II. OBJECTIVES AND SCOPE). If the application is judged by the National Cancer Institute not to be responsive, the applicant will have the opportunity of having the application considered along with other unsolicited applications received by the National Institutes of Health.

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

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

2. Research experience and competence of the Principal Investigator and staff to conduct the proposed studies.

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

4. Adequacy of existing/proposed facilities and resources. Applications which specify a proposed use of human cells/tissues/fluids/excreta, need to provide assurance and details concerning the nature, source, and availability of those specimens.

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

6. Reasonableness of proposed costs.

V. METHOD OF APPLYING

A. Format of Applications

Applications must be submitted on form PHS 398 (Revised 5/80), 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 in format and detail 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-DCT-BRMP-81-5 MONOCLONAL ANTIBODY IN CANCER THERAPY" should be typed in bold letters across the top of the face page of the application.

B. Application Procedure

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

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

To ensure their review, applications must be received by December 15, 1981. Applications received after that date will be returned. 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. Long at the address shown below.

VI. INQUIRIES MAY BE DIRECTED TO;

Dr. Cedric Long
Biological Resources Branch
Biological Response Modifiers Program
Division of Cancer Treatment
National Cancer Institute
Landow Building, Room 8C03
Bethesda, Maryland 20205

Telephone: (301) 496-9664

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NIH-NCI-DCT-BRMP-81-6

MONOCLONAL ANTIBODY IN ANIMAL TUMOR MODELS

NATIONAL CANCER INSTITUTE

Application receipt date: December 15, 1981

The Division of Cancer Treatment of the National Cancer Institute (NCI) invites grant applications from interested investigators for basic and applied studies to evaluate the therapeutic efficacy of monoclonal antibody administration in animal tumor models.

Grants are awarded only to 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 toencourage invetigator-initiated research projects in areas of special importance to the National Cancer Program. Applicants funded under the RFA are supported through the customary National Institutes of Health (NIH) grant-in-aid, in accordance with PHS policies applicable to Reserch 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 NIH Initial Review Group.

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This program is described in the Catalog of Federal Domestic Assistance number 13-395, Cancer Treatment 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.

The components of the BRM program include immunoaugmenting agents, immunomodulating treatments, immunorestorative agents, interferon inducers; interferon and cytokine factors; thymic hormones and factors; tumor antigens and cell surface modifiers, anti-tumor antibodies, anti-tumor immune cells; maturation and differentiation factors.

This RFA addresses the component anti-tumor antibodies and specifically hybridoma derived monoclonal antibodies. Experimental studies have been carried out on the therapeutic effects of anti-umor antibodies in animal models and, to a lesser extent, in man. Such studies have been hampered in animals by the lack of potent antibody and in man by the lack of solid evidence for the presence of tumor specific antigens and therefore for the anti-tumor specificity of the antibody employed. The recent utilization of hybridomas for the production of monoclonal antibodies should help in identifying tumor antigens on animal tumor. It may also provide large quantities of highly specific high-titered anti-tumor antibody for possible therapeutic evaluation in a variety of animal systems as a means of selectively eliminating tumor populations directly or indirectly by eliminating or inactivating suppressor cellular components of the immune system.

II. OBJECTIVES AND SCOPE

Studies to be proposed should evaluate the therapeutic efficacy of monoclonal antibody administration in animal tumor models. Currently available monoclonal antibodies directed against specific antigens expressed on tumor cells or on lymphoid cells suppressing an effective anti-tumor immune response may be evaluated either alone or coupled with drugs, toxins, or isotopes for in vivo anti-tumor properties. Therapeutic potential of these antibodies may be evaluated in the treatment of transplanted, induced and spontaneous animal tumors or human tumor xenographs in nude athymic mice. Studies may examine such parameters as: effects of passive administration of antibody or antibody conjugates on survival and cure rate; differences in ability of antibody of different isotype tomediate and to modulate anti-tumor effects; antibody halflife and tissue distribution, degree and specificity of antibodybinding to tumorcells, in vivo amd in vitro fate of tumor cells, modulation of tumor cell antigens, optimal dose schedule and short and long-term toxicity.

