

# NIH GUIDE

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# for GRANTS and CONTRACTS

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Vol. 4, No. 4, June 1, 1975

CANCER RESEARCH EMPHASIS GRANTS  
(CREG)

ANNOUNCEMENT

## TITLE - *REPLICATION OF RNA TUMOR VIRUSES*

*SCIENTIFIC PROGRAM REQUIREMENT* The National Cancer Institute is accepting applications for support of research projects to study the mechanism of replication of RNA tumor virus nucleic acids. Included under this topic are the structure of viral RNA; the mechanism of transcription of viral RNA to DNA including the action of viral RNA dependent DNA polymerase; the mechanism of integration of viral DNA into the host DNA; the structure of integrated viral DNA; the transcription of integrated viral DNA to viral RNA and other areas directly relevant to the replication of viral nucleic acids. The process of viral penetration into the cell and the synthesis and assembly of viral proteins are not to be included.

*SIGNIFICANCE TO NCI PROGRAM GOALS* A number of animal cancers are caused by RNA viruses and there is good evidence that similar viruses may cause human cancer. The discovery that all these viruses have a RNA dependent DNA polymerase has greatly clarified our understanding of how these viruses multiply in the animal cell. However, there are many areas where our knowledge is deficient, e.g. the transcription of viral DNA to RNA, the initiation of DNA synthesis by RDDP, etc. A better understanding of the complex process of viral nucleic acid replication is central to the aims of the Virus Cancer Program, namely, to determine how viruses cause cancer and how virally caused cancer can be prevented.

## APPLICATIONS REQUIREMENTS

1. *ELIGIBILITY* Nonprofit organizations and institutions, State and local governments and their agencies, authorized Federal institutions, and individuals according to NIH grants policies.

2. *THE APPLICATION* Applicants should propose an individual project. Applicants may elaborate on the purposes, objectives, rationale, and

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*The GUIDE is published at irregular intervals to provide policy and administrative information to individuals and organizations who need to be kept informed of requirements and changes in grants and contracts activities administered by the National Institutes of Health.*

*Supplements, printed on yellow paper, are published by the respective awarding units concerning new projects, solicitations of sources, and requests for proposals.*

significance stated in this announcement and must complete portions of the applications pertaining to procedural details, the investigator's related experience, facilities available, budgets, and biographical information for key professional personnel. The application should also state the duration of time for which the support is requested. It is anticipated that the initial project period will not exceed three years but may be renewable. The level of effort per year should be at least one professional man-year. The National Cancer Institute expects to fund several projects in this area.

3. SUBMISSION Use application form NIH-398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title, number DCCP-1 and the date of publication as the one to which the application responds. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014.

4. RECEIPT DATE Applications must be received in the Division of Research Grants, NIH, no later than October 1, 1975 in order to be considered in the competition under this announcement.

#### REVIEW

Upon receipt, applications will be reviewed for responsiveness to this announcement by the Division of Research Grants (DRG) in consultation with the NCI staff. If an application is judged unresponsive, the applicant will be given an opportunity to withdraw the application or to submit it for consideration in the traditional grant programs of NIH. Applications judged responsive will be reviewed initially for scientific merit by DRG study sections and secondly by the National Cancer Advisory Board.

DRG will not accept an application in response to a CREG announcement that is identical to any other application concurrently being considered by NCI or other NIH awarding units.

For further information potential applicants may contact Dr. Elke Jordan, Virus Cancer Program, Division of Cancer Cause and Prevention, National Cancer Institute.

TITLE - *GENETICS OF RNA TUMOR VIRUSES*

*SCIENTIFIC PROGRAM REQUIREMENT* The National Cancer Institute is accepting applications for support of research on the genetics of RNA tumor viruses. This will include the isolation and characterization of mutants of RNA tumor viruses as well as studies on the mechanism of action of viral genes. Particular emphasis should be placed on the role of viral genes in malignant transformation. Also included in this area of research is the identification and characterization of host cell genes that affect viral functions.

*SIGNIFICANCE TO NCI PROGRAM GOALS* The Virus Cancer Program is interested in elucidating how viruses cause cancer and how virally caused cancer can be prevented. The study of viral genetics provides an excellent and direct tool for understanding viral functions including the transformation of cells to malignancy.

