

# NIH Guide for Grants and Contracts

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U.S. DEPARTMENT OF HEALTH  
AND HUMAN SERVICES

Vol. 14, No. 11, October 11, 1985

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The NIH 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.

#### Have You Moved?

If you 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.

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**NOTICE**

**RESEARCH TRAINING OF NURSES**

P.T. 44; K.W. 0720005, 0785130

This notice calls the attention of National Research Service Award (NRSA) training program directors seeking highly qualified applicants for trainee appointments to the fact that there is a recruitment pool in the nurse community which may have been overlooked.

In May 1984, Dr. James Wyngaarden, Director, NIH, appointed an NIH Task Force charged with reviewing NIH activities involving nursing research. Recommendations made by the Task Force in its final report included several relative to the research training of nurses. In particular, it was noted that many nurse graduates with baccalaureate and doctoral degrees were unaware that they may be eligible to apply for appointments as predoctoral or postdoctoral trainees on NRSA institutional training grants or as applicants for individual NRSA fellowships.

NIH is taking steps to acquaint the nursing community with the eligibility requirements for these programs and the locations and names of the program directors of Institutional NRSAs. NRSA training program directors should also make information about their programs available to the nursing profession.

**NOTICE**

**NURSE SCIENTISTS SOUGHT FOR INITIAL REVIEW GROUPS**

P.T. 22, 34; K.W. 0710030, 0720005

**DIVISION OF RESEARCH GRANTS (NIH)**

The National Institutes of Health (NIH) encourages and welcomes the submission of names of nurse scientists with research experience as potential members of the various initial review groups (study sections) that carry out the review of grant applications for the support of research and training. Names and curricula vitae should be sent to:

Mischa E. Friedman, Ph.D.  
Chief, Referral and Review Branch  
Division of Research Grants  
National Institutes of Health  
Bethesda, Maryland 20892

**NOTICE****MULTIPURPOSE ARTHRITIS CENTERS****P.T. 34; K.W. 0715010, 0785195, 0705050, 0403004, 0500000****NATIONAL INSTITUTE OF ARTHRITIS, DIABETES, AND DIGESTIVE AND KIDNEY DISEASES**

The National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK) supports a series of Multipurpose Arthritis Centers through the Comprehensive Research Center grant mechanism (P60). In a recent notice (NIH Guide for Grants and Contracts, Vol. 14, No. 7, June 21, 1985) the NIADDK fixed the length of project periods for all centers at five years, except under unusual circumstances.

In accord with this policy, the Multipurpose Arthritis Center Program announces two changes in its Application Guidelines:

1. Developmental and feasibility study support will, subject to the recommendations of the Initial Review Group, now be provided for the full five year period of award, based on the number and quality of the approved studies.
2. The present three-component structure of the Multipurpose Arthritis Centers (Research, Education, and Community/Health Services Research components) will be changed to two components. The first component will be biomedical research. The second component will encompass the Education and Community/Health Services Research Components. Applicants will, accordingly, propose a full five-year program for each of the two components.

These changes become effective immediately. Questions regarding these changes and requests for the addendum to the Application Guidelines should be directed to:

Dr. Steven J. Hausman  
Director, Multipurpose Arthritis  
Centers Program  
National Institute of Arthritis, Diabetes,  
and Digestive and Kidney Diseases  
National Institutes of Health  
Westwood Building - Room 403  
Bethesda, Maryland 20892

Telephone: (301) 496-7495

**ANNOUNCEMENT**

**AVAILABILITY OF REQUEST FOR APPLICATIONS: RFA**

**86-CA-01**

**CANCER CONTROL TECHNICAL DEVELOPMENT IN HEALTH AGENCIES**

P.T. 34; K.W. 0715035, 0730070, 0403004

**NATIONAL CANCER INSTITUTE**

Application Receipt Date: January 15, 1986

The Division of Cancer Prevention and Control (DCPC) of the National Cancer Institute (NCI) invites grant applications to enhance the technical capabilities of health agencies in cancer prevention and control.