III. MECHANISM OF SUPPORT

This RFA will use the 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 multiple projects, with total costs amounting to approximately $1.0 million for the first year. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. Also, although this program is provided for in the financial plans of the National Cancer Institute, the award of grants pursuant to this RFA is contingent upon the 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 Division of Research Grants, National Institutes of Health, and (2) the National Cancer Advisory Board. All applications will be evaluated by a single review panel in competition with each other.

Future renewal applications will not compete for earmarked funds. Instead, all renewal applications will be considered as unsolicited grant applications which will compete with all other unsolicited applications received by NIH.

B. Review Criteria

Applications must be responsive to this RFA, in the sense of being directed towards the attainment of the stated programmatic goals (see II. OBJECTIVES AND SCOPE). If the application is judged by the National Cancer Institute not to be responsive, the applicant will have the opportunity of having the application considered along with other unsolicited applications received by the National Institutes of Health.

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

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

2. Research experience and competence of the Principal Investigator and staff to conduct the proposed studies.

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

4. Adequacy of existing/proposed facilities and resources. Applications which specify a proposed use of human cells/tissues/fluids/excreta, need to provide assurance and details concerning the nature, source, and availability of those specimens.

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

6. Reasonableness of proposed costs.

V. METHOD OF APPLYING

A. Format of Applications

Applications must be submitted on form PHS 398 (Revised 5/80), 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 Grans, NIH. The conventional presentation in format and detail 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-DCT-BRMP-81-6 MONOCLONAL ANTIBODY IN ANIMAL TUMOR MODELS" should be typed in bold letters across the top of the face page of the application.

B. Application Procedure

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

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

To ensure their review, applications must be received by December 15, 1981. Applications received after that date will be returned. 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. Long at the address shown below.

VI. INQUIRIES MAY BE DIRECTED TO:

Dr. Cedric Long
Biological Resource Branch
Biological Response Modifiers Program
Division of Cancer Treatment
National Cancer Institute
Landow Building, Room 8C03
Bethesda, Maryland 20205

Telephone: (301) 496-9664

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NIH-NCI-DCT-BRMP-81-8

ANIMAL TUMOR MODELS FOR ANTIPEPTIDE GROWTH FACTOR AND MATURATION FACTOR THERAPY

NATIONAL CANCER INSTITUTE

Application receipt date: December 15, 1981

The Division of Cancer Treatment of the National Cancer Institute (NCI) invites grant applications from interested investigators for basic and applied studies in which a transplanted or spontaneous animal tumor will be developed to determine the therapeutic efficacy of anticancer agents which act by specifically blocking the actions of specific peptide growth factors.

Grants are awarded only to 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 National Institutes of Health (NIH) grant-in-aid, in accordance with PHS policies applicable to Research Project Grants including cost-sharing. However, the RFA solicitation represent 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 NIH Initial Review Group.

The present RFA announcement is for a single competition with a specified deadline of December 15, 1981, for receipt of applications. Applications should be prepared and submitted in accordance with the aims and requirements described in the following sections:

I. BACKGROUND INFORMATION

Biological response modifiers refers to agents or approaches that alter the relationship between tumor and host by modifying the host's biological reponse to tumor cells, with a resultant therapeutic benefit. The application of these agents with a primary intent of therapy is the major focus of the Biological Response Modifiers Program.

This program is described in the Catalog of Federal Domestic Assistance number 13-395, Cancer Treatment 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.

The components of the BRM program include immunoaugmenting agents, immunomodulating treatments, immunorestorative agents, interferon inducers; interferon and cytokine factors; thymic hormones and factors; tumor antigens and cell surface modifiers, anti-tumor antibodies, antitumor immune cells; maturation and differentiation factors.

This RFA addresses maturation and differentiation factors. 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 is theoretically considered that some agents may be developed which will not kill the tumor cells but will actually cause their further differentiation from the malignant state.

Low molecular weight peptide growth factors which promote cell division and anchorage-independent growth of normal and transformed human cells in vitro and which may be required for tumor growth in vivo have been recently identified and characterized. In order to assess the potential therapeutic efficacy of agents which specifically block these growth factors, suitable animal models need to be developed. In addition, other peptide growth factors and certain other substances, have been shown to induce maturation (terminal differentiation) of tumor cells in vitro. Animal tumor models are also required to assess these substances as potential anticancer agents.