APPLICATION REQUIREMENTS

1. ELIGIBILITY Nonprofit organizations and institutions, State and local governments and their agencies, authorized Federal institutions, and individuals according to NIH grants policies.
2. THE APPLICATION Applicants should propose an individual project. Applicants may elaborate on the purposes, objectives, rationale, and significance stated in this announcement and must complete portions of the applications pertaining to procedural details, the investigator's related experience, facilities available, budgets, and biographical information for key professional personnel. The application should also state the duration of time for which the support is requested. It is anticipated that the initial project period will not exceed three years but may be renewable. The level of effort per year should be at least one professional man-year. The National Cancer Institute expects to fund several projects in this area.
3. SUBMISSION Use application form NIH-398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title, number DCCP-2 and the date of publication as the one to which the application responds. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014.
4. RECEIPT DATE Applications must be received in the Division of Research Grants, NIH, no later than October 1, 1975 in order to be considered in the competition under this announcement.

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For further information potential applicants may contact Dr. Elke Jordan, Virus Cancer Program, Division of Cancer Cause and Prevention, National Cancer Institute.

TITLE - IN VITRO CHEMICAL CARCINOGENESIS

*SCIENTIFIC PROGRAM REQUIREMENT* The National Cancer Institute (NCI) is accepting applications for support of research projects in the area of in vitro carcinogenesis. The objective of this research is to study the interaction of chemical carcinogens and mammalian cells in vitro with particular emphasis on the following problems:

(1) development of new model systems for neoplastic transformation induced by chemical or physical agents including consideration of the use of human and non-human primate cells;

(2) the development and/or refinement of methodology for the early identification and quantitation of neoplastic transformation of cells in culture using new biochemical, cytological or immunological markers (relative to identification of transformation) in established systems; and

(3) the development and characterization of new approaches for metabolic activation systems for carcinogens and procarcinogens which can be applied to existing in vitro neoplastic transformation systems.

*SIGNIFICANCE TO NCI PROGRAM GOALS* A goal of the In Vitro Chemical Carcinogenesis Program is to develop new approaches that can lead to reducing the effect of carcinogenic agents by detecting and identifying chemical carcinogens using in vitro cell systems and by studying their mode of action and possible inhibition of that action.

Since limitations exist with present in vitro methodologies, it is anticipated that the above studies may provide more effective and efficient in vitro systems. It is necessary that continuing efforts be directed toward achieving approaches and methodologies which can define in vitro systems that are more applicable to the basic problems of prevention, inhibition and reversal of carcinogenesis in man.

APPLICATION REQUIREMENTS

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2. THE APPLICATION Applicants should propose an individual project. Applicants may elaborate on the purposes, objectives, rationale, and significance stated in this announcement and must complete portions of the applications pertaining to procedural details, the investigator's related experience, facilities available, budgets, and biographical information for key professional personnel. The application should also state the duration time for which the support is requested. It is anticipated that the project period will not exceed three years and that the level of effort per year should not exceed two-three man-years in the category of professional personnel.

3. SUBMISSION Use application form NIH-398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title and the number DCCP-3 and the date of publication as the one to which the application responds. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014.

4. RECEIPT DATE Applications must be received in the Division of Research Grants, NIH, no later than October 1, 1975 in order to be considered in the competition under this announcement.

#### REVIEW

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For further information potential applicants may contact either Dr. Robert Depue or Dr. Virginia C. Dunkel, Project Director, Division of Cancer Cause and Prevention, National Cancer Institute.

TITLE - *EPIDEMIOLOGY OF CANCER OF THE ESOPHAGUS*

*SCIENTIFIC PROGRAM REQUIREMENT* The National Cancer Institute (NCI) is accepting applications for support of research projects on the etiology of cancer of the esophagus. Large geographic variations in incidence and mortality rates of this disease indicate that environmental factors are most likely involved. Some factors that have been considered as possible etiologic agents include the use of alcohol and tobacco, consumption of hot foods and beverages, heavy seasoning of foods, chewing of betel nut, Plummer-Vinson syndrome, radiation exposure from natural sources, exposure to asbestos, air pollution, trace metal deficiencies, vitamin C deficiency, contamination of food with silica particles, and consumption of tannin-rich foods.

Investigators may propose either a retrospective or a prospective approach to this problem. Populations at low or high risk for esophageal cancer should be identified for study of all factors potentially associated with this disease. Plans for data analysis should also be included in the proposal.

*SIGNIFICANCE TO NCI PROGRAM GOALS* We estimate 7,400 new cases in 1975 including 5,500 in males and 1,900 in females. Although incidence rates for whites have declined slightly since 1940, the rates for blacks have increased 2 to 3-fold during the same period. There are some indications that a large portion of esophageal cancers are preventable, but a causative relationship has not been proven for any of the suspected etiologic agents.