**RESEARCH GOALS AND SCOPE**

The goal of this RFA is to enable health agencies at State or selected local levels to enhance their capacity to plan, implement and evaluate cancer control programs. NCI support will provide for access to technical expertise in needs assessment, prioritization, program planning and evaluation. Health agencies are expected to provide for funding of any implementation and operation of resulting cancer control programs.

**ELIGIBILITY**

Applicant must be a State, territorial or local public health department or other agency designated by, operated by or under contract with a State, territorial or local government, with primary cancer control responsibility for a population of at least 500,000. An applicant other than a health department must demonstrate the direct involvement of a health department in the application. Applications that include more than one jurisdiction to meet minimum population requirements will be accepted.

**MECHANISM OF SUPPORT**

Awards will be made as grants. Funding is limited to a maximum of five years. Between 5-10 awards are anticipated depending on the availability of quality applications and funding.

**INQUIRIES**

Copies of the complete RFA and additional information may be obtained from:

Dr. Lawrence Bergner, Program Director  
Cancer Control Applications Branch  
Science Program, Division of Cancer Prevention  
& Control  
National Cancer Institute  
Blair Building - Room 4A01  
9000 Rockville Pike  
Bethesda, Maryland 20892-4200  
Telephone: (301) 427-8597

**ANNOUNCEMENT****AVAILABILITY OF REQUEST FOR APPLICATIONS: RFA****86-HD-01****TROPHECTODERM/BLASTULA DEVELOPMENT**

P.T. 34; K.W. 0413002, 1002059, 1002019, 1002008

**NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT**

Application Receipt Date: February 18, 1986

The Reproductive Sciences Branch (RSB), of the Center for Population Research (CPR), of the National Institute of Child Health and Human Development (NICHD), announces the availability of a Request for Applications (RFA) on trophoctoderm/blastula development. The purpose of this program is to encourage and support research on genetic, biochemical, biophysical, morphological and molecular biological approaches to the problem of the formation of the animal egg into the first epithelium, referred to as the trophoctoderm in mammals and the blastula in non-mammals. The fact that trophoctoderm formation is the predominant activity of preimplantation development underscores its importance to mammalian reproduction. This genetic and epigenetic emphasis on trophoctoderm/blastula development is part of an RSB program on the developmental biology of reproduction that encompasses gametogenesis through implantation research. This initiative is a critical aspect of the mission of the RSB to provide a research base for improved understanding of human and animal reproduction with implications for the control of fertility and infertility.

This program will be funded through the individual research project grant mechanism. Grant applications will be reviewed at a single competition by an initial review group convened by NICHD. It is anticipated that 8-10 grants will be awarded contingent on scientific merit and availability of funds.

Requests for copies of the full RFA should be addressed to:

Richard J. Tasca, Ph.D.  
Reproductive Sciences Branch  
Center for Population Research  
National Institute of Child Health  
and Human Development  
National Institutes of Health  
Landow Building - Room 7C33  
Bethesda, Maryland 20892

Telephone: (301) 496-6515

This program is described in the Catalog of Federal Domestic Assistance No. 13.864, Population Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

ANNOUNCEMENT

AVAILABILITY OF REQUEST FOR APPLICATIONS: (RFA)

86-AM-01

KIDNEY AND UROLOGICAL RESEARCH CENTERS

P.T. 04; K.W. 0785055, 0785095, 0785220, 0705030, 0705075, 0715135, 0755030,  
1002004, 1002008, 1002019, 0785035

NATIONAL INSTITUTE OF ARTHRITIS, DIABETES, AND DIGESTIVE AND KIDNEY  
DISEASES

Application Receipt Date: March 15, 1986

The Division of Kidney, Urologic and Hematologic Diseases (DKUHD) of the National National Institute of Arthritis, Diabetes and Digestive and Kidney Diseases (NIADDDK) announces a national competition to encourage the submission of research center applications (P50), which will establish a limited number of Kidney and Urological Research Centers for the purpose of investigating the epidemiology, causes, prevention and treatment of kidney and urinary tract disorders.

