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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 8368MM, Building 31,
Bethesda, Maryland 20892, 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 organisations 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
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BIOTECHNOLOGY RESOURCES DIRECTORY

SECOND REVISION

The second revision of Biotechnology Resources, A Research Resources Directory has been completed and is now available free.

Describing the biotechnology resources of NIH's Division of Research Resources, the 64-page booklet identifies 38 current DRR grant facilities which may be used by biomedical researchers. These resources provide the national biomedical community with new technologies and processes for the conduct of biomedical research investigations.

Facilities supported by the Biotechnology Resources Program include large-scale and mini-computer systems, biochemical and biophysical instruments (mass spectrometers, nuclear magnetic resonance spectrometers, electron spin resonance spectrometers), million-volt electron microscopes, electron microprobes, biomedical engineering technologies, and production of biochemical and cellular materials. Also included are grantee listings for PROPHET, a national time-sharing computer resource; and SUMEX-AIM, a program which has evolved into a burgeoning artificial-intelligence-in-medicine network.

To guide prospective users in identifying potential sources of research assistance, the Directory details the instruments, services, and current research applications at the individual resources. Complete names, addresses and phone numbers of the Principal Investigators and User Contact Persons are also included.

A geographical index is provided, listing available resources by state, and within each state.

A single free copy of Biotechnology Resources, A Research Resources Directory, Revised 1980 may be secured by writing to the Research Resources Information Center, 1776 East Jefferson Street, Rockville, Maryland 20852, or by request from the Office of Science and Health Reports, Division of Research Resources, National Institutes of Health, Bethesda, Maryland 20205.
The National Institutes of Health has announced publication of a new booklet entitled The Seeds of Artificial Intelligence: SUMEX-AIM. The new booklet, developed by the Division of Research Resources, describes in detail the evolution of the computer and its eventual successful application to artificial intelligence in biomedical research.

The main emphasis of SUMEX-AIM is to design computer programs that capture the medical knowledge and reasoning processes of highly intelligent specialists, thus making specialized expertise more generally accessible. The principles of how knowledge accrues and how it is retrieved in logical sequences are extracted. They are then programmed into the computer.

This process of modeling scientific thought and knowledge then makes it possible for researchers to quickly explore the expertise of leaders in a given field.

The first practical application of artificial intelligence was conceived some 15 years ago when Drs. Joshua Lederburg, Edward F. Feigenbaum and Carl D. Djerassi of Stanford University formulated a project known as DENDRAL. The project was initially begun as a prototype to demonstrate that computerized symbolic reasoning could be successfully applied to molecular problems in chemistry. In 1969, the DRR Biotechnology Resources Program lent support to the project.

In 1973, SUMEX (Stanford University Medical Experimental System) was funded by NIH as a national resource and has since evolved to a burgeoning artificial intelligence network encompassing major projects at Carnegie-Mellon University; University of California, Santa Cruz; University of California, Los Angeles; University of Colorado; University of Pittsburgh; Rutgers University; Stanford University; Veterans Hospital at Palo Alto, California; Michigan State University; University of Texas; Massachusetts Institute of Technology; Tufts University; and others.

Containing 42 photos, charts and illustrations, the new 74-page booklet describes projects designed for application in chemistry, medicine and psychology. Chapters on the history of computing, various program approaches, and the future of knowledge-engineering are also included, as well as a complete SUMEX-AIM directory of projects and project managers.

A single free copy of The Seeds of Artificial Intelligence: SUMEX-AIM may be secured from the Office of Science and Health Reports, Division of Research Resources, National Institutes of Health, Bethesda, Maryland 20205; or from the Research Resources Information Center, 1776 East Jefferson Street, Rockville, Maryland 20852.
USE OF FORM HEW 596, "PROTECTION OF HUMAN SUBJECTS"

This notice is intended to clarify that the submission of form HEW 596, "Protection of Human Subjects" is not required in instances where the applicant has properly checked the "No" box on the application form, indicating that no studies involving human subjects are planned. NIH staff still has the responsibility of resolving instances in which they believe that the "No" box may have been checked inappropriately. The instructions to the revised application form PHS 398 state:

"If studies involving human subjects, or derived materials or data which contain personal identifiers or which can be linked to personal identifiers, are neither planned nor contemplated, check the box marked "No"; the form HEW 596 provided with the application need not then be submitted."
GUIDELINES FOR PATHOLOGY REVIEW

NATIONAL CANCER INSTITUTE

The National Cancer Institute supports a number of studies and projects involving review of human pathology material. The Institute has recently developed procedures to improve the design of such reviews and provide the results to investigators involved in such studies. The following guidelines pertain to all NCI supported studies and projects requiring review of human pathology material:

1. Such projects should include a pathologist as principal investigator or co-investigator.

2. Each Division Director in NCI has the following responsibilities in promoting appropriate practices with respect to pathology evaluations in all research projects in his/her respective programs:
   a. Appointment of an appropriate staff person as a Pathology Coordinator, who shall serve as a member of the Pathology Working Group, and shall review projects within his/her Division to determine whether the pathology section(s) of the project meet the guidelines promulgated by the Pathology Working Group.
   b. Maintain, directly or through the Pathology Coordinator, proper liaison with the Pathology Working Group.