The overall goal is to develop the means to reduce the incidence, morbidity and mortality of cancer in humans. This goal may be achieved by developing the means to reduce the effectiveness of external carcinogenic agents, by developing the means to prevent transformation of normal cells to cells capable of forming cancers, and by making effective methods of cancer prevention available to the public and health professionals.

APPLICATION REQUIREMENTS

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3. SUBMISSION Use application form NIH-398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title and the number DCCP-4 and its date of publication. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014.

4. RECEIPT DATE Applications must be received in the Division of Research Grants, NIH, no later than October 1, 1975 in order to be considered in the competition under this announcement.

#### REVIEW

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For further information, potential applicants may contact Dr. James L. Murray, Division of Cancer Cause and Prevention, National Cancer Institute.



TITLE - *FREQUENCY OF CANCER IN GENETIC ISOLATES*

*SCIENTIFIC PROGRAM REQUIREMENT* The National Cancer Institute (NCI) is accepting applications for support of research projects in determining the frequency of cancer in genetic isolates both in the United States and elsewhere. These populations, though small, might rapidly provide clues to cancer etiology because of the homogeneity of genetic and environmental factors. There is a high degree of inbreeding, and dietary and social habits are often uniform.

*SIGNIFICANCE TO NCI PROGRAM GOALS* Certain cultural units in the United States have a low frequency of cervical cancer, attributed to high standards of personal hygiene. In one identified group, three cousins with Hodgkin's disease have been reported and many familial syndromes of birth defects and immune defects have been recognized with ease among the members of this group. Subsequently, patients with these syndromes have been recognized in the general population where they would have long been ignored because of their scarcity. The cancer experience in other genetic isolates or unique communities of people, is poorly documented. Groups are often well-studied by geneticists who take biologic specimens for genetic markers. Little additional expense would allow collection of history, clinical and biologic specimens relating to carcinogenesis.

APPLICATION REQUIREMENTS

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2. THE APPLICATION Applicants should propose an individual project. Applicants may elaborate on the purposes, objectives, rationale, and significance stated in this announcement and must complete portions of the applications pertaining to procedural details, the investigator's related experience, facilities available, budgets, and biographical information for key professional personnel. The application should also state the duration of time for which the support is requested. It is anticipated that the project period will not exceed three years, and that the level of effort per year will approximate two professional man-years and two technician man-years.
3. SUBMISSION Use application form NIH-398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title and the number DCCP-5 and the date of publication as the one to which the application responds. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014.
4. RECEIPT DATE Applications must be received in the Division of Research Grants, NIH, no later than October 1, 1975 in order to be considered in the competition under this announcement.

REVIEW

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) and NCI staff for responsiveness to this announcement. If an application is judged unresponsive, the applicant will be given an opportunity to withdraw the application or to submit it for consideration in the traditional grant programs of NIH. Applications judged responsive will be reviewed initially for scientific merit by DRG study sections and secondly by the National Cancer Advisory Board.

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For further information potential applicants may contact Dr. Thomas W. Pendergrass, Division of Cancer Cause and Prevention, National Cancer Institute.

TITLE - *RISK OF HUMAN CANCER IN HETEROZYGOTES WITH RECESSIVE  
MUTANT GENES PREDISPOSING TO CANCER IN THE HOMOZYGOTE  
AND HEMIZYGOTE STATES*

*SCIENTIFIC PROGRAM REQUIREMENT* The National Cancer Institute (NCI) is accepting applications for support of research projects in defining the frequency of neoplasia among relatives of patients with recessively inherited conditions that predispose to malignancy, such as Fanconi's anemia ataxia telangiectasia, xeroderma pigmentosum, Bruton's agammaglobulinemia, Wiskott-Aldrich syndrome, Rothmund-Thomson syndrome, albinism, testicular feminization, and familial hemochromatosis.

*SIGNIFICANCE TO NCI PROGRAM GOALS* Although each of these syndromes is rare, much has been learned about cancer etiology and biology by intensively studying the affected patients, that is, those with a double dose of the mutant gene in the case of autosomal recessive conditions. The patients' first-degree relatives, many of whom will have a single dose of the mutant, have been neglected. If the single gene predisposes to cancer, its impact on the cancer burden in the general population might be considerable. For autosomal recessive traits as rare as 1 in 10,000 ( $=q^2$ ) in the general population, the Hardy-Weinberg principle ( $p^2 + 2pq + q^2$ ) determines that the frequency of the heterozygotes ( $2pq$ ) is 1 in 50 ( $= 2 \times \sqrt{1/10,000} \times [1 - \sqrt{1/10,000}]$ ).