I. BACKGROUND

Kidney and urologic diseases account for substantial and increasing morbidity and financial burden in the United States; cumulatively they are responsible for a large number of work days lost and the loss of all or a part of a normal healthy life. Although considerable progress has been made in understanding the basic physiology and pathophysiology of the normal renal and urologic system, there has been little progress in the understanding of fundamental disease processes. Nevertheless, major progress has been made in the management of the clinical sequelae of these diseases. For example, renal dialysis and transplantation have been developed as life-saving procedures and the surgical management of benign prostatic hyperplasia (BPH) has also made substantial progress over the past twenty years. Unfortunately, these advances are not curative procedures and are costly. The proposed multidisciplinary research centers should provide appropriate expertise to investigate the topical areas of immunologically mediated diseases; diabetes mellitus and other endocrine and metabolic disorders; primary renal hypertension; genetic abnormalities; developmental and obstructive disorders; nephrotoxins and toxic cell injury.

This program is described in the Catalog of Federal Domestic Assistance No. 13.849, Kidney, Urologic, and Hematologic 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 the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

## II. RESEARCH GOALS AND SCOPE

The emphases of this initiative are threefold: (1) to attract new scientific expertise into the study of the basic mechanisms of kidney and urological diseases; (2) to encourage interdisciplinary research; and (3) to extend these basic investigations into innovative clinical and epidemiologic studies of the causes, therapy and prevention of kidney and urologic disorders. In approaching one or more of the disease processes outlined above, it is anticipated that extensive collaboration will be required between individuals in the basic sciences, including cell biology, molecular biology, immunology, genetics, epidemiology, biochemistry, physiology and pathology with clinical sciences. Thus it is an express intent to engage into the the field investigators not currently active in renal and urinary tract research and to explore new basic areas which may then be applied to clinical research projects. Individual institutions with both basic and clinical research capabilities would qualify for applying; however, the arrangement for inter-institutional collaborative research activities is another means of meeting the intent of this announcement. It is anticipated that initially NIADDK will fund six Centers at a level not to exceed \$1.0M/year/Center including indirect costs. These awards will be made for five years and the progress of each Center will be evaluated annually.

## III. MECHANISM OF SUPPORT

Support for this program will be through the traditional grant-in-aid. Successful applicants will direct and carry out the center's research projects.

## IV. APPLICATION AND REVIEW PROCEDURES

The applications for Centers solicited in this announcement will be evaluated in national competition by a special review committee convened by the NIADDK. Deadline for the receipt of the applications will be March 15, 1986 and letter of intent should be received from all prospective applicants by the close of business on January 15, 1986.

## V. INQUIRIES

Potential applicants may request additional information and copies of the entire RFA from:

M. J. Scherbenske, PH.D.  
Assistant to the Director for Administration  
Renal Physiology/Pathophysiology Program Director  
DKUHD/NIADDK  
Westwood Building - Room 621  
5333 Westbard Avenue  
Bethesda, Maryland 20892

**ANNOUNCEMENT**

**AVAILABILITY OF REQUESTS FOR APPLICATIONS: (RFA)**

**86-HL-01-B**

**HEMOSTATIC DEFECTS IN RENAL FAILURE: PATHOGENESIS AND TREATMENT**

P.T. 34; K.W. 0785070, 0785095, 0785165

**DIVISION OF BLOOD DISEASES AND RESOURCES**

**NATIONAL HEART, LUNG, AND BLOOD INSTITUTE**

Application Receipt Date: February 18, 1986

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

The program will support research addressing the hemostatic defect observed in some patients with chronic renal failure. The scope of this program includes identification of factors responsible for the bleeding tendency and development and evaluation of possible therapeutic interventions to correct such hemostatic defects. The long range goal of this activity is to expand the knowledge base on hemostatic mechanisms.

Awards in response to this announcement will be made to foreign institutions only for research of very unusual merit, need, and promise, and in accordance with Public Health Service policy governing such awards.

