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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 20, No. 23
June 14, 1991

NOTICES

NOTICES OF AVAILABILITY (RFPs AND RFAs)

ONGOING PROGRAM ANNOUNCEMENTS

NOTICES

JAMES A. SHANNON DIRECTOR'S AWARD

P.T. 34; K.W. 1014006, 0710030

National Institutes of Health

I. SUMMARY

The National Institutes of Health (NIH) announces a new award, the James A. Shannon Director's Award, that will be awarded in FY 1991. The award will provide limited support to scientists whose research applications fall short of the institute/center funding cutoff but are at the margin of funding in which high quality grants are not awarded due to lack of funds. Institutes and centers will recommend pending R01 (traditional research grant), R29 (FIRST Award), and, to a limited extent, R03 (small grant) applications to the Director, NIH, for consideration. The Director intends to make approximately $30 million available for this award. Each award will consist of up to $80,000 direct costs and up to $20,000 indirect costs (20 percent of total costs) for a total of up to $100,000 for a twenty-four-month grant period. Funding for R03 applications will be considerably less. Annual expenditures on these Awards may not exceed 50 percent of the total allocation. INVESTIGATORS MAY NOT APPLY FOR THE SHANNON AWARD.

II. BACKGROUND

The NIH has been concerned that its award rate has dropped precipitously in the last five years from 34.9 percent in 1987 to 26.9 percent in 1991. This has been occurring at a time when there has been increasing Congressional concerns about technology transfer and sustained scientific leadership in biomedical science and biotechnology. Highly meritorious applications have

not been funded. Many of these applications have been from young scientists trying to establish research careers and experienced scientists frustrated by the ever increasing difficulty in obtaining grant renewals.

Cognizant of these issues, the new Director of NIH, Dr. Bernadine Healy, has announced that one of her first initiatives is the James A. Shannon Director's Awards to provide limited support for investigators whose applications are on the margin of funding. Approximately $30 million is available for the awards, with funds derived from two sources--the NIH Director's Discretionary Fund and the NIH Director's transfer authority established in P.L. 101-517. Funds ordinarily set aside for investigator-initiated research projects will not be used. Therefore, this award will not be a redirection of funds that would have been used to fund the traditional NIH investigator-initiated research grants.

III. OBJECTIVE

The objective of the Shannon Award is to provide limited research support for exploration and development based on the merit of a pending application. These grants will underwrite exciting applications that are at the cutting edge of science and that would be missed opportunities if not funded. The Shannon Award is intended to provide support to test the feasibility of an innovative approach; develop further tests and refine research techniques; perform secondary analysis of available data sets; and conduct other activities that are within the original specific aims of the approved application in order to demonstrate research capabilities or lend additional weight to an already meritorious application.

IV. GENERAL FEATURES

A. The Shannon Award will apply to R01, R29, and a limited number of outstanding R03 applications. Foreign applications will not be considered.

B. Investigators may not apply for a Shannon Award. Competing applications, prepared and submitted in accordance with NIH procedures, will have been peer reviewed and provided a percentile rating. Nominees will be from among applications pending FY 1991 funding and reviewed by the Sept./Oct. 1990, Jan./Feb. 1991, May/June 1991 Advisory Boards and Councils. Nominees for the award must be in the top half of the percentile range. Previously approved, but inactivated, applications from this time period may be considered and, if awarded, will be converted to a Shannon Award (R55).

C. The application upon which the Shannon Award is funded will remain active for its entire period of support. However, the investigator is advised to submit a revised application at the earliest convenient date to be considered for future funding as either an R01 or R29.

D. If a competing application (R01 or R29) is subsequently funded while the Shannon Award is active, the balance of the Shannon Award will be deducted from the total approved amount of the competing award.

E. The Shannon Award is a two-year award for up to $100,000 total costs. The distribution of funds will be $80,000 for direct costs ($60,000 in personnel and $20,000 in supplies for budgetary flexibility) and a maximum of $20,000 indirect costs. The level of funding for R03 awards will be considerably less with the same 20 percent of total costs limitation on indirect costs. PHS special grants administration provisions as outlined in the "PHS Grants Policy Statement" interim update of November 15, 1990 apply to these awards. However, expenditures during the first year may not exceed 50 percent of the total award and additional funds may not be rebudgeted into indirect costs.

