

NIH GUIDE

for GRANTS and CONTRACTS

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

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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.

INFORMATION ITEMS

Release of Grant Applications

Under the Freedom of Information Act (P.L. 93-502, 1974) as amended, the National Institutes of Health releases to third parties funded grant applications after the grantee has been informed of the name and affiliation of the requestor and given an opportunity to delete material affecting patent or other valuable rights. NIH also deletes information that would constitute a clearly unwarranted invasion of personal privacy if released, such as individual salaries.

The Public Health Service policy is stated in the instruction sheet accompanying form PHS 398. Grantees and applicants are advised to read carefully the two paragraphs under Release of Information headed, "General Public Information" so that they understand that successful grant applications must be released to third parties upon request.

New grant applications that are disapproved, unfunded, or withdrawn are not required to be released (see page 1 of Vol. 9, No. 13, October 31, 1980, of the NIH Guide for Grants and Contracts).

Use of United States Flag Carriers for Grantee and Contractor Travel

The Deputy Assistant Secretary, Finance, DHHS, has reminded all Departmental components of the requirement for individuals traveling on official business to or from any possessions of the United States and foreign countries **to use only U.S. Flag Carriers whenever service by these carriers is available.** This requirement also applies to grantees and contractors. No exceptions may be made for such factors as cost, convenience or personal preference of the traveler.

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NIH-NHLBI-DLD-81G-B

CELL-TO-CELL INTERACTIONS IN THE DEVELOPING LUNG

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application receipt date: March 16, 1981

The Division of Lung Diseases of the National Heart, Lung, and Blood Institute invites grant applications for research to study the role of cell-to-cell interactions in the developing lung. The scope of this program includes studies directed towards elucidating the functional and structural interactions which occur between cells of the normal developing lung.

This type of solicitation (the RFA) is utilized when the Division wishes to stimulate investigator interest in a particular research area that is important to the National Program. The RFA identifies the scope of the Division's interest but does not require that the proposal conform to specific research requirements. The RFA is supported through the customary NIH grant-in-aid and is governed by the policies for regular research grants. However, the RFA solicitation represents a single competition with a specified deadline for receipt of applications. All applications in response to the RFA will be reviewed by the same initial review group.

The present announcement is for a single competition with a specified deadline of March 16, 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

Methods for the separation and culture of specific lung cells have paved the way for more detailed studies of lung cell functions. There is an inherent problem with isolated cell systems, however, since the cell-to-cell interactions which may influence cell behavior are lost. Studies in other organs have revealed that contacts between cells may involve short-range

This program is described in the Catalog of Federal Domestic Assistance number 13.838, Lung Diseases 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 A-95 Clearinghouse or Health Systems Agency Review.

interactions between adjacent cells or interactions over longer distances via chemical mediators and that such interactions are intimately related to the molecular biology of cell differentiation and organogenesis. Information available on the lung in this regard is very limited, although it has been known for nearly 50 years that morphologic development of embryonic lungs depends upon interactions between mesenchyme and epithelium. Little is known, however, about interactions between cells in the later stages of fetal or neonatal lung development. Understanding of cell-to-cell interactions in the normal developing lung should help to increase knowledge of the functions of individual lung cell types as well as the types of communications between them.

Recent findings suggest that regulation and maintenance of human fetal type II lung cell function may depend upon factors released from fibroblasts. Stimulatory as well as inhibitory effects of fibroblasts have been described, and these may be mediated by some biochemical factor(s). However, the chemical mediators involved, their cellular origin, and the molecular interactions important to the function of type II cells are not yet known.

The possibility that endothelial cells and pulmonary vascular smooth muscle cells communicate with each other also needs to be explored. It is not known, for example, if some pulmonary vascular muscle functions require the presence of intact endothelium. Interactions between interstitial cells and both epithelial and endothelial cells could influence specific functions of both epithelial and endothelial cells. Yet there is little information available concerning these possibilities.

II. GOALS AND SCOPE

The specific goal of this program is to encourage research to elucidate functional and structural interactions between normal lung cells in the fetal or neonatal lung. For the purpose of this announcement, fetal lung denotes the lung in the period beyond the canalicular stage of development. Investigations may include studies of epithelial and endothelial, as well as interstitial mesenchymal cells, and should attempt to define the role of cell-to-cell interactions in processes of differentiation, maturation, multiplication, and metabolic functions of specific cell types. Studies on the adult lung may be included if the intent is to compare it to the developing lung, but major emphasis must be on the latter. Proposals should have as their main objective the study of cellular interactions in the normal developing lung. However, investigations may also include relevant studies of injury and repair. Applications dealing with cells isolated from lungs which are in pre-canicular stages of development would not be considered an acceptable response to this announcement. Studies may use intact lungs or isolated cells, but must be designed to explore interactions suspected to occur in the lung in vivo. For example, proposals on fortuitous or random intermixing of cell types in culture would not be considered an adequate response to this announcement. If isolated cells are to be used, the applicant must show evidence of relevant expertise; de novo studies on cell separation

methodology will not be supported. Each application should clearly define the rationale, background, and specific aims of proposed studies and provide details of methods and procedures to be used.