II. OBJECTIVES AND SCOPE

Studies are encouraged to develop a transplanted or spontaneous animal tumor 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 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 or similar cell lines might form the basis of a suitable animal tumor model

III. MECHANISM OF SUPPORT

This RFA will use the 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 multiple projects, with total costs amounting to approximately $300,000 for the first year. This funding level is dependent on the receipt of a sufficient number of applications of high

scientific merit. Also, although this program is provided for in the financial plans of the National Cancer Institute, the award of grants pursuant to this RFA is contingent upon the 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 Division of Research Grants, National Institutes of Health, and (2) the National Cancer Advisory Board. All applications will be evaluated by a single review panel in competition with each other.

Future renewal applications will not compete for earmarked funds. Instead, all renewal applications will be considered as unsolicited grant applications which will compete with all other unsolicited applications received by NIH.

B. Review Criteria

Applications must be responsive to this RFA, in the sense of being directed towards the attainment of the stated programmatic goals (see II. OBJECTIVES AND SCOPE). If the application is judged by the National Cancer Institute not to be responsive, the applicant will have the opportunity of having the application considered along with other unsolicited applications received by the National Institutes of Health.

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

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

2. Research experience and competence of the Principal Investigator and staff to conduct the proposed studies.

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

4. Adequacy of existing/proposed facilities and resources. Applications which specify a proposed use of human cells/tissues/fluids/excreta, need to provide assurance and details concerning the nature, source, and availability of those specimens.

5. Scientific technical or medical significance and originality of proposed research.

6. Reasonableness of proposed costs.

V. METHOD APPLYING

A. Format of Applications

Applications must be submitted on form PHS 398 (Revised 5/80), 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 in format and detail 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-DCT-BRMP-81-8 ANIMAL TUMOR MODELS FOR ANTIPEPTIDE GROWTH FACTOR AND MATURATION FACTOR THERAPY" should be typed in bold letters across the top of the face page of the application.

B. Application Procedure

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

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

To ensure their review, applications must be received by December 15, 1981. Applications received after that date will be returned. 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. Long at the address shown below.

VI. INQUIRIES MAY BE DIRECTED TO:

Dr. Cedric Long
Biological Resources Board
Biological Response Modifiers Program
Division of Cancer Treatment
National Cancer Institute
Landow Building, Room 8C03
Bethesda, Maryland 20205

Telephone: (301) 496-9664

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NIH-NCI-DCT-BRMP-81-9

THERAPEUTIC USE OF LYMPHOKINES IN CANCER

NATIONAL CANCER INSTITUTE

Application receipt date: December 15, 1981

The Division of Cancer Treatment of the National Cancer Institute (NCI) invites grant applications from interested investigators for basic and applied studies to evaluate the therapeutic value of defined lymphokines in anti-tumor immunity.

Grants are awarded only to 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 National Institutes of Health (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 NIH Initial Review Group.

The present RFA announcement is for a single competition with a specified deadline of December 15, 1981, for receipt of applications. Applications should be prepared and submitted in accordance with the aims and requirements described in the following sections:

I. BACKGROUND INFORMATION

Biological response modifiers refers to agents or approaches that alter the relationship between tumor and host by modifying the host's biological response to tumor cells, with a resultant therapeutic benefit. The application of these agents with a primary intent of therapy is the major focus of the Biological Response Modifiers Program.

The components of the BRM program include immunoaugmenting agents,

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This program is described in the Catalog of Federal Domestic Assistance number 13-395, Cancer Treatment 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.

immunomodulating treatments, immunorestorative agents, interferon inducers; interferon and cytokine factors; thymic hormones and factors; tumor antigens and cell surface modifies, anti-tumor antibodies, anti-tumor immune cells; maturation and differentiation factors.

This RFA addresses Cytokines (Lymphokines). These factors are 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 cytocidal or antiproliferative activity, some to modulate and exert selective regulatory effects on various components of immune responses and others to affect bone marrow proliferation, or ossification or vessel proliferation. Production and purification of lymphokines have been a problem in the past. More recently, means have been developed to obtain lymphokines from lymphoid lines in culture thus helping to resolve the problem. Administration of lymphokines that can selectively activate or suppress certain components of the immune system may produce a beneficial anti-tumor effect in vivo.