3. The Pathology Working Group should be composed of the Division Pathology Coordinators and appropriate consultants. Meetings of the Group will be held at least quarterly. The Pathology Working Group should promulgate and recommend guidelines and should make decisions on all matters brought before it.

4. Investigators, intramural and extramural, proposing studies to be supported by NCI involving review of human pathologic material should include the following information in their proposal:
   a. How the pathologist investigator will interact with the contributing institutional pathologists, including the methods to be used to collect, review, report and exchange appropriate data;
   b. The methods to be used in (a) to code the information to insure proper compliance with the Freedom of Information and Privacy Acts and to protect the patient;
   c. Measures to insure that the mechanism for reporting results of pathology reviews to the contributing institutional pathologists conforms to usual ethical standards of medical practice, as well as complying with regulations for the protection of human subjects (45 CFR 46), and is accomplished in a timely fashion so that the
attending physician would be apprised of the most current status of the subject.

5. Investigators, proposing studies to be supported by NCI involving review of human pathologic material, should keep Institutional Review Boards informed about plans and procedures outlined in #4 above.
RESEARCH GRANTS RELATED TO

REYE'S SYNDROME

The National Institute of Neurological and Communicative Disorders and Stroke (NINCDS), in co-sponsorship with the National Institute of Allergy and Infectious Diseases (NIAID), the National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD), and the National Institute of Child Health and Human Development (NICHD), is encouraging the submission of applications for research grants in the area of Reye's Syndrome (RS), a clinically important childhood encephalopathy.

BACKGROUND

Reye's Syndrome is a childhood disorder which was first recognized and described by Dr. Douglas Reye in Australia in 1963. The disease is characterized by several clinical features, manifested progressively in a quick succession. It is usually preceded by a prodromal viral infection, usually influenza B or varicella, either alone or accentuated by another virus or by environmental factors. This is followed by vomiting, fatty infiltration of liver and viscera, impairment of oxidative metabolism, high concentrations of serum ammonia, high serum transaminase activities, and high intracranial pressure leading to progressive cerebral edema. In approximately 20-40% of affected children, the encephalopathy proceeds to irreversible brain damage and even death. Thus, this disease constitutes a major health problem and poses a great risk to the younger generation.

RESEARCH GOALS AND SCOPE

Since RS is suspected to be caused by several factors, efforts need to be directed toward the identification of the causative factor(s), elucidation of their mechanisms of action, control and elimination of these intrinsic and/or extrinsic factors, with the expectation of developing techniques for early diagnosis, improving the existing therapeutic modalities and developing new ones in the management and control of RS.

Many investigators have concluded that even though Reye's Syndrome may result from a number of causes, the common pathway resulting in clinical symptoms is injury to the mitochondria. These findings suggest that there is some unknown factor in serum that damages mitochondria. Continued studies of Reye's Syndrome are of great importance because a clearer understanding of the cellular pathophysiology of this disorder may lead to a better understanding of the damaging effects of all acute encephalopathies upon the brain. Cellular metabolic functions such as respiration, fatty acid oxidation, mechanisms affecting urea and ammonia production, protein synthesis, glycolysis and

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.
other specific dysfunctions need to be investigated. Morphological aspects of liver dysfunction and their possible correlation with biochemical abnormalities provide additional areas of interest.

Many of the features of acute encephalopathies appear to result from abnormalities in transport of water, electrolytes, and chemicals from plasma into the extracellular and intracellular fluid spaces in brain, with resulting alterations in the osmolality and pH of brain tissue. Transport of ions and metabolites in and out of cells is energy-dependent, but links between defects in transport, energy production and acute cerebral encephalopathy are not known and need further definition.

Exposure to pesticides, solvents and drugs alone or in combination with virus has been implicated as a possible cause of this syndrome. Several metabolic disturbances seem to occur in Reye's Syndrome as a result of these exposures, each of which could result in an acute disturbance of brain function. These and other related factors such as cellular immune responses, neurotransmitters, etc., need to be investigated.