Requests for copies of the RFA should be addressed to:

Carol H. Letendre, Ph.D.  
Division of Blood Diseases and Resources  
Federal Building - Room 5A12  
7550 Wisconsin Avenue  
Bethesda, Maryland 20892

Telephone: (301) 496-5911

**ANNOUNCEMENT**

**AVAILABILITY OF REQUEST FOR APPLICATIONS: (RFA)**

**85-HL-02-B**

**MEMBRANE TRANSPORT, PERMEABILITY AND VOLUME CONTROL IN SICKLE CELL DISEASE**

P.T. 34; K.W. 0790005, 0785070, 0715040

**DIVISION OF BLOOD DISEASES AND RESOURCES**

**NATIONAL HEART, LUNG, AND BLOOD INSTITUTE**

Application Receipt Date: February 18, 1986

The Sickle Cell Disease Branch, Division of Blood Diseases and Resources, National Heart, Lung, and Blood Institute (NHLBI) announces the availability of a Request for Applications (RFA) on the above mentioned subject. Copies of the RFA, 86-HL-2-B, may be obtained from the staff of the NHLBI.

The purpose of this program is to encourage research on the red cell membrane with relation to transport, permeability, and volume control in sickle cell disease. Studies have shown that sickle cell disease involves alterations of the erythrocyte membrane and that the sickling phenomenon is accompanied by decreased membrane deformability. This research would provide innovative approaches to elucidate the role of the erythrocyte membrane in hemoglobin S gelation and ultimately to apply this knowledge to the development of therapeutic approaches for sickle cell disease. Awards in response to this announcement will be made to foreign institutions only for research of very unusual merit, need, and promise, and in accordance with Public Health Service policy governing such awards.

Requests for copies of the RFA should be addressed to:

John I. Hercules, Ph.D  
Sickle Cell Disease Branch  
Division of Blood Diseases and Resources  
National Heart, Lung, and Blood Institute  
National Institutes of Health  
Federal Building - Room 508A  
Bethesda, Maryland 20892

Telephone (301) 496-6931

**ANNOUNCEMENT**

**AVAILABILITY OF REQUEST FOR APPLICATIONS: RFA**

**86-HL-03-L**

**DEVELOPMENT AND DIFFERENTIATION OF AIRWAY EPITHELIUM**

P.T. 34; K.W. 0705065, 1002059, 1002004, 1003002, 0765035, 0710100

**DIVISION OF LUNG DISEASES**

**NATIONAL HEART, LUNG, AND BLOOD INSTITUTE**

Application Receipt Date: April 1, 1986

The Structure and Function Branch of the Division of Lung Diseases, National Heart, Lung, and Blood Institute (NHLBI) announces the availability of a request for applications (RFA) on the above subject. Copies of the RFA are currently available from staff of the NHLBI.

This program will support basic research on the cellular and molecular mechanisms that influence and regulate development of epithelial cells in normal prenatal and early postnatal lung. It is expected that research applications will encompass a variety of approaches (morphologic, biochemical, molecular, etc.) and will require expertise from a wide variety of disciplines including cell biology, biochemistry, pathology, and pharmacology.

A letter of intent is requested by February 15, 1986, and the deadline for receipt of applications is April 1, 1986. The earliest award date for successful applications will be in September, 1986. Awards in response to this announcement will be made to foreign institutions only for research of very unusual merit, need, and promise, and in accordance with Public Health Service policy governing such awards.

Requests for copies of this RFA should be addressed to:

Dorothy Berlin Gail, Ph.D.  
Chief, Structure and Function Branch  
Division of Lung Diseases, NHLBI  
5333 Westbard Avenue - Room 6A07  
Bethesda, Maryland 20892

Telephone: (301) 496-7171

**ANNOUNCEMENT**

**AVAILABILITY OF REQUEST FOR APPLICATIONS: RFA**

**86-HL-04-H**

**FUNDAMENTAL STUDIES OF CARDIAC MORPHOGENESIS**

P.T. 34; K.W. 0705015, 1002059, 0710030

**DIVISION OF HEART AND VASCULAR DISEASES  
NATIONAL HEART, LUNG, AND BLOOD INSTITUTE**

Application Receipt Date: March 15, 1986

The Cardiac Functions Branch of the Division of Heart and Vascular Diseases, National Heart, Lung, and Blood Institute (NHLBI) announces the availability of a Request for Applications (RFA) on the above subject.

This program will support interdisciplinary research on fundamental mechanisms which underlie normal development of the heart. The emphasis of the program is on the interplay of developmental processes, particularly in terms of structure/function relationships.