The research topics presented below are intended to provide a perspective of the scope of research that would meet the goals of this program. It is not required that all or any of these topics be included. Investigators are encouraged to consider other relevant approaches designed to yield information on cell-to-cell interactions in the developing lung.

A. Epithelial-mesenchymal Interactions

It is well recognized that preparation of the fetal lung for air breathing is dependent, among other things, on the production by epithelial type II cells of complex lipoproteins which stabilize the terminal respiratory units. Recent findings suggest that this biochemical activity of type II cells is stimulated by hormones and that mesenchymal-epithelial cell interaction may be necessary to elicit a full response to corticosteroids. Although it is suspected that a fibroblast factor is the humoral mediator in this interaction, the nature of the factor and its precise role remain unknown. The possibility that other hormone-induced changes in epithelial cell function depend on similar mesenchymal-epithelial cell interactions has not been examined.

Communications are suspected to exist among epithelial cells and between epithelial and fibroblast cells. For example, the pinocytotic macromolecular transport processes recently recognized in type I cells may be the expression of interactions between the cells of the alveolus and the interstitium. Elucidation and understanding of such processes are relevant to neonatal lung function and lung maturation.

B. Pulmonary Vascular Cells

Smooth muscle and endothelial cells may interact to influence the reactivity of the vessel wall. The role of this interaction in the formation of new blood vessels and its contribution to active vasoconstriction needs further investigation. For example, how circulating vasoactive agents gain access to vascular smooth muscle is not clear. Myoendothelial junctions have been observed between the two cell types in the adult lung, but their function is not known. They may serve in the transfer of information from endothelial cells to smooth muscle cells. It also is not known whether or when these junctions occur in the developing lung. Nor is it known if both endothelial cells and vascular smooth muscle cells possess hormone receptors. Whether some pulmonary vascular muscle functions require the presence of intact endothelium also needs to be investigated.

C. Pulmonary Macrophages

Pulmonary macrophages secrete a number of biologically active materials, including enzymes, that cause degradation of connective tissue and factors which promote growth of fibroblasts. Thus, macrophages may have a crucial role in the growth of connective tissue in the lung. Investigations to define the role of the pulmonary macrophage in the growth of connective tissue in the lung and the nature of its interactions with fibroblasts are needed.

The topics cited above are for illustrative purposes only. Other approaches are encouraged as long as the rationale, background, and specific objectives are clearly stated and meet the objective of the program.

III. MECHANISM OF SUPPORT

The support mechanism for this program will be the traditional 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.

Although this program is included and provided for in the financial plans for Fiscal 1981, award of grants pursuant to this request for grant applications is contingent upon ultimate receipt of appropriated funds for this purpose. It is anticipated that a limited number of awards (more than one but not more than four to six) will be made under this program. A variety of approaches would represent valid responses to this announcement. Accordingly, it is anticipated that there will be a range of costs among individual grants awarded. Applicants are requested to furnish their own estimates of the time required to achieve the objectives of the proposed research project; however, the total project period of this proposal must not exceed 5 years. At the end of the project period, renewal proposals may be submitted for competitive review. A project period start date of September 30, 1981 is anticipated.

The current policies and requirements which govern the research grant program 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 received after the March 16, 1981 deadline or is judged to be unresponsive, the applicant will be contacted and given the opportunity to withdraw the application or to submit it for consideration in the regular grant program of NIH. Initial technical merit review will be by a single review group arranged by the Division of Research Grants (DRG). Secondary review will be undertaken by the National Heart, Lung, and Blood Advisory Council.

If a proposal submitted in response to this RFA is identical to a research grant application already submitted to 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 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

A. Letter of Intent

Prospective applicants are asked to submit a one-page letter of intent which includes a very brief synopsis of proposed areas of research and identification of any other participating institutions. This letter should be sent no later than January 15, 1981 to Dr. Dorothy Berlin Gail, Division of Lung Diseases, National Institutes of Health, 5333 Westbard Avenue, Room 6A03, Bethesda, Maryland 20205.

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.