Brain edema is a final neurological manifestation of all the complexities of this syndrome. Clinically, CSF pressure is invariably increased in children who subsequently die. Despite the obvious existence of brain edema and coma in Reye's Syndrome, little is known of the mechanisms involved and virtually no means are at hand for early diagnosis and treatment, although early recognition and treatment of RS is of paramount importance in reducing mortality and morbidity.

Although some of the areas for research have been described above, the applicant by no means is restricted to any one or more of these avenues of research. Any investigational aspect directly or indirectly related to the etiology, pathology, diagnosis, prevention and treatment of Reye's Syndrome is encouraged. Development of animal models of this syndrome forms an integral part of this announcement.

MECHANISMS OF SUPPORT

Applications may be submitted for a) program project grants (P01) or b) for individual research project grants (RO1).

a) Program projects may include clinical research as well as experimental approaches, depending upon local (or cooperative) facilities which include technical and professional expertise, interest, resources, and patient availability to carry out the desired research objectives. Applicants should develop a comprehensive research program, each phase to be directed to a specific aspect of Reye's Syndrome. Potential applicants are encouraged to consult with the appropriate institute representative (listed below) as early as possible in the planning stages. Deadlines for receipt of P01 applications are June 1, October 1, and February 1.
b) Applicants may propose individual research projects involving any investigational aspect of Reye's Syndrome. Deadlines for receipt of RO1 applications are July 1, November 1, and March 1.

REVIEW PROCEDURES AND CRITERIA

Applications should be prepared on form PHS 398 following regular instructions contained in the application kit. Submitted applications will be assigned by Division of Research Grants to awarding units and for peer review in accordance with the usual Referral Guidelines. Applications will be reviewed for scientific merit and relevance to program goals in accordance with the standard review procedures of the NIH; that is, each application will be assessed first for scientific merit review by a group of mostly non-Government scientists having appropriate expertise and then for both scientific merit and program relevance by the appropriate National Advisory Council.

Applicants may request amounts commensurate with the objectives to be accomplished for a period not to exceed five years. The support mechanism referred to in this announcement will be grants-in-aid and these awards will be made on a competitive basis to those applicants who have successfully competed with all applicants for funds from the sponsoring programs of the institutes involved.

The phrase "Prepared in Response to the Program Announcement for Research Grants in the Area of Reye's Syndrome" should be typed across the top of the first (face) page of the application.

Completed applications should be submitted according to the deadlines for the review schedule mentioned above and also supplied in the application kit and mailed to the following address:

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

INQUIRIES AND CORRESPONDENCE

One copy of the application is to be sent to each of the addresses below. Applicants needing further information may contact:

Kenneth Surrey, Ph.D.
Neurological Disorders Program
NINCDS, National Institutes of Health
Room 710, Federal Building
Bethesda, Maryland 20205

John R. LaMontagne, Ph.D.
Influenza Program Officer
National Institutes of Health
NIAID/MIDP/DAB
Room 750, Westwood Building
Bethesda, Maryland 20205
Robert Katz, Ph.D.
Metabolic Diseases Research Program Director
NIAMDD-EP, National Institutes of Health
Room 603, Westwood Building
Bethesda, Maryland 20205

Delbert Dayton, M.D.
Chief, Genetics and Teratology Section
CNED/CRMC/NICHD, National Institutes of Health
Room 7C08, Landow Building
Bethesda, Maryland 20205
BIOTECHNOLOGY RESOURCES PROGRAM

DIVISION OF RESEARCH RESOURCES

The Biotechnology Resources Program, Division of Research Resources, announces the continued availability of biotechnology resource center grants for research, development and provision of complex technological capabilities, generally large instruments and/or computation equipment needed in biomedical or clinical research. The purpose of the grants is to make advanced state-of-the-art instruments and equipment available to the biomedical research community on a shared basis. Emphasis is also on research and development on instruments, equipment and/or accompanying methodology which increases uses of the instruments and equipment in biomedical or clinical research.

Biotechnology resources currently supported have capabilities in large-scale, mini and microcomputer systems, and an array of specialized instruments and equipment for analysis and characterization of biological structures. The latter include mass spectrometers, nuclear magnetic resonance spectrometers, electron spin resonance spectrometers, million-volt electron microscopes, scanning transmission electron microscopes, electron microprobe, multivire x-ray diffractometer, equipment for studying fast biochemical and biophysical reactions, laser systems for use in cell biology research, and equipment to use synchrotron radiation in research. Details on instruments, equipment, services and current research applications at individual biotechnology resources are given in the Biotechnology Resources Directory. This Directory is available from the Research Resources Information Center, 1776 East Jefferson Street, Rockville, Maryland 20852.