This announcement may be of particular interest to investigators with expertise in anatomy, biochemistry, biomedical engineering, biology, biophysics, computer modelling, embryology, genetics, microscopy, molecular biology, pathology, pediatric cardiology, pharmacology, and physiology. Awards in response to this announcement will be made to foreign institutions only for research of very unusual merit, need, and promise, and in accordance with Public Health Service policy governing such awards.

**TIMETABLE**

|                          |                       |
|--------------------------|-----------------------|
| Letter of Intent         | December 31, 1985     |
| Application Receipt Date | March 15, 1986        |
| Technical Review         | May-June 1986         |
| Advisory Council Review  | September 11-12, 1986 |
| Award Date               | September 1986        |

**INQUIRIES**

Inquiries concerning this program and requests for copies of the RFA should be addressed to:

Constance Weinstein, Ph.D.  
Division of Heart and Vascular Diseases  
National Heart, Lung, and Blood Institute  
Federal Building - Room 304  
7550 Wisconsin Avenue  
Bethesda, Maryland 20892

Telephone: (301) 496-1627

**ANNOUNCEMENT**

**AVAILABILITY OF REQUEST FOR APPLICATIONS: (RFA)**

**86-HL-06-H**

**BIOLOGICAL MECHANISMS OF NUTRIENT EFFECTS ON BLOOD PRESSURE**

P.T. 34; K.W. 0705015, 0715115, 1002034, 1002004, 1002008, 0710100, 1003002,0710095

**DIVISION OF HEART AND VASCULAR DISEASES**

**NATIONAL HEART, LUNG, AND BLOOD INSTITUTE**

Application Receipt Date: April 1, 1986

The Hypertension and Kidney Diseases Branch of the Division of Heart and Vascular Diseases, National Heart, Lung, and Blood Institute (NHLBI) announces the availability of a request for applications (RFA) on the above subject. Copies of the RFA are currently available from staff of the NHLBI.

This program will support basic and clinical research designed to elucidate the mechanism or mechanisms by which nutrients affect blood pressure. It is expected that the applications will encompass a variety of approaches (humoral, vascular, biochemical, molecular, etc.). Numerous basic and clinical disciplines are applicable, including physiology, cell biology, molecular biology, pharmacology, biochemistry and clinical nutrition. Awards in response to this announcement will be made to foreign institutions only for research of very unusual merit, need, and promise, and in accordance with Public Health Service policy governing such awards.

Requests for copies of the RFA should be addressed to:

John B. Dunbar, Dr. P.H.  
Division of Heart and Vascular Diseases  
National Heart, Lung, and Blood Institute  
National Institutes of Health  
Federal Building - Room 4C10  
Bethesda, Maryland 20892

Telephone: (301) 496-1857

**ANNOUNCEMENT**

**AVAILABILITY OF REQUEST FOR APPLICATIONS: RFA**

**86-HL-09-P**

**PHYSICAL ACTIVITY AND FITNESS ASSESSMENT METHODS**

P.T. 34; K.W. 0785055, 0755015, 0745030, 0404021, 0735015, 0745020

**DIVISION OF EPIDEMIOLOGY AND CLINICAL APPLICATIONS**

**NATIONAL HEART, LUNG, AND BLOOD INSTITUTE**

Application Receipt Date: February 18, 1986

The Epidemiology and Biometry Program of the Division of Epidemiology and Clinical Applications, National Heart, Lung, and Blood Institute (NHLBI) announces the availability of a Request for Applications (RFA) on the above subject. Copies of the RFA are currently available from staff of the NHLBI.

The special grant program will support research investigating physical activity and fitness measurement methods for use in epidemiological and clinical trials research. Three general areas have been identified that could be addressed by grant applications:

1. Validation and reproducibility of current physical activity and/or fitness questionnaires or other measures for epidemiological and clinical trials research.
2. Validation of movement sensors or other devices for objective measurement.
3. Development of blood or other biological markers of recent past or current physical activity and fitness status.

Awards in response to this announcement will be made to foreign institutions only for research of very unusual merit, need, and promise, and in accordance with Public Health Service policy governing such awards.

