

Full Text AR-95-002

NEW HORIZONS IN OSTEOARTHRITIS RESEARCH

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PURPOSE

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and the National Institute on Aging (NIA) invite investigators to submit grant applications for "New Horizons in Osteoarthritis Research." The applications may be for fully independent research projects or for a group of independent research projects that use the interactive research project grant (IRPG) mechanism. The research should be specifically targeted towards understanding the disease processes in osteoarthritis. This Request for Applications (RFA) requests basic and applied research projects, but not epidemiological or clinical treatment projects.

HEALTHY PEOPLE 2000

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, New Horizons in Osteoarthritis Research, is related to the priority areas of chronic disabling conditions and of older adults and preventive services. 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, DC 20402-9325 (telephone 202-783-3238).

ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Foreign institutions are not eligible for First Independent Research Support and Transition (FIRST) (R29) Awards. Racial/ethnic minority individuals, women, and persons with disabilities are encouraged to apply as Principal Investigators.

MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) research project grant (R01), FIRST (R29) award, and the Interactive Research Project Grant (IRPG). Normal collaborative approaches, such as using co-investigators, consultants or sub-contracts, may be utilized as appropriate to achieve the aims of each independent research application.

The IRPG mechanism encourages interaction and collaboration among independent scientists with common goals. It is intended to bring together research projects from investigators who wish to collaborate but who do not require extensive shared resources. There should be constructive interchange of ideas, data and/or materials. A minimum of two independent investigators are encouraged to submit concurrent, collaborative, cross-referenced individual regular research (R01) or FIRST (R29) applications. These applications must be free-standing and contain independent hypotheses and aims. An application that provides only a service to other applicants is not acceptable. Applicants may be from one or several institutions. Detailed information about this mechanism of support is available in the NIH Program Announcement PA-94-086 in the NIH Guide for Grants and Contracts, Volume 23, Number 28, July 29, 1994.

The total project period for applications submitted in response to the present RFA may not exceed four years for R01s or five years for R29s.

Responsibility for the planning, direction, and execution of the proposed project will be solely that of each independent applicant.

The anticipated award date is September 30, 1995. Awards will be administered under PHS grants policy as stated in the Public Health Service Grants Policy Statement, DHHS Publication No. (OASH) 94-50-000 (rev. 4/1/94).

This RFA is a one-time solicitation. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed according to customary peer review procedures.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resource for conducting the proposed research. If so, a letter of agreement from either the GCRC program director or Principal Investigator could be included within the application.

FUNDS AVAILABLE

It is anticipated that six to eight awards will be made as a result of applications for the "New Horizons in Osteoarthritis Research." The estimated funds available for the first year of support for this program are \$1,400,000 in total costs. Actual funding is dependent on the receipt of a sufficient number of applications of high scientific merit and the availability of funds for this purpose. The direct cost of each R01 is limited to \$160,000 for the first year and R29s are limited to \$70,000 average per year. Funding beyond the first and subsequent years of the grant will be contingent upon satisfactory progress during the preceding years and the availability of funds.

RESEARCH OBJECTIVES

The osteoarthritic diseases (OA) are the most prevalent disorders of the joint, with radiographic evidence seen in at least 70 percent of the population over age 65. In 1984, the economic cost of OA was estimated at \$8 billion. OA is a group of overlapping distinct diseases that may have different etiologies but similar biologic, morphologic, and clinical outcomes. The disease processes not only affect the articular cartilage but involve the entire joint including the subchondral bone, ligaments, capsule, synovial membrane and periarticular muscles. Ultimately, the articular cartilage degenerates with fibrillation, fissures, ulceration and full thickness loss of the joint surface.

A workshop entitled "New Horizons in Osteoarthritis" was held April 23-26, 1994, to bring together an interdisciplinary group of leading clinicians and scientists to discuss the current knowledge and delineate future research directions on the etiopathogenesis of OA.

The workshop was sponsored by the American Academy of Orthopaedic Surgeons (AAOS), the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute on Aging (NIA), the National Arthritis Foundation, and the Orthopaedic Research and Education Foundation.