Characteristics of Technologies Supported

Program requirements for the nature of technologies supported are:

- Expense and/or complexity requires it to be shared by investigators on a regional or national level.

- Uses of it span interests of a variety of disciplines or NIH categorical areas.

- State is such that further technological development is needed to fulfill its potential in biomedical and clinical research.

This program is described in the Catalog of Federal Domestic Assistance number 13.371. 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.
Characteristics of a Biotechnology Resource

The biotechnology resource center grant contains funds for five activities:

- **Core research** in methodological and analytical techniques or development of new instruments.

- **Collaborative research** between resource equipment experts and scientists requiring special technical developments to solve biomedical research problems.

- **Service** is provision of equipment and necessary technical personnel to researchers; fees may be charged for services in some resources.

- **Training** in the use of the equipment and interpretation of results.

- **Dissemination** of the capabilities and research accomplishments of the resource.

Support Provided by the Grant

The Biotechnology Resources Program makes possible the establishment and initial operation of resources. After an initial start-up and development period, a resource is expected to derive support for operating the routine service components and the mature collaborative projects from sources other than the Biotechnology Resources Program.

The Program plans to award $2 million or more to new competing resource grants in fiscal year 1981, contingent on receipt of the scientifically meritorious applications and appropriated funds.

Application Procedures and Program Guidelines

More detailed Program and application guidelines are available from the Program. Prospective applicants should consult these guidelines and discuss the proposed resource with Program staff. Inquiries and requests for Program and application guidelines should be addressed to:

Director
Biotechnology Resources Program
Division of Research Resources
National Institutes of Health
Room 5B-41, Building 31
Bethesda, Maryland 20205

Telephone: (301) 496-5411
The deadlines for applications are October 1, February 1, and June 1. Applications will undergo initial review by an appropriate study section of the Division of Research Grants. Secondary review will be by the National Advisory Research Resources Council.
RESEARCH ON DISEASES OF THE
BILIARY TRACT AND EXOCRINE PANCREAS,
NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM,
AND DIGESTIVE DISEASES

As a part of its mission to support research and related training into the causes, diagnosis, prevention, and treatment of the diseases of the biliary tract and the exocrine pancreas, the Biliary Tract and Pancreatic Diseases Program of the National Institute of Arthritis, Metabolism, and Digestive Diseases desires to expand its support of research, both basic and clinical, into the normal function and the relevant diseases of these organs.

Applications for research grants relating to areas such as those listed below are invited. This list is not intended to be either comprehensive or exclusive, nor is it in order of priority. Rather, it is intended to exemplify the wide variety of new and/or continuing Program emphases. For background information regarding opportunities for investigator-initiated research in the broad area of this announcement, it is suggested that prospective applicants refer to the publication: "Report to the Congress of the United States of the National Commission on Digestive Diseases," Volume IV, Parts 2A and 2B, DHEW Publication No. (NIH) 79-1884 and (NIH) 79-1885. Copies of this publication may be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402 (G.P.O. Order No. 017-045-00090-3; Price: $8.50).

I. Biliary Tract

1. Continuation of multidisciplinary studies on pigment gallstone disease, including:

   (a) determination of the factors and mechanisms regulating bilirubin, carbonate, phosphate, and calcium secretion into bile;

   (b) understanding the events leading to nidation and growth of pigment stones;

   (c) prevention of such precipitation;

   (d) determination of the composition of pigment stones, including the nature of the black pigment and of the large unmeasured organic component (presumably protein) in these stones;

   (e) identification of patients with pigment stones prior to cholecystectomy;

   (f) development of method(s) for dissolution of pigment stones.
2. Determination of the effect of manipulation of plasma lipids either by diet or by drugs upon biliary cholesterol saturation in man and other primates. Identification of drugs which are lithogenic coupled with knowledge of their pharmacological effects should provide further insights into mechanisms affecting cholesterol excretion in bile.

3. Search for agents other than chenodeoxycholic acid which might induce cholesterol unsaturated bile, can be given orally, and are nontoxic and cheaper than chenodeoxycholic acid. The finding that ursodeoxycholic acid may induce greater cholesterol desaturation than chenodeoxycholic acid without producing diarrhea deserves follow-up in terms of efficacy, safety, and mechanism of action in both short-term and long-term clinical trials.