F. One final progress report, final financial status report, and final invention statement (HHS 568) will be required 90 days after the end of the twenty-four-month grant period. The progress report must identify those portions of the original proposal pursued with the Shannon Award. If the awardee is successful with a subsequent application, the progress report in the amended application will suffice as a progress report for the Shannon Award and a final invention statement will not be required.

V. REVIEW CRITERIA AND PROCEDURES

A. NIH staff, initial review groups, and Advisory Councils and Boards will have reviewed all R01, R29, and R03 applications in the usual manner. Program administrators will submit to their institute or center director for further consideration pending applications that have creative and innovative approaches and meet the mission of the institute.

B. On July 15, the institutes and centers will submit their nominees for the Shannon Award to the Office of the Director, NIH. The Deputy Director for Extramural Research, NIH, will convene a committee of senior NIH officials to review the nominated applications and make recommendations to the Director, NIH. The Director, NIH, will make the final selection.

C. The Director will notify the institutes and centers of her decision by August 15, 1991. The institutes and centers will issue the FY 1991 Shannon Awards before September 30, 1991.

NOTICES OF AVAILABILITY (RFPs AND RFAs)

PROGRAM PROJECTS ON AUTOIMMUNITY

RFA AVAILABLE: AI-91-09

P.T. 34; K.W. 0715015, 0745027, 0745070, 0710030

National Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: August 1, 1991
Application Receipt Date: November 13, 1991

BACKGROUND INFORMATION

The Autoimmunity Section of the Division of Allergy, Immunology and Transplantation (DAIT) of the National Institute of Allergy and Infectious Diseases (NIAID) supports research aimed at elucidating the causes and mechanisms of tolerance and autoimmune diseases and to promote application of this basic biomedical knowledge to the development and implementation of new preventive and treatment modalities for these diseases.

This Request for Applications (RFA) is intended to encourage and invite the development of program projects applications from collaborating basic science and clinical research investigators who are interested in developing integrated novel studies on autoimmune diseases.

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000", a PHS-led national activity for setting priority areas. This RFA, Program Projects on Autoimmunity, is related to the priority area of diabetes and chronic disabling diseases. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402-9325 (telephone 202-783-3238).

RESEARCH GOALS AND SCOPE

The major goals of these program projects are: increased understanding of the etiology and pathogenetic mechanisms involved in autoimmune diseases; generation of new information and the expansion of the current knowledge base; and the application of this knowledge to the development of new or improved measures of risk assessment, prevention, early diagnosis, and treatment of a wide variety of autoimmune diseases and disorders in which the autoimmune response is a major contributor to pathogenesis.

Broad and innovative applications that address all aspects of the immune responses related to self reactivity may include studies concerned with relevant areas of genetics, cell and molecular biology, biochemistry, physiology, microbiology, pathology, and pharmacology. Of special interest to NIAID are program projects that emphasize new ideas, novel approaches, and state-of-the-art technology in basic research that elucidate pathogenetic mechanisms and that show promise for clinical application in the prevention, diagnosis, and treatment of autoimmune diseases.

There is overwhelming evidence that implicates immune mechanisms in the pathogenesis of diseases of the skin, nervous system, endocrine system, and gastrointestinal tract. Thus, in addition to studies of well recognized autoimmune disorders, such as systemic lupus erythematosus, rheumatoid arthritis, antibody-mediated thrombocytopenia, and autoimmune hemolytic anemia, NIAID encourages investigators to design and develop studies aimed at establishing the role of the immune system in the pathogenesis of endocrine, dermatologic, neurologic, and gastrointestinal diseases and the development of new preventive and treatment modalities specific for these disorders through the manipulation of the immune response.

Protocols focused on the study of mechanisms of autoimmune diseases should be designed based on integrated and coordinated intra-institutional clinical investigations or experimental studies with demonstrated relevance to human autoimmune disease. Inclusion of basic research components utilizing in vitro procedures and samples from human source materials are encouraged, as are preclinical studies using appropriate animal models of human autoimmune disease. Inclusion of clinical investigative components drawing upon immunologically relevant areas in medicine, pediatrics, surgery, dermatology, neurology, pathology, and their subspecialties is highly recommended.