A book that summarizes this workshop on OA includes extensive discussion in the areas of definition, epidemiology, classification, cartilage changes in aging and degeneration, changes in the joint as an organ, role of mediators and inflammation in degradative mechanisms, repair of cartilage, monitoring of preclinical and clinical progression, and treatment of OA. It contains six sections with individual chapters, which define the present state of knowledge and identify future research directions. This book will be published by AAOS in February 1995.

This RFA for the "New Horizons in Osteoarthritis Research" is intended to stimulate further scientific investigations on a broad range of topics in this area of high public health impact. Research may be basic and/or applied in nature. Epidemiological and clinical treatment applications will not be accepted. Applications must be targeted to an aspect of the disease osteoarthritis rather than a fundamental study of the biology of normal joint tissues. As indicated above under Mechanism of Support, applications may be in the standard fully independent R01 and R29 format or interactive in nature using the IRPG format.

This RFA is purposefully not restrictive in defining a narrow range of OA topics to be studied. Appropriate research areas may include, but are not limited to, the following:

- o Exploration of the genetic basis for some types of OA.

- o Study of the altered metabolic control in OA of synthetic and degradative processes in cartilage.

- o Study of the effects of altered biological and mechanical factors on control of chondrocyte activity in OA degeneration.

- o Investigation of the interactive roles of the component structures of the joint as an organ in the development and progression of OA.

- o Elucidation of the age-related changes in joint tissues and their role in the development and progression of osteoarthritis.

- o Evaluation of the "point of no return" at which cartilage appears to have diminished reparative ability and the degradation proceeds rapidly.
- o Exploration of the role of inflammatory responses and their mediators in the initiation and progression of OA.
- o Study of the nature and significance of wear debris from articular cartilage in initiating and sustaining the degradative process.
- o Exploration of tissue engineering or other approaches for biological repair of cartilage.
- o Development of markers of OA.

INCLUSION OF WOMEN AND MINORITIES IN RESEARCH INVOLVING HUMAN SUBJECTS

It is the policy of the NIH that women and members of minority groups and their subpopulations must be included in all NIH supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale and justification is provided that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This new policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43) and supersedes and strengthens the previous policies (Concerning the Inclusion of Women in Study Populations, and Concerning the Inclusion of Minorities in Study Populations), which have been in effect since 1990. The new policy contains some provisions that are substantially different from the 1990 policies.

All investigators proposing research involving human subjects should read the "NIH Guidelines For Inclusion of Women and Minorities as Subjects in Clinical Research," which have been published in the Federal Register of March 28, 1994 (FR 59 14508-14513) and reprinted in the NIH Guide for Grants and Contracts, Volume 23, Number 11, March 18, 1994.

Investigators also may obtain copies of the policy from the program staff listed under INQUIRIES. Program staff may also provide additional relevant information concerning the policy.

LETTER OF INTENT

Prospective applicants are asked to submit, by January 20, 1995, a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, the number RFA AR-95-002, and the title "New Horizons in Osteoarthritis Research".

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains allows NIAMS and NIA staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

Dr. Tommy Broadwater
Extramural Program
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Natcher Building, Room 5AS-25E
45 Center Drive MSC 6500
Bethesda, MD 20892-6500
Telephone: (301) 594-9979 (until 11/18/94) (301) 594-4952 (after
11/18/94)
FAX: (301) 480-4543

APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research; from the Office of Grants Information, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/435-0714; and from the NIH program administrator listed under INQUIRIES.

The RFA label available in the PHS 398 (rev. 9/91) application form must be affixed to the bottom of the face page of the application. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title (New Horizons in Osteoarthritis Research) and number must be typed on line 2a of the face page of the application form and the YES box must be marked.

Applications for the FIRST Award (R29) must include at least three sealed letters of reference attached to the face page of the original application. FIRST Award (R29) applications submitted

without the required number of reference letters will be considered incomplete and will be returned without review.

Submit a signed, typewritten original of the applications, including a cover letter (if appropriate), the checklist, and three signed, photocopies, in one package (including IRPGs whether or not the applications arise from the same institution) to:

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

At the time of submission, two additional copies of the application must also be sent to Dr. Tommy Broadwater at the address listed under LETTER OF INTENT.