Requests for copies of the RFA should be addressed to:

Dr. Richard Donahue  
Epidemiology and Biometry Program  
National Heart, Lung, and Blood Institute  
Federal Building - Room 2C08  
Bethesda, Maryland 20892

Telephone: (301) 496-2327

**ANNOUNCEMENT**

**BIOMEDICAL RESEARCH SUPPORT GRANT APPLICATIONS FOR FISCAL YEAR 1986**

P.T. 34; K.W. 0710030

**DIVISION OF RESEARCH RESOURCES**

Application Receipt Date: January 2, 1986

**I. BACKGROUND**

The Biomedical Research Support Grant (BRSR) Program is designed to provide funds to eligible institutions (i.e., those heavily engaged in health-related research) to strengthen their programs by allowing flexibility to meet emerging opportunities in research; to explore new and unorthodox ideas; and to use these research funds in ways and for purposes which, in the judgment of the grantee institution, would contribute most effectively to the furtherance of their research program.

**II. ELIGIBILITY**

Awards are made to non-profit institutions, not directly to individual investigators. Health professional schools, other academic institutions, hospitals, state and municipal health agencies, and research organizations may apply if during FY 1985 (October 1, 1984 through September 30, 1985) the institution was awarded a minimum of three allowable PHS biomedical or health-related behavioral research grants, totaling \$200,000 (including direct and indirect costs). Federal institutions and institutions located in a foreign country are not eligible.

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

**III. AWARD CONDITIONS**

The BRSR award is for one year and must be renewed annually. The start date is April 1. It is estimated that approximately 556 BRSR awards will be made in FY 1986.

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This program is described in the catalog of Federal Domestic Assistance, No. 13.337, Biomedical Research Support. Grants will be awarded under the authority of the Public Health Service Act, Section 301 (a)(3); Public Law 86-798, (42 USC 241) and administered under PHS grant policies and Federal Regulations 45 CFR Part 74 and the Biomedical Research Support Grant Information Statement and Administrative Guidelines. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

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

IV. METHOD OF APPLYING

BRSG application kits (Form NIH-147-1) will be mailed on or about November 26 to institutions that, according to NIH records, are eligible to apply for a BRSG.

Completed BRSG applications must be received by January 2, 1986. If an institution believes that it is eligible and has not received an application kit by December 5, 1985, please submit a letter of request to:

Mrs. Gilda Polletto  
Grants Management Specialist  
Office of Grants and Contracts Management Division of  
Research Resources  
National Institutes of Health  
Building 31 - Room 5B-32  
9000 Rockville Pike  
Bethesda, Maryland 20892

ANNOUNCEMENT

**COMBINED IN VIVO APPLICATION OF MULTINUCLEAR MAGNETIC RESONANCE  
IMAGING AND SPECTROSCOPY**

P.T. 34; K.W. 0706030, 0745020, 0715035, 0735015, 1003001, 0785190

**NATIONAL CANCER INSTITUTE**

Initial Application Receipt Date: November 1, 1985  
Subsequent Application Receipt Dates: February 1, June 1, October 1

The Radiation Research Program (RRP), Division of Cancer Treatment (DCT), National Cancer Institute (NCI) supports a variety of research programs in the area of medical imaging for the diagnosis and treatment of cancer. The present program announcement is to encourage the submission of scientifically meritorious grant applications in the specific area of magnetic resonance. The RRP anticipates that the described research can be completed in a period of three to four years and depending on the nature of the awarded projects, renewal applications may be considered.

The pressing need for accurate noninvasive cancer diagnosis mandated this initiative. This announcement is to emphasize the continuing interest of the Diagnostic Imaging Research Branch (DIRB), RRP, DCT, NCI in innovative research in magnetic resonance imaging (MRI) and encourages the submission of applications leading to the advancement and improvement of the state-of-the-art in this important area of cancer diagnosis and tumor monitoring.

The major thrust in magnetic resonance imaging has been in the direction of visualizing the resonating hydrogen nucleus (proton imaging), there being an abundant supply of hydrogen in the body, chiefly in water, but also in various tissues. The intrinsic differences in proton relaxation times between fluid, fat, muscle, blood, tumor and bone are major determinants of the contrast available for use in proton imaging.