II. OBJECTIVES AND SCOPE

Studies to be proposed should evaluate the therapeutic value of defined lymphokines in anti-tumor immunity. Currently available lymphokines, 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 analyusis could involve testing the therapeutic efficacy of various lymphokine preparations in transplantable and spontaneous animal tumor models. Investigators may restrict their study to a single lymphokine or may wish to perform comparative studies on various lymphokines. A goal of the studies should be to provide information relevant to the choice of a lymphokine(s) for preliminary clinical testing and the type(s) of tumor host relationship most amenable to effective biological modification using lymphokines.

III. MECHANISM OF SUPPORT

This RFA will use the 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 multiple projects, with total costs amounting to approximately $250,000 for the first year. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. Also,although this program is provided for in the financial plans of the National Cancer Institute, the award of grants pursuant to this RFA is contingent upon the 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 Grants, National Institutes of Health, and (2) the National Cancer Advisory Board. All applications will be evaluated by a single review panel in competition with each other.

Future renewal applications will not compete for earmarked funds. Instead, all renewal applications will be considered as unsolicited grant applications which will compete with all other unsolicited applications received by NIH.

B. Review Criteria

Applications must be responsive to this RFA, in the sense of being directed towards the attainment of the stated programmatic goals (see II. OBJECTIVES AND SCOPE). If the application is judged by the National Cancer Institute not to be responsive, the applicant will have the opportunity of having the application considered along with other unsolicited applications received by the National Institutes of Health.

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

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

2. Research experience and competence of the Principal Investigator and staff to conduct the proposed studies.

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

4. Adequacy of existing/proposed facilities and resources. Applications which specify a proposed use of human cells/tissues/fluids/excreta, need to provide assurance and details concerning the nature, source, and availability of those specimens.

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

6. Reasonableness of proposed costs.

V. METHOD OF APPLYING

A. Format of Applications

Applications must be submitted on form PHS 398 (Revised 5/80), 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 in format and detail 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-DCT-BRMP-81-9 THERAPEUTIC USE OF LYMPHOKINES IN CANCER" should be typed in bold letters across the top of the face page of the application.

B. Application Procedure

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

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

To ensure their review, applications must be received by December 15, 1981. Applications received after that date will be returned. 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. Long at the address shown below.

VI. INQUIRIED MAY BE DIRECTED TO:

Dr. Cedric Long
Biological Resources Branch
Biological Response Modifiers Program
Division of Cancer Treatment
National Cancer Institute
Landow Building, Room 8C03
Bethesda, Maryland 20205

Telephone: (301) 496-9664

ANNOUNCEMENT

DENTAL IMPLANT RESEARCH

NATIONAL INSTITUTE OF DENTAL RESEARCH

I. BACKGROUND

In June 1978 at the Harvard School of Dental Medicine a consensus development conference on dental implants was conducted. A summary of the conference appeared in the Journal of the American Dental Association, Vol. 98, March 1979, pages 373 to 377. The full proceedings are available from the NIDR. One of the effects of this conference on the dental profession was the reassessment by the Council on Dental Materials, Instruments, and Equipment of the American Dental Association on the use of endosseous implants. In the March 1981 issue of the Journal of the American Dental Association (Vol. 102, page 350), the Council reported that it has "extended its Acceptance Program to include endosseous implants."

Many of the leading investigators in dental implant research participated in this conference. The data that had already been published on dental impalnt research and practice was reviewed. Four implants in clinical practice at that time were discussed. Guidelines for use of these implants are provided in the conference proceedings. The background literature and the data presented and discussed at the conference indicate that many unanswered questions still remain in the field of dental implants.

II. RESEARCH GOALS

The specific goal of this program announcement is to encourage investigator initiated research grant applications in dental implant research. The topics presented below are not listed in any order of priority and are intended only to provide examples of research areas of interest to the Restorative Materials Program. However, investigators are encouraged to consider any other relevant topics and approaches that would lead to a better understanding of dental implants.

A. Clinical Studies

A major conclusion of the consensus development conference was that prospective clinical trials should be carried out to validate the retrospective data reported. Reports at the conference showed variability in 5 year survival data for the most commonly used implant, the endosseous blade, to be as high as 90% or as low as 65%.