Already Swift et al., have reported an elevated cancer risk for heterozygotes in autosomal recessive Fanconi's anemia (Nature 230:370-373, 1971) and ataxia telangiectasia (in press). Additional investigators need to repeat Swift's pioneering study and approach other genetic diseases predisposing to malignancy, with xeroderma pigmentosum, Bruton's disease and Wiskott-Aldrich syndrome being prime candidates.

APPLICATION REQUIREMENTS

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2. THE APPLICATION Applicants should propose an individual project. Applicants may elaborate on the purposes, objectives, rationale, and significance stated in this announcement and must complete portions of the applications pertaining to procedural details, the investigator's related experience, facilities available, budgets, and biographical information for key professional personnel. The application should also state the duration of time for which the support is requested. It is anticipated that the project period will not exceed four years, and that the level of effort per year will approximate two professional man-years and three technician man-years.
3. SUBMISSION Use application form NIH-398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title and the number DCCP-6 and the date of publication as the one to which the application responds.

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Mail the application and letter to Division of Research Grants,  
National Institutes of Health, Bethesda, Maryland 20014.

4. RECEIPT DATE Applications must be received in the Division of Research Grants, NIH, no later than October 1, 1975 in order to be considered in the competition under this announcement.

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For further information potential applicants may contact Dr. Thomas W. Pendergrass, Division of Cancer Cause and Prevention, National Cancer Institute.

TITLE - *IS HODGKIN'S DISEASE A COMMUNICABLE DISEASE?*

*SCIENTIFIC PROGRAM REQUIREMENT* The National Cancer Institute (NCI) is accepting applications for support of research projects in determining whether Hodgkin's disease is a communicable disease. The study design should stress the methodologic aspects of choosing comparison groups that would generate reliable expectations for case to case and case to "carrier" to case contacts with which to compare to that observed. Accommodation of the influences of age, latent period and pathophysiology should also be incorporated.

*SIGNIFICANCE TO NCI PROGRAM GOALS* Several studies in the past few years have described "extended clusters" for this disease. All of these studies suffer from a lack of an appropriate expectation for such "extended clusters". Because of its significance to both cancer etiology and control, it would seem that this is the most important question within the area of the possible relationship of cancer to infectious agents that is amenable to the epidemiologic approach.

APPLICATION REQUIREMENTS

1. *ELIGIBILITY* Nonprofit organizations and institutions, State and local governments and their agencies, authorized Federal institutions, and individuals according to NIH grants policies.
2. *THE APPLICATION* Applicants should propose a program project. Applicants may elaborate on the purposes, objectives, rationale, and significance stated in this announcement and must complete portions of the applications pertaining to procedural details, the investigator's related experience, facilities available, budgets, and biographical information for key professional personnel. The application should also state the duration of time for which the support is requested. It is anticipated that the project period will not exceed two to four years, and that the level of effort per year will approximate one to two professional man-years and three to five technician man-years.
3. *SUBMISSION* Use application form NIH-398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title and the number DCCP-7 and the date of publication as the one to which the application responds. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014.
4. *RECEIPT DATE* Applications must be recieved in the Division of Research Grants, NIH, no later than October 1, 1975 in order to be considered in the competition under this announcement.

REVIEW

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) and NCI staff for responsiveness to this announcement. If an

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application is judged unresponsive, the applicant will be given an opportunity to withdraw the application or to submit it for consideration in the traditional grant programs of NIH. Applications judged responsive will be reviewed initially for scientific merit by DRG study sections and secondly by the National Cancer Advisory Board.

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For further information potential applicants may contact Dr. Thomas W. Pendergrass, Division of Cancer Cause and Prevention, National Cancer Institute.

TITLE - *ASSESSING THE EFFECTS ON OFFSPRING OF PRECONCEPTION  
AND IN-UTERO IMMUNOSUPPRESSION*

*SCIENTIFIC PROGRAM REQUIREMENT* The National Cancer Institute (NCI) is accepting applications for support of research projects in determining the effect on offspring of immune suppression prior to or during pregnancy. Such a study should assess the effects on fertility, fetal wastage, congenital defects and disease in the offspring.