4. Continuation of the safety evaluation of chenodeoxycholic acid, ursodeoxycholic acid, other primary and secondary bile acids, and their metabolites and potentially cholelitholytic analogs in terms of:

   (a) hepatotoxicity;
   (b) their effects on fluid secretion, mucosal permeability, and mucosal morphology in the colon;
   (c) their role in large bowel carcinogenesis;
   (d) induction of DNA damage and repair;
   (e) mutagenesis;
   (f) neoplastic transformation of mammalian cells in culture.

5. Continuation of investigations into the mechanism of regulation of hepatic cholesterol synthesis and secretion and the effects of agents (e.g., chenodeoxycholate and ursodeoxycholate) on these processes. Studies should be pursued which will quantify hepatocyte cholesterol pools and define their relationships with extrahepatic pools. From which pool, if any, does biliary cholesterol derive and how does the cholesterol reach bile? Does newly synthesized cholesterol gain preferential access to bile?

6. Continuation of studies on the regulation of bile acid synthesis, secretion, pool size, and circulation. The role of the gallbladder in bile acid storage and discharge should be studied insofar as it affects biliary bile acid excretion rate and bile cholesterol saturation. Small bowel transit time as well as jejunal bile acid absorption under physiological conditions should be studied as factors which influence bile acid pool size and cycling frequency and, hence, biliary acid excretion rate in man.

7. Initiation of limited controlled clinical trials with patients with retained common duct stones or hepatic duct stones using agents currently efficacious in gallstone dissolution (e.g., chenodeoxycholic acid, ursodeoxycholic acid). For those patients who still have an access to the common duct, agents more efficacious and less toxic than cholic
acid should be explored as gallstone solvents.

8. Development of new techniques in this field, including:

(a) noninvasive methods for the diagnosis of potential gallstone formers;

(b) a method for quantitatively investigating gallbladder function in animals;

(c) noninvasive techniques for the quantitative determination of the contraction of the gallbladder, its effect on bile composition, and the enterohepatic circulation in patients.

II. Exocrine Pancreas

1. Conduct of epidemiological studies to identify those individuals who are at greatest risk for pancreatic disease and to determine what characteristics (e.g., the roles of diet, alcohol, exposure to environmental pollutants and regional factors) predispose certain individuals or groups of individuals to the development of pancreatitis.

2. Studies aimed at developing meaningful animal models of acute and chronic human pancreatitis. Other types of systems that could be explored for their potential of being used to establish models of human pancreatic diseases are pancreatic tissue maintained in tissue or organ culture.

3. Development of the ability to obtain percutaneous or transduodenal biopsy samples of the pancreas from patients with pancreatitis as well as other disorders.

4. Continuation of investigations aimed at developing methods for the diagnosis of pancreatic diseases, including:

(a) development of a radioimmunoassay technique for the measurement of serum pancreatic enzymes, including their precursor forms, and determination of the comparative value of this technique to current enzymatic procedure;

(b) simplification and standardization of the technology of pancreatic secretory function tests;

(c) prospective evaluation, comparison, and determination of the relative cost-effectiveness of the various newer imaging procedures in the diagnosis of pancreatic disease, including computerized tomography, ultrasonography, and endoscopic retrograde pancreatography.
5. Continuation of basic research on the exocrine pancreas along the following lines:

(a) fundamental research directed toward the understanding of the control processes of regeneration and repair of the pancreas after injury;

(b) further studies on the basic cell biology of the acinar, centroacinar, and duct cells of the gland, including:

(i) morphological and biochemical characterization of secretagogue receptors;

(ii) rigorous biochemical studies on the types of inhibitors known or suspected to be present in pancreatic juice from normal man and comparison with those in pancreatic juice from patients in an attempt to define breakdown of the cell's first line of defense against premature activation of pancreatic proenzymes;

(iii) systematic biochemical characterization of membranes from intracellular compartments as well as of the cell's bounding plasma membrane in order to define the basis for the normal resistance of such membranes to enzymes secreted in active form;

(iv) detailed quantitative studies using freeze-fracture electron microscopy of pancreatic tissue afflicted with pancreatitis to determine whether or not tight junctions are primarily or secondarily disrupted.

6. Studies of the potential role of the immune system in pancreatic disease.

7. Further research on the treatment of acute and chronic pancreatitis, including:

(a) development of more effective methods to reduce pancreatic metabolic and secretory activity;

(b) development of more potent pancreatic enzyme preparations and oral delivery systems that will prevent gastric acid-pepsin inactivation of pancreatic enzymes;

(c) evaluation from both a pathophysiologic as well as a clinical point of view in appropriate controlled clinical trials of the value of pancreatectomy, subtotal pancreatectomy, longitudinal pancreaticoduodenostomy, and other forms of surgical therapy used in the treatment of acute and chronic pancreatitis.
General Information

The mechanism of support will be the traditional research grant. Applications in response to this announcement will be reviewed on a nationwide basis in competition with each other and in accordance with the usual National Institutes of Health peer review procedures. The initial review for scientific and technical merit will be by an appropriate study section of the Division of Research Grants, NIH; secondary review will be by the National Arthritis, Metabolism, and Digestive Diseases Advisory Council. The review criteria customarily employed by the National Institutes of Health for regular research grant applications will prevail. Funding decisions will be based upon relative scientific merit, program relevance, and the availability of appropriated funds. 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.