Applications must be received by February 21, 1995. If an application is received after that date, it will be returned to the applicant without review. The Division of Research Grants (DRG) will not accept any application in response to this RFA that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. The DRG will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed for completeness by DRG and responsiveness by the NIAMS and NIA. Incomplete applications will be returned to the applicant without further consideration. If the application is not responsive to the RFA, NIAMS staff will contact the applicant to determine whether to return the application to the applicant or submit it for review in competition with unsolicited applications at the next review cycle.

Applications that are complete and responsive to the RFA will be evaluated for scientific and technical merit by an appropriate peer review group convened by the NIAMS in accordance with the review criteria stated below.

As part of the initial merit review, a process (triage) may be used by the initial review group in which applications will be determined to be competitive or non-competitive based on their

scientific merit relative to other applications received in response to the RFA. Applications judged to be competitive will be discussed and assigned a priority score. Applications determined to be non-competitive will be withdrawn from further consideration and the Principal Investigator and the official signing for the applicant organization will be notified.

Review criteria for this RFA are generally the same as those for unsolicited research grant applications:

- o extent to which the proposed research addresses the goals of the RFA;
- o scientific, technical, or medical significance and originality of proposed research;
- o appropriateness and adequacy of the experimental approach and methodology proposed to carry out the research;
- o qualifications and research experience of the Principal Investigator and staff, particularly, but not exclusively, in the area of the proposed research;
- o availability of the resources necessary to perform the research;
- o adequacy of the mechanisms for quality control, study monitoring, data management and reporting and data analysis;
- o appropriateness of the proposed budget and duration in relation to the proposed research;
- o In the case of human tissue samples, adequacy of plans to include both genders and minorities and their subgroups as appropriate for the scientific goals of the research.
- o Adequacy of plans to include both genders and minorities and their subgroups as appropriate for the scientific goals of the research. Plans for the recruitment and retention of subjects will also be evaluated.

The initial review group will also examine the provisions for the protection of human and animal subjects and the safety of the research environment.

When appropriate, the special value of the cooperative and interactive nature of the individual research applications and applicants comprising an IRPG should be emphasized in each application, under Section 7 of form PHS 398.

AWARD CRITERIA

The anticipated date of award is September 30, 1995.

Applications will compete for available funds with all other applications responsive to this RFA.

The following items will be considered in making funding decisions:

- o quality of the proposed program project grants as determined by peer review;
- o availability of funds; and
- o programmatic priorities.

INQUIRIES

Inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Dr. Stephen L. Gordon
Musculoskeletal Diseases Branch
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Natcher Building, Room 5AS-251
45 Center Dr MSC 6500
Bethesda, MD 20892-6500
Telephone: (301) 594-9951 (until 11/18/94) (301) 594-4977 (after
11/18/94)
FAX: (301) 480-4543
Email: GORDONS@EP.NIAMS.NIH.GOV

Dr. David Finkelstein
Biology of Aging Program
National Institute on Aging
Gateway Building, Suite 2C231

7201 Wisconsin Avenue
Bethesda, MD 20892
Telephone: (301) 496-6402
FAX: (301) 402-0010
Email: FD6@CU.NIH.GOV

Direct inquiries regarding fiscal matters to:

Ms. Diane M. Watson
Grants Management Branch
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Natcher Building, Room 5AS-53
45 Center Dr MSC 6500
Bethesda, MD 20892-6500
Telephone: (301) 594-9965 (until 11/18/94) (301) 594-3505 (after
11/18/94)
FAX: (301) 480-5450
EMAIL: WATSOND@EP.NIAMS.NIH.GOV

Mr. Robert Pike
Grants and Contracts Management Office
National Institute on Aging
Gateway Building, Suite 2N212
Bethesda, MD 20892
Telephone: (301) 496-1472
FAX: (301) 402-3672
Email: PikeB@NIHNIAGW.BITNET

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance Nos. 93.846, 93.847, and 93.866. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 410, 78th Congress, as amended, 42 USC 241 and administered under PHS grants policies and Federal Regulations 42 CFR 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 Public Health Service (PHS) strongly encourages all grant recipients to provide a smoke-free workplace and promote the non-use of all tobacco products. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

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