*SIGNIFICANCE TO NCI PROGRAM GOALS* Immuno-suppressed persons have a markedly and uniquely altered risk of malignancy. The influence of immune suppression on products of conception may provide valuable insights into the preconception and in-utero determinants of cancer.

APPLICATION REQUIREMENTS

1. ELIGIBILITY Nonprofit organizations and institutions, State and local governments and their agencies, authorized Federal institutions, and individuals according to NIH grants policies.

2. THE APPLICATION Applicants should propose a program project. Applicants may elaborate on the purposes, objectives, rationale, and significance stated in this announcement and must complete portions of the applications pertaining to procedural details, the investigator's related experience, facilities available, budgets, and biographical information for key professional personnel. The application should also state the duration of time for which the support is requested. It is anticipated that the project period will not exceed three to five years, and that the level of effort per year will approximate one professional man-years and three or four technician man-years.

3. SUBMISSION Use application form NIH-398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title and the number DCCP-8 and the date of publication as the one to which the application responds. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014.

4. RECEIPT DATE Applications must be received in the Division of Research Grants, NIH, no later than October 1, 1975 in order to be considered in the competition under this announcement.

REVIEW

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TITLE - *LONG-TERM HEALTH SEQUELAE OF ESTROGEN REPLACEMENT THERAPY*

*SCIENTIFIC PROGRAM REQUIREMENT* The National Cancer Institute (NCI) is accepting applications for support of research projects in determining the long-term health effects of estrogen replacement therapy in menopausal women, with particular emphasis on mortality from all causes and the incidence of cancers of the breast, endometrium and colon.

*SIGNIFICANCE TO NCI PROGRAM GOALS* As has been pointed out in a not-so-recent editorial (J. Nat. Cancer Inst. 51:729, 1973), this question is one of the most important ones that epidemiologists need to answer. There is evidence from the laboratory and from case reports that the form of estrogens used for this purpose may be carcinogenic. On the other hand, there are several studies that suggest "protection" against all causes of death and against the incidence of all forms of cancer. Since this is the fifth most prescribed drug in the United States, these questions need immediate attention while contracts do exist to evaluate this exposure in relation to one or two specific diseases, what is needed is an across-the-board estimate of the influence of this drug on chronic disease in order to make a risk-benefit decision on its use.

APPLICATION REQUIREMENTS

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3. SUBMISSION Use application form NIH-398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title and the number DCCP-9 and the date of publication as the one to which the application responds. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014.
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For further information potential applicants may contact Dr. Thomas W. Pendergrass, Division of Cancer Cause and Prevention, National Cancer Institute.

TITLE - *SURVEILLANCE FOR DRUGS THAT MAY BE CARCINOGENIC*

*SCIENTIFIC PROGRAM REQUIREMENT* The National Cancer Institute (NCI) is accepting applications for support of research projects in uncovering previously unsuspected drugs associated with cancer, and following up these leads with analytic studies. This basically calls for the establishment of a resource with access to large numbers of cancer patients and controls, that would systematically evaluate lifetime drug histories and collect data to control for potential confounding variables.

*SIGNIFICANCE TO NCI PROGRAM GOALS* The area of drug exposures has been one of the most productive of etiologic clues to causes of cancer and to biologic mechanisms involved. A program whose mission is primarily to evaluate toxic drug effects has shown how it can identify leads to causes of cancer also (Boston Collaborative Drug Surveillance Program). It has been constrained by small numbers of cases (since cancer is not its main emphasis) and the ability to evaluate only recent drug exposures (within three months of hospital admission). Lifetime drug histories on large numbers of cases might be considerably more productive.

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3. *SUBMISSION* Use application form NIH-398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title and the number DCCP-10 and the date of publication as the one to which the application responds. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014.
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For further information potential applicants may contact Dr. Thomas W. Pendergrass, Division of Cancer Cause and Prevention, National Cancer Institute.

TITLE - *DEVELOPMENT AND STUDY OF THE AVIAN MODEL FOR OVARIAN TUMORS*

*SCIENTIFIC PROGRAM REQUIREMENT* The National Cancer Institute (NCI) is accepting applications for support of research projects in development of the avian model for ovarian cancer and study of the laboratory and epidemiologically identifiable factors associated with the development (or non-development) of tumors. The purpose of the study is to provide a model with a high natural frequency of ovarian cancer (ovarian cancer is a main cause of death in old chickens), and which progresses from prodromal through subclinical through overt disease in a relatively short time span (ovarian tumors are prevalent in chickens greater than 2 years of age and reach a peak around 3 years).