Application Procedure

Applications should be submitted on form PHS 398, which is available in the business or grants and contracts offices of most academic and research institutions or from the Division of Research Grants, NIH. The phrase "RESPONSE TO NIAID DD PROGRAM ANNOUNCEMENT ON RESEARCH ON DISEASES OF THE BILIARY TRACT AND EXOCRINE PANCREAS" should be typed across the top of the first (face) page of the application. Additionally, a brief covering letter should accompany the application indicating it is being submitted in response to this program announcement.

Applications will be accepted on an indefinite basis in accordance with the usual receipt dates for new research grant applications: July 1, November 1, and March 1.

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

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

For further information concerning this announcement and for information regarding other mechanisms of support for research and training available in this connection, investigators are encouraged to contact:

Dr. G. G. Roussos
Program Director for Biliary Tract and Pancreatic Diseases
Room 602, Westwood Building
National Institutes of Health
Bethesda, Maryland 20205

Telephone: (301) 496-7121
In order to alert the Biliary Tract and Pancreatic Diseases Program to the submission of proposals as requested above, a copy of the covering letter accompanied by copies of the face page and summary page of such applications should be forwarded under separate cover to Dr. Roussos.
RESEARCH GRANTS RELATED TO MOTOR NEURON DISEASES,
SPINOCEREBELLAR AND SYSTEM DEGENERATIONS, NINCDS

The Neurological Disorders Program of the National Institute of Neurological and Communicative Disorders and Stroke, a component of the National Institutes of Health, invites grant applications for support of research on motor neuron, spinocerebellar, and related system degenerations.

Amyotrophic Lateral Sclerosis, the most common of the motor neuron diseases (MND), is characterized by degeneration of the corticospinal tracts, and by atrophy and loss of motor neurons of the precentral gyri, cranial nerve nuclei and anterior horns of the spinal cord. These changes are associated with weakness and atrophy of the affected skeletal muscles. Onset of the disease usually occurs between 40 and 64 years of age. Some forms are familial.

Friedreich's ataxia, a relatively common form of the hereditary ataxias, affects spinocerebellar and corticospinal tracts, posterior columns, and peripheral nerves. The disease usually appears before 20 years of age. Many cases are familial and transmitted in an autosomal recessive fashion. Damage to the heart is often present and some of the patients suffer from diabetes mellitus.

"Linking forms" between these and other system degenerations have suggested a spectrum of possibly related disorders. The etiology of these diseases and effective treatments are unknown.

RESEARCH GOALS AND SCOPE

There is a paucity of understanding about these disorders at all but clinical and pathological levels and therefore additional basic research is essential. Studies might include normal and abnormal biology of motor and other neurons, CNS response to injury and the effects of environmental toxins, new and more sensitive probes for detection of conventional and unconventional infectious agents, development of new animal models, identification of metabolic and endocrine abnormalities and changes in extraneural tissue more accessible to biopsy, tests for "populations at risk," early diagnosis, epidemiology and experiments with new therapeutic modalities.

This program is described in the Catalog of Federal Domestic Assistance number 13.852. 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.
MECHANISMS OF SUPPORT

Applications may be submitted for program project grants (P01), or individual research project grants (R01).

a) Program projects may include clinical research as well as experimental approaches, depending upon the local facilities or those of cooperating institutions. These should include technical and professional expertise, interest, resources, possibly patients and the ability to carry out the desired objectives. Applicants should develop a comprehensive research program, each phase of which is directed to a specific aspect of amyotrophic lateral sclerosis or other system degenerations. Potential applicants are encouraged to consult with the staff of the Neurological Disorders Program early in the planning stage. Deadlines for receipt of P01 applications are October 1, February 1, and June 1.

b) Individual applicants may propose any investigational aspect of amyotrophic lateral sclerosis or system degenerations. Deadlines for receipt of R01 applications are July 1, November 1, and March 1.