The participants of the conference reached consensus for the statement, "To have a sound statistical basis, conference data should be validated in new clinical trials with panel review, tighter patient selection, and uniform data collection and evaluation criteria." Therefore, we encourage clinical studies on those implants considered appropriate by the investigator. The investigator should provide a well documented protocol with particular attention and justification for the implant chosen, the patient selection criteria, and the safeguards to the patient during the course of the study and on follow-up. Criteria for success and failure should be clearly described.

B. Tissue Implant-Interface

1. Mechanical Function

Dental implants perform a mechanical function in transmitting loads to supporting bone and soft tissue structures. More information is desirable regarding the mechanical function of these implants in situ. A quantitative knowledge of functional loading could help clarify the extent by which implants differ when in service and how this influences the device performance. Some approaches that might be considered are, for example: (1) direct measurements in situ (humans or animals) using techniques which would provide data concerning mechanical function and (2) biomechanical analysis using suitable modeling technique(s) for calculating the mechanical function and its validation in vivo.

2. Design Factors

a. Shape and size - Investigations of the effect of shape and size on implant performance are needed. Since the scope of this investigation could be almost limitless, the variables would have to be carefully chosen and justified to insure adequate control and relevance.

b. Material - Concern has been expressed by many investigators as to the biocompatibility and durability of implant materials. The mechanical properties of candidate materials must be demonstrated to be adequate to withstand the occlusal loads transmitted to the implants. This includes the problems of biodegradability, corrosion, shear of coating materials, etc.

c. Surface Texture - The influence of surface texture on implant performance is not well understood, e.g., surfaces having smooth, rough, porous, crenulated, bonding, etc., can be studied and compared. The comparison should document the selection of a surface texture based on tissue reaction studies.

C. Animal Models

Some investigators believe there is a serious question regarding which animal is best suited for testing dental implants. Experience has been gained with dogs, swine, baboons and primates other than baboons. Some factors which could be considered in light of how they relate to the human situation or as models, per se, are as follows: (1) the gross and microanatomy of the dentition, mandibular and maxillary structures, (2) the functional characteristics of mandibular motion during mastication and the rest position, (3) the physiological factors of the bone and soft tissues as they relate to healing and predisposition to disease (such as periodontal disease), (4) dietary factors, (5) oral hygiene considerations, and (6) cost and avaialability of the animals.

III. MECHANISM OF SUPPORT

The mechanism of support for this program will be through research project grants (RO1 and R23). The legislative authority is Section 301 of the Public Health

Service Act (P.L. 78-410 as amended, 42 USC 241). The Catalog of Federal Domestic Assistance number is 13.843, Restorative Materials Research. Policies that govern research grant programs of the National Institutes of Health will prevail. This program is not subject to A-95 Clearinghouse or Health Systems Agency review. The award of grants pursuant to this request for grant applications is contingent upon receipt of applications with high scientific merit and the availability of appropriated funds.

IV. REVIEW PROCEDURES AND CRITERIA

Applications will be received by the Division of Research Grants (DRG), National Institutes of Health and will be reviewed in accordance with the usual NIH peer review procedures. Factors considered in the scientific merit evaluation of each application will include an assessment of the importance of the proposed research problem, the novelty and originality of the approach, the training experience and research competence of the investigator(s), the adequacy of the experimental design, the suitability of the facilities, and the appropriateness of the requested budget relative to work proposed. Following study section review, the application will be evaluated for program relevance by the NIDR Advisory Council. Funding decisions will be based upon relative scientific merit and the Institute's ability to fund.

Applications will be accepted in accordance with the usual date for new applications on an indefinite basis. The deadlines for receipt of new applications for the three annual review cycles are: March 1, July 1, and November 1.

V. METHOD OF APPLYING

Applications should be submitted on form PHS 398 (Rev. 5/80) which is available in the business or grants office at most academic or research institutions. If not, an application form may be obtained from:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Westwood Building, Room 449
Bethesda, Maryland 20205

Telephone: (301) 496-7441

The phrase "PREPARED IN RESPONSE TO NIDR DENTAL IMPLANT ANNOUNCEMENT" should be typed across the top of the first page of the application or on line 2 of the form PHS 398 (Rev. 5/80). The original and six copies of the application should be sent or delivered to:

Application Receipt Office
Division of Research Grants
National Institute of Health
Westwood Building, Room 240
Bethesda, Maryland 20205