*SIGNIFICANCE TO NCI PROGRAM GOALS* A recent comprehensive review on the etiology of cancer of the ovary (J. Nat. Cancer Inst. 53:1603-1618, 1974) calls attention to the paucity of clues which exist as to suspected chemical or physical agents in human ovarian cancer, and further calls attention to the fact that as far as is known, "only chickens develop significant numbers of ovarian adenocarcinomas similar in histologic appearance and behavior to the common human epithelial carcinomas, but these have not been adequately investigated". While it is well recognized that findings from animals are not necessarily applicable to man, it is equally well recognized that clues derived from laboratory studies can be of great value in developing and investigating new hypotheses (etiology of cancer). In this instance it should be possible to study various hormone levels in a flock to determine what changes might be associated with the subsequent development of ovarian tumors, and which might be associated with resistance to the development of such tumors. Although no special poultry strain has yet been noted to have excessive ovarian cancer, one may exist, and if so might be useful in study of physiologic differences between average and high risk flocks, as well as genetic studies within flocks to determine the importance of heredity in development of the tumors. If particular hormone ratios seem to be associated with the development of ovarian cancer, study could be made as to how these ratios might be modified and what the effect would be on the development of cancer.

APPLICATION REQUIREMENTS

1. ELIGIBILITY Nonprofit organizations and institutions, State and local governments and their agencies, authorized Federal institutions, and individuals according to NIH grants policies.
2. THE APPLICATION Applicants should propose an individual project. Applicants may elaborate on the purposes, objectives, rationale, and significance stated in this announcement and must complete portions of the applications pertaining to procedural details, the investigator's related experience, facilities available, budgets, and biographical information for key professional personnel. The application should also state the duration of time for which the support is requested. It is anticipated that the project period will not exceed three years, and that the level of effort per year will approximate .3-.5 professional man-years and one technician man-year.

3. SUBMISSION Use application form NIH-398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title and the number DCCP-11 and the date of publication as the one to which the application responds. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014.

4. RECEIPT DATE Applications must be received in the Division of Research Grants, NIH, no later than October 1, 1975 in order to be considered in the competition under this announcement.

#### REVIEW

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) and NCI staff for responsiveness to this announcement. If an application is judged unresponsive, the applicant will be given an opportunity to withdraw the application or to submit it for consideration in the traditional grant programs of NIH. Applications judged responsive will be reviewed initially for scientific merit by DRG study sections and secondly by the National Cancer Advisory Board.

DRG will not accept an application in response to a CREG announcement that is identical to one concurrently being considered by NCI or other NIH awarding units.

For further information potential applicants may contact Dr. Thomas W. Pendergrass, Division of Cancer Cause and Prevention, National Cancer Institute.

TITLE - *CANCER EPIDEMIOLOGY IN COLLABORATION WITH THE NCI PROGRAM  
OF CANCER SURVEILLANCE, EPIDEMIOLOGY AND END RESULTS (SEER)*

*SCIENTIFIC PROGRAM REQUIREMENT* The National Cancer Institute (NCI) is accepting applications for support of research projects in the field of cancer epidemiology and etiology which will be conducted in collaboration with cancer registries participating in the SEER Program of cancer Surveillance, Epidemiology and End Results. The SEER Program provides information on trends in the incidence of the various forms of cancer in the United States, variation in the occurrence of cancer among different population groups and in different geographic areas, changes in diagnostic and treatment practices, and the associated end results in the general run of cancer patients. Data are obtained from a selected number of population-based cancer registries that provide uniform information on a continuing basis and participate in ad hoc studies designed to identify and assess etiologic and prognostic factors.

Only limited pilot or feasibility studies can be supported under the present contract agreement with the participating registries. Therefore, NCI is now soliciting CREG proposals for full-scale comprehensive research efforts on the epidemiology and etiology of all types of cancer, and especially research which may lead to identification of factors which can be modified to reduce the incidence and mortality of cancer. Although specific research protocols are requested, the actual approaches and methods will be left to the initiative of the applicants. Studies may be either retrospective or prospective in design.