SPECIAL INSTRUCTIONS FOR THE INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included or adequately represented in the study populations for clinical studies, a specific justification must be provided. Application without such documentation will not be accepted for review.

MECHANISM OF SUPPORT

Program project (P01) grants are awarded to an institution on behalf of a program director for the support of a broadly based, multidisciplinary, long-term research program that has a specific major goal or basic theme. A program project generally involves the organized efforts of groups of investigators who conduct research projects related to the overall program goal. The grant can provide support for the projects and for certain basic resources shared by individuals in the program project if sharing facilitates the total research effort. Each project supported by a program project grant is expected to contribute to and be directly related to the common theme of the program; the projects, under the direction of a Principal Investigator, should demonstrate an essential element of unity and interdependence. In Fiscal Year 1992 the NIAID plans to award at least two program project grants submitted in response to this RFA and, depending on availability of funds and scientific merit, more than two. Budgetary requests must be limited to no more than $500,000 direct costs per year.

ELIGIBILITY

ONLY DOMESTIC INSTITUTIONS ARE ELIGIBLE TO APPLY. Applications may be submitted by any domestic, public or private, nonprofit or profit-making organizations.

METHOD OF APPLYING

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

Olivia Preble, Ph.D.
Allergy, Immunology and Transplantation Research Committee
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Westwood Building, Room 3A-07
Bethesda, MD 20892
Telephone: (301) 496-3528

LETTER OF INTENT

Prospective applicants are asked to submit by August 1, 1991, a letter of intent that includes a descriptive title of the overall proposed research, the name of the Principal Investigator, and a list of the names of key investigators and their institution(s). The letter of intent is requested in order to provide an indication of the number and scope of applications to be reviewed to allow early preparations for review, as well as to promote early interactions between applicants and NIAID staff. The letter of intent is not binding and does not commit the sender to submit an application, nor is it a requirement for submission of an application. The letter of intent is to be directed to Dr. Preble at the address given above.

STAFF CONTACT

A more detailed RFA may be obtained from:

Susana A. Serrate-Sztein, M.D.
Chief, Autoimmunity Section
Division of Allergy, Immunology and Transplantation
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Westwood Building, Room 755
Bethesda, MD 20892
Telephone: (301) 496-7985
Telefax: (301) 402-0175

Inquiries regarding fiscal matters may be addressed to Mr. Carow:

Mr. Jeffrey Carow
Chief, Immunology Grants Management Section
GMB, DEA, NIAID, NIH
Westwood Building, Room 726
Bethesda, MD 20892
Telephone: (301) 496-7075

This program is described in the Catalog of Federal Domestic Assistance No. 93.855, Immunology, Allergic and Immunologic 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 grants policies and Federal Regulation 42 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

ONGOING PROGRAM ANNOUNCEMENTS

STUDIES ON THE INTERACTIONS BETWEEN ENVIRONMENTAL TOXICANTS AND THE IMMUNE SYSTEM

PA: PA-91-66

P.T. 34; K.W. 0705040, 1007009, 0715120, 1002004, 1002008

National Institute of Environmental Health Sciences
National Institute of Allergy and Infectious Diseases

Application Receipt Dates: February 1, June 1, October 1

BACKGROUND

The National Institute of Environmental Health Sciences (NIEHS) and the National Institute of Allergy and Infectious Diseases (NIAID) announce their interest in receiving individual research grant applications (R01s and R29s) for support of studies on the interactions between environmental substances and their effects on immune function. The objective is to promote research at the molecular and cellular level to better understand mechanisms of environmentally induced aberrations within the immune system in order to gain insight into approaches to mitigate the effects of such agents. These agents are substances that may be present in the natural environment or have been added by human activities and are known or or thought to induce illnesses that affect or involve the immune systems.