REVIEW PROCEDURES AND CRITERIA

Applications should be prepared on form PHS 398 following instructions contained in the application kit. Application kits are available at most institutional business offices or from the Division of Research Grants, NIH. Program projects should conform to the style and format recommended by this Institute; this information is available from the staff contacts listed below. Program project applications will be reviewed initially and judged for scientific merit by one of the NINCDS program project review committees. Individual research projects receive a similar review by the appropriate study section of the Division of Research Grants. Both reviews will be conducted in accordance with NIH policy and procedures involving peer review. Applicants may request amounts commensurate with the objectives to be accomplished for a period not to exceed five years. The support mechanism for this program will be the grant-in-aid. Awards will be made to the applicants who have successfully competed with all those requesting funds from the Neurological Disorders Programs.

The phrase "Prepared in Response to NINCDS Invitations for Research Grants in the area of Motor Neuron Diseases, Spinocerebellar and System Degenerations" should be typed across the top of the first (face) page of the application.

Completed applications should be submitted according to the deadlines for the review schedule mentioned above (also supplied in the application kit) and mailed to the following address:

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

One copy of the application should be sent to the address below. Applicants needing further information including format for program project applications may contact:

Dr. A. P. Kerza-Kwiatecki  
Health Scientist Administrator  
Neurological Disorders Program  
Room 710, Federal Building  
Bethesda, Maryland 20205  
Telephone: (301) 496-1431

or

Dr. Emanuel M. Stadlan, Chief  
Research Programs in Multiple Sclerosis, Sclerosing and Infectious Diseases  
National Institute of Neurological and Communicative Disorders and Stroke  
Room 810, Federal Building  
Bethesda, Maryland 20205  
Telephone: (301) 496-2313
BIOBEHAVIORAL APPROACHES TO THE TREATMENT
OF HYPERTENSION, NHLBI

The Behavioral Medicine Branch of the National Heart, Lung, and Blood Institute wishes to encourage clinical research projects dealing with evaluation of combinations of pharmacologic and non-pharmacologic therapies in the treatment of patients with diagnosed essential hypertension and requests investigators to consider applying for regular research grant support in this area.

Pharmacologic antihypertensive therapy has been particularly effective in reducing blood pressure in severely and moderately hypertensive patients. Lifetime maintenance of lowered blood pressure by pharmacologic means has proven particularly nettlesome, with long term (five year) compliance with drug regimes estimated to be less than 20% of the target population. Short term side effects, cost and the unknown long-term implications of lifetime drug regimens have been major contributors to the compliance problem.

Exercise, diet, relaxation techniques, biofeedback, meditation, psychotherapy, as examples of non-pharmacologic approaches, have been less effective in lowering blood pressure than pharmacologic agents, but pilot studies have demonstrated their potential utility in maintaining pharmacologically lowered pressure. Medication requirements have been significantly reduced or completely eliminated by such procedures. Apparently, the combinations of pharmacologic and non-pharmacologic therapies may also produce a synergistic effect, i.e., the non-pharmacologic techniques may potentiate the effect of the drugs. The above issues need further exploration in well-controlled studies which can assess the efficacy and preferred configuration of "biobehavioral" approaches to the treatment of hypertension.

This is the third of three announcements of this research interest to be made during the year prior to the regular application receipt dates of July 1, 1980 and November 1, 1980. Applications should be made in the usual manner (except for the two items noted below), and the regular review procedure will be followed.

Individuals who submit proposals in response to this announcement are asked to:

This program is described in the Catalog of Federal Domestic Assistance number 13.837. 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.
1. Use the STANDARD TITLE: "Biobehavioral Approaches to the Treatment of Hypertension" and mail the completed PHS 398 form directly to the Division of Research Grants as instructed in the application kit; and

2. Submit a brief LETTER OF INTENT stating that such an application has been, or will be, submitted. The letter should be addressed to:

   Behavioral Medicine Branch
   National Heart, Lung, and Blood Institute
   National Institutes of Health
   Room 3A-13, Federal Building
   Bethesda, Maryland 20205

Questions about this announcement should be directed to the Behavioral Medicine Branch; telephone (301) 496-9380.
The Senior International Fellowship Program of the Fogarty International Center, NIH, provides opportunities to non-Federal U.S. biomedical research and graduate-level educational institutions to nominate outstanding staff members at mid-career, who have demonstrated productive scholarship and have recognized stature in their profession, to go abroad to study and share their expertise as representatives of the best in the American health sciences. It is intended that this award be a career-enhancing educational experience with mutual benefits to all involved.

Fellowship awards are made for periods of 3 to 12 months for research and study in the health sciences at foreign host institutions. An applicant must be a U.S. citizen or permanent resident, have a full-time appointment at the U.S. institution, have at least five years' experience beyond the doctorate, and possess the linguistic skills appropriate to the host institution. Transportation costs, host institution allowance, stipend and foreign living allowance are provided.