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. The Institute requests such letters only to provide an indication of the number and scope of applications to be received. A 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. This letter should be addressed to and further information may be obtained from:

Thomas M. Valega, Ph.D.
Chief, Restorative Materials Program Branch
Extramural Programs
National Institute of Dental Research
Room 506, Westwood Building
Bethesda, Maryland 20205

Telephone: (301) 496-7491

ANNOUNCEMENT

EFFECTIVE FERTILITY REGULATION

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

I. BACKGROUND AND GOALS

The Social and Behavioral Sciences Branch (SBSB) of the Center for Population Research (CPR) of the National Institute of Child Health and Human Development (NICHD) invites grant applications for the support of research on the effective/ineffective use of contraceptives, especially for groups who are at higher than average risk for pregnancy or who have not been extensively studied.

II. PROGRAM SCOPE AND CONTENT

The effectiveness of fertility regulating methods as used by certain U.S. groups has not yet been studied extensively. These groups include Hispanics, Blacks, males, adolescents,and those experiencing one or more unwanted pregnancies. Some of these groups are at higher than average risk for pregnancy. Indepth studies of contraceptive effectiveness centering on such groups as those identified above are needed. Such research may address the following questions and objectives.

What are the differences in the effectiveness of fertility regulating methods as used by each of the groups? What are the explanations for these differences? A major goal is to determine the interrelationships among the characteristics of individuals, fertility regulating methods, and the manner in which contraceptives are obtained, in the effective or ineffective control of fertility. The selection, use, and effectiveness of fertility regulating methods may be influenced by demographic, psychological, social, economic, and other factors.

Concentrating on groups such as those identified, it is requested that applicants indicate the type of population(s) to which they have access, furnishing as much detail as possible about the type and size of population, distribution of relevant personal characteristics, methods being used, and delivery system(s) being utilized. Familiarity with the literature concerning factors in effective and effective fertility regulation, especially with regard to the group(s) under investigation, should be demonstrated.

Individual characteristics which may be considered include age, race, sex, ethnicity, education, religion, socioeconomic status, marital status and history, partner characteristics and relationships, pregnancy history, and use of fertility regulating methods.

Attention should also be given to the characteristics and use of fertility regulating methods which may include method(s) used, method switching, regularity of use, accuracy and adequacy of use, side effects, and ease and convenience.

This program is supported under Title III, Section 301 and Title IV, Section 441 (Public Law 78-410, as amended; 42 USC 241). The Catalogue of Federal Domestic Assistance number is 13.864, Population Research. Awards will be administered under PHS Grant Policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74, and Section 472, 42 USC 2891-1 and administered under 42 CFR Part 66.

In relating the manner in which contraceptives are obtained to the characteristics of group members and methods used, the following could be considered: how people find out about the methods, how people obtain the methods, and characteristics of professionals or non-professionals from whom methods are obtained.

It may be of benefit to the research to include a conceptual model of the interrelationships among factors influencing effective fertility regulation for the groups being studied. Innovative research designs may be able to accomplish research objective with fairly small-scale studies in which there has been careful selection of variables and samples within a well-defined meaningful conceptual framework. Research designs do not necessarily have to limit the scale of studies, but careful attention should be paid to developing efficient and cost-effective designs. One objective of the research should be findings with implications for feasible, workable approaches to increasing the effectiveness of fertility regulating behavior of the various groups under study.

III. MECHANISMS OF SUPPORT

A variety of mechanisms are available for obtaining grant support under this program:

1. The Research Project Grant, the traditional NICHD research support mechanism;

2. The New Investigator Research Award, a mechanism described in the NIH Guide for Grants and Contracts Volume 9, Number 1, January 3, 1980; and

3. The Program Project Grant, a mechanism available for multi-disciplinary research involving at least three projects with a common focus.

IV. CRITERIA FOR REVIEW

Applications compete on the basis of relative scientific merit with all grant applications before the NICHD. They are formally reviewed by NIH peer review groups and by the NICHD National Advisory Council. The number of awards made will reflect both relative merit and the availability of grant funds. Some applications reflect overlapping interests of more than one Institute, and in these cases, may be assigned to more than one Institute for funding purposes. The criteria for review are the traditional considerations underlying scientific merit which include adequacy and appropriateness of the approach; training, experience, and research competence or promise of the investigator(s); the adequacy of the research design; the suitability of the facility; and the appropriateness of the requested budget relative to the work proposed.