NIAID is the principal Federal funding component that supports fundamental research concerned with the structure and function of the immune system in health and disease. The acquisition of new and deeper knowledge about the immune system is requisite to the development of improved procedures for prevention, diagnosis, and treatment of immunological diseases and of diseases having a major immunological component. The interest of the NIAID in environmental toxicology is predicated on the strong likelihood that the analysis of interactions between noxious substances in the environment and the immune system can provide insight, from a largely ignored perspective, on some of the typical functions of the immune system, the adaptability and plasticity of the immune system, and the susceptibility of the immune system to chemical and physical insult.

The NIEHS is the principal Federal funding component for support of basic research on environmental factors that contribute to human health problems and disease. Major emphasis by NIEHS is placed upon research examining those physical and chemical substances resulting from industrial progress. However, there also are many natural environmental substances that have been found to have deleterious effects on human health and are within the purview of the NIEHS mission. Many of these substances cause human health problems by disrupting normal immune function that can lead to a disease state.

RESEARCH GOALS AND SCOPE

The effects of environmental toxicants may be divided into three broad categories: suppression/inhibition of immunological competence; initiation or triggering of autoimmunity; and stimulation of allergic/hypersensitivity reactions. Although the NIEHS and NIAID have overlapping interests with respect to each of these categories of effect, it is reasonable to state that the interests of NIEHS center on the effects of chemical/physical agents that suppress or reduce the capacity of the immune system. The interests of NIAID are more focussed on the actions of chemical/physical agents that precipitate or lead to autoimmune and allergic disorders. Interests of the NIEHS are to identify and characterize the mechanisms of action of substances that affect the immune system and to determine the magnitude and consequences of exposure to such substances. NIAID is concerned with understanding the immuno-physiological processes that are affected by environmental agents and elucidating the pathogenesis of the disorders that they cause. Both Institutes are interested in approaches that may mitigate the noxious effects of environmental agents and in the development of improved animal and in vitro models for studying the effects of noxious substances. Examples of projects/topics that would be of primary interest to each Institute follow:

OF PRIMARY INTEREST TO NIEHS:

- Analysis of the precise effects of toxicants on individual components of the immune system; e.g., on cellular components such as antigen-processing cells (APC), B-lymphocytes, and T-lymphocytes.

- Development of in vitro systems for systematic quantitative analyses and mechanisms of action of toxicants on individual cellular components of the immune system: APC, B-cells, and T-cells.

- Studies on dual effects of toxic agents such as simultaneous inactivation of certain components of the immune system and activation of other components.

- Studies on the genetics and pharmacological control of susceptibility and resistance to the effects of toxic substances on the immune system.

OF PRIMARY INTEREST TO NIAID:

- Identification of the actual immunogenic components (e.g., fragments, molecular conjugates) and epitopes of toxicants that trigger allergic/hypersensitive responses or autoimmunity, and detailed analyses of their processing by APC and presentation to T- and B-cells.

- Comprehensive studies on toxicant-induced allergic/hypersensitive responses designed to reveal the roles of components such as T-cells, APC, IgE-producing B-cells, IgE molecules, leukocytes, and mediator substances in the development and manifestation of those responses.

- Development of approaches to prevent or reduce the undesirable effects of toxicants on the immune system; e.g., appropriate pre-immunization ("vaccination") against toxicants or preparation of monoclonal antibodies capable of nullifying the effects of toxicants.

- Studies on the genetic control of susceptibility and resistance to those effects of toxicants that lead to autoimmune or allergic disorders.

OF INTEREST TO BOTH INSTITUTES

- Studies on toxicant-triggered expression of stress proteins (e.g., heat-shock proteins) and special receptors such as those for aromatic hydrocarbons controlled by the "Ah" genetic locus and found in leukocytes; and the roles of such proteins in the effects of toxicants on immune functions.

- Studies on aberrations in the elaboration and functions of cytokines and cytokine receptors induced by toxicants.

- Synergistic actions of physical/chemical agents either with each other (e.g., a chemical and UV-B or two chemicals) or with other

agents such as viruses or oncogenes. NIAID is most interested in those responses that lead to autoimmune or allergic disorders.

SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group, together with a rationale for its choice. In addition, general and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Section 2, A-D of the Research Plan AND summarized in Section 2, E, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial /ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks. Hispanics). The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

MECHANISM OF SUPPORT

The mechanism of support for this activity will be the individual research grant - Research Project Grant (R01) and First Independent Research Support and Transition (FIRST) Award (R29) as applicable.