During the Fellowship period at the host institution the applicant is expected to pursue a specific, well-designed project of mutual interest related to his or her ongoing work as well as to that which will be continued upon return. The type of project would be dependent upon the professional discipline of the applicant, such as basic laboratory or clinical research, data collection and analysis, or operational research. The intrinsic technical merit of the project is one of several important factors to be considered in evaluating the totality of an application as to its fulfillment of the basic purposes of the Program. The following factors will be given weight in review of an application:

- qualifications of the applicant
- potentiality for career enhancement
- opportunity for close, interpersonal technical interchange
- benefit to the U.S. nominating institution
- benefit to the foreign host institution
- technical merit and significance of the project.
Applications cannot be considered as fulfilling the purposes of the Program where there is not a sufficient period of time for in-depth interaction by the applicant with the host institution or where the benefit is primarily for only one of the parties. Thus applications having any of the following as the major feature cannot be accepted:

- visits to multiple institutions for brief periods
- attendance at conferences
- attendance in formal training courses
- provision of full-time clinical or teaching services
- completely independent study.

Application kits will be available from March 15 - September 15, 1980 and will be sent only upon request from the offices of deans or equivalent institutional officials. Information brochures will be sent to individuals on request. In addition to a project description and other supporting material, applications require nomination by the U.S. institution and a letter of invitation by a foreign host institution. The deadline for applications is October 1, 1980 with selection of awards April 1981.

Further information may be obtained from:

Senior International Fellowship Program
Scholars and Fellowships Program Branch
Fogarty International Center
National Institutes of Health
Bethesda, Maryland 20205
SENIOR INTERNATIONAL FELLOWSHIPS
OF THE
FOGARTY INTERNATIONAL CENTER, NIH
IN SPECIAL FIELDS
- AGING
- ARTHRITIS
- DIABETES
- EPILEPSY
- TROPICAL DISEASES

As part of its Senior International Fellowship Program and in cooperation with certain Institutes of NIH, the Fogarty International Center announces that several Senior International Fellowship awards will be allocated each year to specified fields for research and study abroad. The fields and cooperating Institutes are:

- Aging - National Institute on Aging
- Arthritis - National Institute of Arthritis, Metabolism, and Digestive Diseases
- Diabetes - National Institute of Arthritis, Metabolism, and Digestive Diseases
- Epilepsy - National Institute of Neurological and Communicative Disorders and Stroke
- Tropical Diseases - National Institute of Allergy and Infectious Diseases

These awards will be in addition to those made under the broad range of fields of its regular program. The number will be dependent upon the availability of special funds for this purpose and the merit of applications.

The eligibility requirements, award levels and general terms are the same as for regular Senior International Fellowships.

Annual Application Deadline - October 1

Annual Notification of Final Selection Decisions - April

Fellowships may be activated at any time within 12 months of issuance of the Notice of Research Fellowship Award (PHS Form 416)
Concurrent Applications - An applicant cannot submit concurrent applications to both the regular Senior International Fellowship Program and the Special Emphasis Fellowship Program. Because of the possibility that an application may be approved but cannot be funded by the applicant's designated Program, an applicant may request consideration by the appropriate administrative agency for the alternate Program. Such dual consideration would apply only to those applications whose objectives are relevant to either Program. Such consideration will be granted only upon written request at the time of submission of an application.

An applicant must be a U.S. citizen or permanent resident, be an experienced investigator at mid-career, hold a full-time staff position at a non-Federal U.S. biomedical research or graduate-level educational institution, be nominated by the institution, and have an invitation by a foreign host institution. Awards are made for periods of 3 to 12 months abroad and provide a stipend, travel costs, host institution allowance and a foreign living allowance. To be given particular consideration in one of the specified fields, the study proposal in the application must be clearly and directly related to that field but may range from basic biological mechanisms to clinical aspects.

Individuals interested in being considered for these special Fellowships should first familiarize themselves with the general program guidelines for Senior International Fellowships. Application kits will be sent only to offices of Deans or equivalent institutional officials upon request. Information brochures will be sent to individuals upon request. In order to assure proper processing, all inquiries and application materials submitted should be clearly identified in the following manner:

"SENIOR INTERNATIONAL FELLOWSHIP - SPECIAL FIELD "(______________________)."
(name of field)

Further information may be obtained from:

Senior International Fellowship Program
Scholars and Fellowships Program Branch
Fogarty International Center
National Institutes of Health
Bethesda, Maryland 20205