B. Format for Applications

Applications should be submitted on Form PHS-398, the application form for the traditional research grant which may be obtained at institution business or research offices. If Form 398 is not available at the institution, it may be obtained by contacting the Division of Research Grants, Office of Grants Inquiries, 5333 Westbard Avenue, Room 449, Bethesda, Maryland 20205; Phone (301) 496-7441. The conventional presentation in format and detail for regular research grant applications should be utilized. Specific attention is directed towards the inclusion of a statement indicating the willingness of the applicant to work cooperatively with other participants in the program and with the National Heart, Lung, and Blood Institute.

c. 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 5:00 p.m. EST on March 16, 1981.

The face page of the application must be labeled to indicate that it is submitted in response to this program announcement: RFA-NHLBI-DLD-81G-B "Cell-to-Cell Interactions in the Developing Lung."

VI. INQUIRIES

Inquiries may be directed to Dr. Dorothy Berlin Gail, Division of Lung Diseases, National Institutes of Health, Westwood Building, Room 6A03, Bethesda, Maryland 20205; Telephone: (301) 496-7171.

NOTICE

AGING AND NUTRITION IN NONHUMAN PRIMATES

A colony of pig-tailed macaques (Macaca nemestrina) dedicated to interdisciplinary research on the biology of aging has been established at the University of Washington. The colony of 72 animals, ranging in age from 3 to more than 23 years, is supported by a grant from the National Institute on Aging. One of the colony is to be maintained on a typical American human diet and half the diet lower in lipid, simple sugar and salt contents. One function of the colony is to provide specimens to investigators at research institutions throughout the U.S. who are interested in characterizing relationships between aging and nutrition in a nonhuman primate species. Short-term experiments of any nature that can be carried out by colony personnel or by visiting scientists are also encouraged. Investigators interested in obtaining specimens or experimental access to the colony should contact:

Dr. Douglas M. Bowden
Regional Primate Research Center SJ-50
University of Washington
Seattle, Washington 98195
Telephone: (206) 543-1430

ANNOUNCEMENT

EXTRAMURAL ASSOCIATES PROGRAM

NATIONAL INSTITUTES OF HEALTH

Application receipt date: January 31, 1981

The National Institutes of Health (NIH) invites nominations for the 1981-82 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, travel 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 September 1, 1981 or February 1, 1982. **Nominations and completed applications are due by January 31, 1981**; selections will be announced by April 30, 1981.

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 1A10
9000 Rockville Pike
Bethesda, Maryland 20205
Telephone: (301) 496-9728

ANNOUNCEMENT

PREVENTIVE CARDIOLOGY ACADEMIC AWARD

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

The Division of Heart and Vascular Diseases, National Heart, Lung, and Blood Institute has initiated the Preventive Cardiology Academic Award to provide a stimulus for the development of a preventive cardiology curriculum in those schools of medicine and osteopathy that do not have one and to strengthen and improve the preventive cardiology curriculum in those schools that do. Each school of medicine or osteopathy in the United States and its possessions or territories is eligible to compete for one award for a project period that does not exceed five years. The number of awards made each year will depend upon the merit of the applications received and availability of funds.

For the purposes of the Preventive Cardiology Academic Award, the term preventive cardiology is used to define the area of cardiovascular medicine having a special concern with the development of knowledge and the application of knowledge directed at the prevention of heart and vascular diseases. This includes the area of primary prevention of cardiovascular diseases in infants, children, and adults who are at risk of developing such diseases and the reduction of preventable complications or disability in persons who have already developed cardiovascular disease.

This award is intended to:

- * encourage the development of a high quality preventive cardiology curriculum in schools of medicine and osteopathy that will significantly increase the opportunities for students and house staff to learn both the principles and practice of preventive cardiology;
- * develop promising faculty whose interest and training are in preventive cardiology teaching, research and practice;
- * develop superior faculty who have a major commitment to and possess educational skills for teaching preventive cardiology;

This program is described in the Catalog of Federal Domestic Assistance Number 13.837, Heart and Vascular Diseases 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 Section 413 (42 USC 287b) and administered under PHS grants policy and Federal Regulation 42 CFR Part 66. This program is not subject to A-95 Clearinghouse or Health Systems Agency Review.

- * facilitate interchange of educational ideas and methods applicable to teaching preventive cardiology among awardees and institutions;
- * develop at the grantee institution the ability to strengthen continuously the improved preventive cardiology curriculum, with local funds, subsequent to the award.