Recent research in MRI shows that nuclei other than hydrogen have been visualized by using higher magnetic field strength plus receiver coils tuned for the specific Larmor frequency. For example, visualization of sodium nuclei, which appear to be in greater concentration in gliomas than in surrounding brain, has been achieved. The phosphorus nucleus has also been visualized, but because of the relatively small amount of phosphorus in tissue, this imaging does not at this time have the clarity of the proton image.

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

Using magnetic resonance spectroscopy murine tumors have been found to exhibit significant change in their in vivo  $^{31}\text{P}$  phosphorus spectra at various stages of growth and in response to various forms of therapy. Preliminary experiments suggest that regional changes in blood flow and pH (using  $^{19}\text{F}$ ,  $^{31}\text{P}$ ) may be documented in localized tumors by combining imaging and spectroscopic methods. Imaging results with  $^{31}\text{P}$  have demonstrated the ability to spatially localize regional ATP, ADP, inorganic phosphate and phosphocreatine, all of which may prove to be indicators of responsiveness versus resistance of tumor. Using phosphorus spectroscopy, researchers have been able to differentiate human small cell from non-small cell carcinoma of the lung. Other tumors that have been differentiated spectroscopically are human neuroblastoma and breast cancer.

This announcement encourages research with the combined in vivo applications of multinuclear MRI and MRS for increasing sensitivity of tumor demonstration spatially and monitoring of biochemical response to therapy by spectroscopic methodology. Special areas of interest specifically identified are:

1. Combined in vivo multinuclear research in MR imaging and spectroscopy.
2. Correlation of magnetic resonance images with spectroscopic biochemical analysis in normal and abnormal tissue, that is, following steady state responses to different interventions by following metabolites.
3. Correlation of magnetic resonance imaging with biochemical and metabolic changes associated with tumor responses to chemotherapy and radiotherapy; determination of response to and distribution of drugs, and response to radiotherapy by evaluating regional differences in tumor using surface coil spectroscopy and imaging.
4. Evaluation of steady state metabolic changes occurring in specific areas of local tumor masses by spatial demonstration of various parts of the tumor mass (MRI) and by multinuclear studies (MRS) for the measurement of steady state bioenergetics ( $^{31}\text{P}$ ), and glycolytic pathways ( $^{13}\text{C}$ ,  $^1\text{H}$ ) and by determination of regional blood flow and pH effects ( $^{31}\text{P}$ ,  $^{19}\text{F}$ ).
5. Determination of the clinical applications of the combined biochemical response and imaging correlates of neoplastic tissue.
6. Determination of spectroscopic data by both invasive and non-invasive techniques. Data may be acquired by local surface coil versus shaped, depth correlated RF pulses.
7. Contrast enhancement studies based on multinuclear imaging, paramagnetic contrast agents and chemical shift imaging to localize and delineate tumor (MRI) and concurrent evaluation of biochemical properties (MRS) in an attempt at tissue characterization.
8. Other areas of pertinent investigation in combined MRI and MRS research inadvertently omitted in this announcement would be appropriate to this program.

#### ELIGIBILITY

Non-profit organizations and institutions, governments and their agencies, for profit organizations, and individuals are eligible to apply.

#### REVIEW PROCEDURES AND CRITERIA

Applications should be submitted on form (PHS-398-Rev 5/82) which is available in the institution's collaborative research or business office. Otherwise an application kit may be obtained from the Office of Grants Inquiries, Division of Research Grants (DRG), NIH. The original and six copies of the application should be sent to:

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

Applications in response to this solicitation will be reviewed on a nationwide basis in competition with other research grant applications, and in accord with the usual NIH peer review procedures. Applications will first be reviewed Federal scientific consultants (Study Section), and then by the National Advisory Council of the appropriate Institute(s). The review criteria customarily employed by the NIH for regular research grant applications will prevail.

The title of this announcement should be typed under item 2 on page 1 of the application, and the word "yes" should be checked to indicate a response to this announcement.

The initial application receipt date is November 1, 1985. Subsequent receipt dates will be February 1, June 1, and October 1.