Registries currently participating in the SEER Program are:

	<u>Registry Institution</u>	<u>Area Covered</u>	<u>Population Covered - 1970</u>
1.	California State Department of Health	San Francisco Bay area, five counties	3,109,519
2.	Connecticut State Department of Health	Entire State of Connecticut	3,031,709
3.	University of New Mexico	Entire State of N.M.	1,016,000
4.	University of Utah	Entire State of Utah	1,059,273
5.	Research Corporation of the University of Hawaii	Entire State of Hawaii	768,561
6.	University of Iowa	Entire State of Iowa	2,824,376
7.	Fred Hutchinson Cancer Research Center	Seattle-Tacoma area, five counties	1,934,628

8. Michigan Cancer Foundation	Detroit Metropolitan area, three counties	4,199,931
9. Charity Hospital of Louisiana at New Orleans	New Orleans area, three parishes	982,224
TOTAL Population covered, present participants:		<u>18,927,221</u>

Applications are not limited to the participation of SEER institutions above.

*SIGNIFICANCE TO NCI PROGRAM GOALS* The SEER Program contributes to Objective No. 5 of the National Cancer Plan, i.e., "develop the means to achieve an accurate assessment of the presence, extent and probable cause of cancer risks in population groups (including attention to precancerous lesions) and of individuals alone (diagnosis) and in groups (detection) as an aid to prevention, cure, or prognosis." The program also provides a means for measuring progress in achieving Objective N. 6, namely, "develop the means to cure as many patients as possible and to maintain maximum control of the cancerous process in patients not cured."

It is anticipated that epidemiologic research supported by this CREG program will produce significant new information which will help achieve the objectives of the National Cancer Plan.

#### APPLICATION REQUIREMENTS

1. ELIGIBILITY All nonprofit organizations and institutions, State and local governments and their agencies, authorized Federal institutions, and individuals are eligible, according to NIH grants policies, regardless of whether or not they are now participating in the SEER Program.
2. THE APPLICATION Applicants should propose an individual project. Applicants may elaborate on the purpose, objectives, rationale, and significance stated in this announcement and must complete portions of the applications pertaining to procedural details, the investigator's related experience, facilities available, budgets, and biographical information for key professional personnel. The application should also state the duration of time for which the support is requested. It is anticipated that the project period will not exceed five years, and that the level of effort per year will approximate one to two professional man-years.
3. SUBMISSION Use application form NIH-398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the applications, identify this CREG announcement by its title and the number DCCP-12 and its date of publication. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014.
4. RECEIPT DATE Applications must be received in the Division of Research Grants, NIH, no later than October 1, 1975, in order to be considered in the competition under this announcement.



REVIEW

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) and NCI staff for responsiveness to this announcement. If an application is judged unresponsive, the applicant will be given an opportunity to withdraw the application or to submit it for consideration in the traditional grant programs of NIH. Applications judged responsive will be reviewed initially for scientific merit by DRG study sections and secondly by the National Cancer Advisory Board.

DRG will not accept an application in response to a CREG announcement that is identical to one concurrently being considered by NCI or other NIH awarding units.

For further information potential applicants may contact Dr. James L. Murray, Division of Cancer Cause and Prevention, National Cancer Institute.

**TITLE - BEDSIDE APPROACH TO THE ETIOLOGY OF CANCER**

*SCIENTIFIC PROGRAM REQUIREMENT* The National Cancer Institute (NCI) is accepting applications for support of research projects in which new clues to the etiology of cancer will be sought at the bedside through deeper-than-usual family and personal histories. For this reason the information should be obtained under the supervision of a medical specialist with an aptitude to think etiologically. The information collected should concern previous major diseases in the patient and his family, as described in a pedigree, and a description of occupational and other environmental exposures of the patient. The quality of the proposal submitted will be judged by its feasibility and by the applicant's comprehension of etiologic aspects of clinical oncology. The stress of the application should be on clinical astuteness, and not on data routinely collected by extensive formal questionnaires. It is anticipated that Departments of Pediatrics or Internal Medicine will be effective settings for supplementing histories as they are routinely obtained. The principal investigator will be expected to identify for such histories, patients who seem to have a high probability of yielding information that will reveal something new about the origins of neoplasia. Some indication should be given in the application as to how new clues developed by bedside observations would be further explored. Progress will be judged on the basis of publications concerning the findings made.

*SIGNIFICANCE TO NCI PROGRAM GOALS* Many of the important findings about the causes of cancer have come from observations first made in man, with respect both to inherited or environmental influences. Until now, there has been no hospital-based program to enhance this source of new information, so important to the goals of NCI.