V. METHOD OF APPLYING

Applicants are asked to notify the Social and Behavioral Sciences Branch, NICHD (see address below) at least one month prior to formal submission of an application. Include name of principal investigator, institutional address, title of application, and abstract of the proposed research. Indicate that the application is in response to this announcement.

For research projects and New Investigator Research Awards, use form PHS 398 (Revised 5/80). If your institution does not have these, copies may be obtained from:

Office of Grant Inquiries
Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20205

Telephone: (301) 496-7441

Information concerning Program Project Grants and how to apply can be obtained from SBSB staff.

After you have completed the application, expedite its routing within NIH by:

1. Printing and underlining NICHD SOCIAL AND BEHAVIORAL SCIENCES BRANCH on the upper margin of the face sheet.

2. Checking the box on the application form indicating that your proposal is in response to this announcement.

3. Enclosing a cover letter repeating that this application is in response to this announcement of the NICHD SOCIAL AND BEHAVIORAL SCIENCES BRANCH.

Forward application and cover letter to:

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

Receipt dates for Research Project Grant and New Investigator Research Award applications are: March 1, July 1, and November 1; receipt dates for the Program Project Grant: February 1, June 1, and October 1.

VI. INQUIRIES AND CORRESPONDENCE

Correspondence, including requests for advice on further development of applications, should be directed to:

Sidney H. Newman, Ph.D.
(Behavioral Scientist Administrator)
Social and Behavioral Sciences Branch
National Institute of Child Health and Human Development
Room 7C25, Landow Building
7910 Woodmont Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-1174

NOTICE

PROGRAM PROJECT RESEARCH GRANT

APPLICATION (PO1) SPECIAL DIRECTIVES

NATIONAL INSTITUTE ON AGING

The National Institute on Aging (NIA) announces special instructions for investigators submitting applications for Program Project Research Grants (PO1's) which are likely to be assigned to NIA for support. These directives will apply to all new and competing program project applications submitted for the NIH-DRG application receipt date, February 1, 1982, and thereafter.

1. SCOPE AND SCALE OF NIA PROGRAM PROJECT APPLICATIONS

POLICY STATEMENT FOR PROGRAM PROJECTS

Program project grants will be regarded as mechanisms to further research and fully exploit existing knowledge to meet well-defined Institute programmatic objectives. A healthy mix of basic and/or clinical research in biomedical, as well as in the behavioral sciences of aging, would be a desirable program design.

o Program projects will be broad in scope involving a number of established investigators drawn from various specialties who have assembled as a team to examine a specific research objective or central theme. Therefore the project shall consist of several individual subprojects submitted and supported, but in which there is a definable advantage to the research effort or to the NIA by combining these into a single overall proposal. Program projects should be in areas defined by Program Announcements. The NIA policy derives from a desire to encourage large interdisciplinary projects of high scientific merit and which relate to well-defined programmatic objectives. However, the Institute recognizes that interdisciplinary research approaches relevant to the Institute's mission can and do arise outside areas defined by Program Announcements. In such cases, where an investigator desires to prepare and submit an unsolicited application for interdisciplinary research, the investigator should, prior to the preparation of the formal application, write a letter of intent to the Associate Director for Biomedical and Clinical Medicine, or to the Associate Director for Behavioral Sciences Research, summarizing the content of the proposed application, its staff, size, research approach and approximate date for submission and subsequent funding, if approved. There should be a clear statement as to why the program project, rather than one or more regular research grants, is the preferred method of work. This letter will be reviewed by the appropriate NIA staff and the investigator will receive advice as to the most appropriate course of action.

o The resolution of issues regarding compliance with overall policy and procedures for program projects, will be the responsibility of the NIA Associate Director for Planning and Extramural Affairs.

o Priority will ordinarily be given to applications that come from interdisciplinary teams who have, or who intend to create, a formal interdisciplinary program in aging.

o The total direct costs requested for the first year should not exceed $500,000. Budget increments for subsequent years may include some necessary cost of living increases.

o Total increments for subsequent years should not exceed 10% of the total budget.

o To be eligible for award as a program project, an approved application must contain a minimum of three subprojects.

o Initial application may be submitted for up to a five-year period and can be renewed for a subsequent five-year period. However, a special review and evaluation will be carried out at the end of the 8th year if the applicant institution plans to submit an application for another renewal for continuation of the project after ten years. The two-year buffer is designed to facilitate minimum disruption and maximum time for planning, evaluation and decision both for the grantee institution as well as the Institute as to the fate of the program if it is not funded for the additional period.