All PHS and NIH grant policies governing regular research project grants, including cost sharing, apply to applications received in response to this program announcement.

For further information contact:

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**ANNOUNCEMENT****STUDIES OF DOSE FRACTIONATION AND VOLUME LATE EFFECTS IN NORMAL  
TISSUES USING ANIMAL MODELS**

P.T. 34; K.W. 0715035, 0725015, 0785190

**NATIONAL CANCER INSTITUTE**

Initial Application Receipt Date: November 1, 1985  
Subsequent Application Receipt Dates: February 1, June 1, October 1

The Radiation Research Program (RRP), Division of Cancer Treatment (DCT), National Cancer Institute (NCI) through its Radiotherapy Development Branch (RDP) supports a broad spectrum of research into radiation biology, radiation physics and radiation therapy. The present program announcement is to encourage the submission of scientifically meritorious grant applications for studies of dose fractionation and volume late effects in normal tissues using animal models, especially as they relate to radiotherapy.

Over the years the doses used in radiotherapy have become increasingly fractionated. Overall treatment duration was protracted until acute responses, e.g., of skin and mucosae, no longer limited the total dose that could be delivered to a tumor. However, when protraction was sufficient to minimize acute reactions, the total dose became limited by the development of late complications, e.g., dermal contraction, necroses, bone fracture. The change in the type of dose limiting tissue reflects one difference in the fractionation response of early- and late-responding normal tissues. Whereas repair of sublethal damage occurs in both, regeneration of surviving target cells during the course of fractionated radiotherapy is less or absent in the late-responding tissues.

There is a considerable diversity in the dose fractionation patterns in use in major radiotherapy centers worldwide. Nevertheless, it seems unlikely that valid inter-institution comparisons of therapeutic ratios can be made from the literature.

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What is considered in the United States to be conventional or standard dose fractionation, consisting of regimens using 1.8-2 Gy/day, 5 days per week, is certainly not the most appropriate for all patients, and may not be the best for even the majority. Experimental evidence, both from the clinic and the laboratory, suggests that better results may be obtained for the same total dose by reducing the dose per fraction and shortening the overall time, and, therefore, the average interval between dose fractions. There is evidence to suggest that reducing the dose per fraction leads to an increase in the "tolerance" dose for lateresponding normal tissues which is greater than the increase in dose needed for a certain probability of tumor control. Shortening the overall treatment time reduces the extent of repopulation by tumor clonogens, although at the risk of compromising reoxygenation.

A second factor believed to modify the response of normal tissues is the volume of tissue irradiated. The volume effect is frequently discussed but rarely written about. It is a generally agreed-upon clinical impression that the phenomenon is important in dermal and spinal cord irradiation and is of course important in situations where the functional integrity of a complete organ is put at risk.

Although the severity of a normal tissue response increases with increase in the volume or area of tissue irradiated, it is not known if this applies to all tissues, nor whether it varies with fractionation pattern. The volume effect has rarely been well quantified and has not been investigated extensively in experimental animals.

The mechanism involved in the change in effect per unit of dose with change in volume is not understood. It is not known whether it is an increased induction of injury per unit of dose with increase in volume or a decreased ability of the host to recover from or compensate for an equal injury per unit of dose. It is important to understand the volume effect because of the clinical dilemma posed by the tolerance of normal tissues being modified to a significant, but poorly quantified, extent by the volume irradiated, while, in general, larger tumors require larger doses and larger treatment volumes for their control.

In the light of all these considerations RDB encourages investigator initiated grant applications:

- (1) to determine appropriate animal models for a variety of human tissues which are dose-limiting for curative radiotherapy;
- (2) to select endpoints and evaluation criteria and develop statistical considerations for dose fractionation and volume effects studies;
- (3) to determine the dose response relationships for late effects for fractionation schemes relevant to radiotherapy;
- (4) to determine whole and partial organ dose response relationships for late effects for fractionation schemes relevant to radiotherapy;
- (5) and to identify methods for predicting and/or measuring the onset and rate of regeneration in irradiated normal tissues as a function of various dose fractionation patterns.

This list is not meant to be exhaustive. Other applications consistent with the spirit of this announcement are welcome.

For further information contact:

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