Criteria for the Award

Competitive review of proposals will include an evaluation of the evidence of commitment of both the sponsoring institution and the head of the cardiology division to the accomplishment of the objectives of the award as well as the qualifications, interest and commitment of the candidate to undertake responsibility for implementing a high quality preventive cardiology curriculum. Sponsorship of the candidate must be by the head of the division responsible for the teaching and practice of cardiology in the institution. Joint appointments with other departments or schools such as Preventive Medicine, Pediatrics or Epidemiology are encouraged when they would lead to a meaningful enhancement of the curriculum, extend concepts of prevention to other teaching areas or enhance the candidate's professional development in preventive cardiology teaching, research or practice. Multidisciplinary programs are encouraged.

The candidate must have sufficient clinical training and research experience in cardiology to be able to develop and implement a high quality curriculum within the institution. If the candidate's background requires further educational development, the plans to acquire this additional training should be described. Relevant training in epidemiology, clinical trials, behavioral science or other areas could be advantageous in the broader role of the candidate in stimulating preventive cardiology concepts among other peer health professionals in the institution.

Provisions of the Award

The non-renewable Preventive Cardiology Academic Award will include funds for the awardee's salary, fringe benefits, developmental funds, and actual indirect costs not to exceed 8% of total allowable direct costs.

The applicant may request salary support up to \$30,000 per year. In addition to this amount, fringe benefits may be requested at the applicable institutional rate.

The applicant's salary which is requested from this grant may not exceed the time or effort (at least 50%) to be devoted to the Preventive Cardiology Academic Award. The total salary on which it is based must be consistent both with the established salary structure at the institution and with salaries actually provided by the institution from its own funds to other staff members of equivalent qualifications, rank, and responsibilities in the department concerned. If full-time salaries are not currently paid to comparable staff members, the proposed salary must be appropriately related to the existing part-time salary structure. The Awardee may devote up to 50% effort as principal or participating investigator on an NIH-supported grant(s) or contract(s) and may be remunerated from the grant(s) or contract(s) accordingly.

Developmental funds may include personnel support necessary to achieve the program objectives; travel funds to enable the awardee to visit other institutions or to attend special meetings, courses or conferences designed to increase his/her knowledge and competence in the teaching/learning process related to preventive cardiology; equipment necessary as teaching aids; supplies necessary to the program objectives; and stipends for a limited number of students to extend their preventive cardiology learning experience during their elective quarter in the academic year. Funds may not be used to support cardiology fellowships or research projects.

Review of Applications

Applications for initial Preventive Cardiology Academic Awards will be appraised in terms of criteria outlined for the institution and the awardee in Criteria for the Award.

The review will include an initial assessment of the written proposal by the Division of Extramural Affairs, NHLBI and will require an interview with the prospective awardee in Bethesda, Maryland. (Travel expenses for this interview must be paid by the applicant institution.) When necessary, a site visit may be made to the institution to determine the institutional environment, the commitment of the sponsoring division or department head and evidence of cooperation that may be needed to implement the candidate's proposed program. The initial review group will recommend applicants for consideration to the National Heart, Lung, and Blood Advisory Council.

Method of Applying

Each prospective applicant should forward a letter of intent, countersigned by the head of the cardiology division or department, by the February 1 preceding the receipt date to:

Centers and Special Projects Section
Review Branch
Division of Extramural Affairs
National Heart, Lung, and Blood Institute
Westwood Building, Room 553
Bethesda, Maryland 20205

These letters will not be considered commitments, but will be used to estimate the number of proposals to be submitted.

Applications for Preventive Cardiology Academic Awards may be submitted for the April 1 receipt date each year to the National Institutes of Health for review by the National Heart, Lung, and Blood Advisory Council the following September. The requested beginning date for funding should be July 1 of the year following the receipt date.

Application forms (PHS 398) may be obtained from the administrative office of the application institution or from the Division of Research Grants, NIH.

Deadlines for Receipt of Applications

Beginning in April 1980, annual receipt dates were established as follows:

<u>APPLICATION RECEIPT</u>	<u>COUNCIL REVIEW</u>	<u>START DATE</u>
April 1	September	July 1*

*Of the year following application receipt.

For Additional Information

Prospective applicants are encouraged to review the Preventive Cardiology Academic Awards Guidelines dated November 1, 1980 which detail the eligibility requirements and application procedures. Requests for copies of these guidelines and questions related to Preventive Cardiology Academic Award should be directed to:

Dr. William T. Friedewald
Acting Chief, Preventive Cardiology Branch
Division of Heart and Vascular Diseases
National Heart, Lung, and Blood Institute
Federal Building, Room 212B
Bethesda, Maryland 20205
Telephone: (301) 496-2533