Applications for competitive renewal of program projects that have already been in existence for five to ten years should be considered as final competitive proposals and should so indicate in the application.

In accordance with this policy to limit the lifespan of POIs, competitive renewals that have been in existence for more than ten years will be closely examined for the rationale for their continuance.

II. PREAPPLICATION PROCESS

A. Applicants are encouraged to communicate with NIA prior to preparation of a formal application. Applicants are requested to communicate with NIA prior to submnission of the application through a "letter of intent" submitted by the prospective principal investigator. It is to the applicant's advantage to submit a letter of intent to the respective Associate Directors for Biomedical Research and Clinical Medicine and Behavioral Sciences Research.

This letter of intent will assist NIA staff to determine whether the proposal falls within the mission and research interests of the Institute and meets the criteria for a program project. It will also permit the applicant to benefit from consultation with NIA staff.

B. The letter of intent should provide, in no more than two single spaced, typewritten pages, the following information:

1. A statement highlighting the central theme and objectives of the proposed program project,

2. A brief description of each subproject including the name of the Project Director and a statement of how each specific subproject will contribute to the overall goal of the program project,

3. An annual budget and the number of years of support requested for the total program project and for each subproject, and

4. Depending on the subject matter of the proposal, a letter of intent should be directed to either:

Associate Director for Biomedical Research
and Clinical Medicine
National Institute on Aging
Room 5C11, Building 31
Bethesda, Maryland 20205

Telephone: (301) 496-4996

or

Associate Director for Behavioral
Sciences Research
National Institute on Aging
Room 5C02, Building 31
Bethesda, Maryland 20205

Telephone: (301) 496-3136

Priority Areas in Biomedical Research and Clinical Medicine

1. Nutrition in relation to health of the aged and aging processes
2. Pharmacology program
3. Gerontological and geriatric dermatology
4. Differentiated cells in culture
5. Senile dementia of the Alzheimer's type
6. Geriatric medicine research
7. Urinary incontinence

Priority Areas in Behavioral Sciences Research

1. Studies of the maintenance of health and effective functioning in the middle and later years.

2. Cohort-longitudinal studies which serve as the data base for interdisciplinary research and potentially for secondary data analyses.

C. In response to the letter of intent, potential applicants will be contacted promptly by an Institute health scientist administrator who will be available for further consultation.

III. THE APPLICATION

Applications should be prepared on form PHS 398 (Revised 5/80), which is available at most institutional business or research offices, or from the Division of

Research Grants, NIH. Type "PROGRAM PROJECT" on the first application page. NIH-DRG receipt and review dates for a program project application are:

Application Receipt Dates	Initial Review	Council Review	Earliest Beginning Dates
February 1	June	September October	December 1
June 1	October November	January February	April 1
October 1	February March	May	July 1

The page limitations stated in PHS 398 kit instructions should be applied to the individual project writings, not to the entire program project application as a whole. Complete information, including budget, should be provided for each component project. In addition overall program budgets (including core facilities where applicable) should be provided with the overview section of the proposal.

Applications should be mailed to:

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

At the time that formal application is mailed to DRG, the applicant is requested to inform the Executive Secretary of the Aging Review Committee NIA, in writing, that his/her program project application has been submitted to DRG. The address is:

Office of Planning and Extramural Affairs
National Institute on Aging
Room 5C12A, Building 31
Bethesda, Maryland 20205

The scientific review of the formal application will be conducted by the Aging Review Committee, the initial review group for the NIA. All communications regarding the review of the application before the meeting of the Aging Review Committee should be addressed to the Executive Secretary, Aging Review Committee, Office of Planning and Extramural Affairs, NIA. Request for information subsequent to the scientific review should be addressed to the associate Director of the appropriate program.

Final review is provided by the National Advisory Council on Aging.

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