APPLICATION AND REVIEW PROCEDURES

A. Deadline: Applications will be accepted in accordance with the usual receipt dates for new research grant applications; i.e., February 1, June 1, and October 1. The earliest possible award dates will be approximately nine months after the respective receipt dates. Applications received too late for one cycle of review will be held until the next receipt date.

B. Method of Applying: Applications will be received by the NIH Division of Research Grants (DRG) and referred to an appropriate study section for scientific and technical merit review. Institute assignment decisions will be governed by normal programmatic considerations as specified in the NIH Referral Guidelines. The review criteria customarily employed by the NIH for research grant applications will prevail. Following the initial scientific review, the applications will be evaluated by the National Advisory Council of the assigned Institute.

Applications must be submitted on form PHS 398 (revised 10/88) which is available in the business or grants and contracts offices at most academic and research institutions and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441. To identify the application as a response to this announcement, check "yes" in Item 2 on the face page of the application and enter the announcement title, "Environmental Toxicants and the Immune System", and PA-91-66.

The original and six copies of the application must be directed to:

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

ADDITIONAL INFORMATION

Applicants are strongly encouraged to contact one of the Program Administrators listed below prior to preparing an application. Inquiries related to this program announcement should be directed to:

Dr. Joseph F. Albright
Program Administrator
Division of Allergy, Immunology and Transplantation
National Institute of Allergy and Infectious Diseases
Westwood Building, Room 757
Bethesda, MD 20892
Telephone: (301) 496-7551

Dr. Jerry A. Robinson
Program Administrator
Scientific Programs Branch
Division of Extramural Research and Training
National Institute of Environmental Health Sciences
P.O. Box 12233
Research Triangle Park, NC 27709
Telephone: (919) 541-7724

Grants management inquiries should be directed to:

David L. Mineo
Chief, Grants Management Branch
Division of Extramural Research and Training
National Institute of Environmental Health Sciences
P.O. Box 12233
Research Triangle Park, NC 27709
Telephone: (919) 541-1373

This program is described in the Catalog of Federal Domestic Assistance Numbers 93.112, Characterization of Environmental Health Hazards; 93.113, Biological Response to Environmental Health Hazards; and 93.855, Allergy, Immunology and Transplantation Research. Awards are made under the authority of Section 487, Public Health Service Act as amended (42 USC 288) and administered under PHS Grants Policies and Title 42 of the Code of Federal Regulations, Part 66. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

BIOLOGY OF THE BASEMENT MEMBRANE ZONE OF SKIN AND EPIDERMOLYSIS BULLOSA

PA: PA-91-67

P.T. 34; K.W. 0715185, 0790005, 0765033, 1002058, 0780020

National Institute of Arthritis and Musculoskeletal and Skin Diseases
National Institute of Child Health and Human Development

I. PURPOSE

The Skin Diseases Program of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) supports research on the structure, function, and diseases of the skin. The Genetics and Teratology Branch of the National Institute of Child Health and Human Development (NICHD) supports research on genetic and congenital malformations of skin. This program announcement is to encourage submission of research grant applications in the area of basement membrane zone of the skin in normal and diseased states with particular reference to epidermolysis bullosa.

II. BACKGROUND

The basement membrane zone of the skin is an area of great biologic importance. The many structures within this zone mediate not only attachment of the epidermis to the underlying dermis but also transport nutrients from the vasculature of the dermis to the nonvascularized epidermis and, in the reverse direction, chemicals, including drugs, into the systemic circulation following topical application. Studies of skin diseases must consider the basement membrane zone in evaluating the underlying mechanisms of their pathogenesis.

Epidermolysis bullosa is a large group of hereditary and at least two acquired skin diseases in which the pathologic defect occurs within the skin basement membrane zone, either within the basal keratinocytes, the electron microscopically identified basement membrane, or the superficial papillary dermis. In the past several years many structures have been identified within this area of skin. Several have been implicated in the pathogenesis of one or more forms of epidermolysis bullosa. Thus, these diseases represent an experiment of nature, the study of which can provide great insights into normal functioning of molecules of the basement membrane zone of skin, as well as potential approaches to the diagnosis and treatment of individuals suffering with these often debilitatiing or even fatal conditions.

The NIAMS supports a National Epidermolysis Bullosa Registry that consists of four clinical sites and a coordinating center. The first five years of this Registry will conclude in September 1991. The Registry facilitates research in epidermolysis bullosa and the biology of the basement membrane zone by providing tissues from banked sources and/or obtaining patients interested in participating in research.

RESEARCH GOALS AND SCOPE

The goal of this program announcement is to stimulate research in the biology of the skin basement membrane zone and into the etiopathogenesis of epidermolysis bullosa. Some research areas appropriate for inclusion in applications responsive to this announcement are:

- Studies of the molecules making up the basement membrane zone, in the normal and/or diseased state;
- Studies seeking early aberrations and biological markers of skin development at the tissue, cellular, and molecular levels;
- Molecular genetic approaches to understanding basic defects in the hereditary forms of epidermolysis bullosa utilizing both candidate gene and anonymous marker approaches;
- Investigations utilizing tissue culture, organ and animal model systems, and other techniques as appropriate to investigate the mechanisms by which defects in the skin basement membrane zone result in disease phenotype;
- Studies leading to clinical trials and the treatment of various forms of epidermolysis bullosa;
- Epidemiology of subsets of epidermolysis bullosa.

MECHANISM OF SUPPORT

Research mechanisms to support these investigations include individual research grants (R01), Clinical Investigator Awards (K08), and First Independent Research and Transition (FIRST) Awards (R29).

SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Section 2, A-D of the Research Plan AND summarized in Section 2, E, Human Subjects. Applicants/offerors are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics).

The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

APPLICATION AND REVIEW PROCEDURES

Applications in response to this announcement will be reviewed in accordance with Public Health Service peer review procedures for research grants. Review criteria include significance and originality of the research goals and approaches; feasibility of the research and adequacy of the experimental design; training, research competence, and dedication of the investigator(s); adequacy of available facilities; and provision for the humane care of animals. Decisions will be based on initial review group and National

Advisory Council recommendations. Applications must be submitted on form PHS 398 (rev. 10/88), available in the business or grants office at most academic or research institutions and from the Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20894, telephone (301) 496-7441.

Applications will be accepted in accordance with the submission dates for new applications on a continuing basis.

February 1, June 1, October 1 for research grant applications.

The phrase "BIOLOGY OF THE BASEMENT MEMBRANE ZONE OF SKIN AND EPIDERMOLYSIS BULLOSA, PA-91-67" must be typed on line 2 of the face page of the application. The original and six copies must be sent or delivered to:

Grant Application Receipt Office
Division of Research Grants
Westwood Building, Room 240
National Institutes of Health
Bethesda, MD 20892-4500**

For further information, investigators are encouraged to contact the following individuals:

Alan N. Moshell, M.D.
Skin Diseases Program Director
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Westwood Building, Room 405
Bethesda, MD 20892
Telephone: (301) 496-7326

Delbert H. Dayton, M.D.
Genetics and Teratology Branch
Center for Research for Mothers and Children
National Institute of Child Health and Human Development
Executive Plaza North Building, Room 643
9000 Rockville Pike
Bethesda, MD 20892
Telephone: (301) 496-5541

For fiscal and administrative matters, contact:

Diane M. Watson
Grants Management Officer
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Westwood Building, Room 407-A
Bethesda, MD 20892
Telephone: (301) 496-7495

Douglas Shawver
Supervisory Grants Management Specialist
Grants Management Branch
Office of Grants and Contracts
National Institute of Child Health and Human Development
Executive Plaza North, Room 505
Bethesda, MD 20892
Telephone: (301) 496-1303

This program is described in the Catalog of Federal Domestic Assistance No. 93.846, Arthritis, Musculoskeletal and Skin Diseases Research and No. 93.865, Research for Mothers and Children. Awards will be made under authorization of the Public Health Service Act, Title III, Section 301(c) (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

**THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:

5333 Westbard Avenue
Bethesda, Maryland 20816