**APPLICATION REQUIREMENTS**

1. ELIGIBILITY Nonprofit organizations and institutions, State and local governments and their agencies, authorized Federal institutions, and individuals according to NIH grants policies.
2. THE APPLICATION Applicants should propose a modest program project. Applicants may elaborate on the purposes, objectives, rationale, and significance stated in this announcement and must complete portions of the applications pertaining to procedural details, the investigator's related experience, facilities available, budgets, and biographical information for key professional personnel. The application should also state the duration of time for which the support is requested. It is anticipated that the project period will not exceed three years, and that the level of effort per year will approximate 0.25 professional man-years, aided by persons who routinely take histories and can readily look more deeply into them.
3. SUBMISSION Use application form NIH-398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title and the number DCCP-13 and the date of publication as the one to which the application responds. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014.

4. RECEIPT DATE Applications must be received in the Division of Research Grants, NIH, no later than October 1, 1975 in order to be considered in the competition under this announcement.

REVIEW

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) and NCI staff for responsiveness to this announcement. If an application is judged unresponsive, the applicant will be given an opportunity to withdraw the application or to submit it for consideration in the traditional grant programs of NIH. Applications judged responsive will be reviewed initially for scientific merit by DRG study sections and secondly by the National Cancer Advisory Board.

DRG will not accept an application in response to a CREG announcement that is identical to one concurrently being considered by NCI or other NIH awarding units.

For further information potential applicants may contact Dr. Thomas W. Pendergrass, Division of Cancer Cause and Prevention, National Cancer Institute.

TITLE - *CELL KINETICS*

*SCIENTIFIC PROGRAM REQUIREMENT* The National Cancer Institute (NCI) is accepting applications for support of research projects in cell kinetics. Studies may focus on one or more of the following areas:

(1) Studies are to be performed in animals comparing the kinetic behavior of critical normal host tissues such as bone marrow, gut, and skin, with that of experimental tumors prior to, during and following the administration of antineoplastic agents that are either of proven clinical value or have been determined to be promising in NCI screening systems or Phase I clinical trials.

The choice of model experimental tumor systems is discretionary, provided that the experimental systems employed are or can be well characterized with respect to their kinetic behavior. Minimum studies on the experimental tumor systems should include growth curves and measurement of tritiated thymidine-associated parameters. Other established techniques may include cell survival, host survival, DNA content distribution studies, studies measuring tritiated thymidine-specific activity in DNA, and morphologic studies. New techniques, assay systems, and cell kinetic parameters may be developed and evaluated in comparison with more established methods.

(2) Studies are to be carried out in experimental animal systems to explore optimal relative dosages and intervals in single drug multiple dose schedules, two drug combinations, and/or combinations of radiation therapy and drugs.

(3) Detailed studies of kinetic interactions among drugs and/or drugs and radiation will be carried out in vivo and/or in vitro to explore basic kinetic, biochemical, pharmacologic, pharmacokinetic, or other mechanisms of such interactions, in order to determine if observations made in a particular test system have broad applicability in other experimental systems and in man.

*SIGNIFICANCE TO NCI PROGRAM GOALS* The primary objectives of the cell kinetics program are to better define the role of cell population proliferative behavior in relation to drug response characteristics in animals and man, to determine those therapeutic principles which relate to population kinetic behavior and are applicable to man, and to devise approaches to the optimization of cancer chemotherapeutic regimens which take such principles into account.

APPLICATION REQUIREMENTS

1. ELIGIBILITY Nonprofit organizations and institutions, State and local governments and their agencies, authorized Federal institutions, and individuals according to NIH grants policies.

2. THE APPLICATION Applicants should propose an individual project. Applicants may elaborate on the purposes, objectives, rationale, and significance stated in this announcement and must complete portions of the application pertaining to procedural details, the investigator's

related experience, facilities available, budgets, and biographical information for key professional personnel. The application should also state the duration of time for which the support is requested. It is anticipated that the project period will not exceed three (3) years, and that the level of effort per year will approximate 1-3 professional man-years and 2-4 technician man-years.

3. SUBMISSION Use application form NIH-398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title and the number DCT-1 and the date of publication as the one to which the application responds. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014.

4. RECEIPT DATE Applications must be received in the Division of Research Grants, NIH, no later than October 1, 1975 in order to be considered in the competition under this announcement.

#### REVIEW

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) and NCI staff for responsiveness to this announcement. If an application is judged unresponsive, the applicant will be given an opportunity to withdraw the application or to submit it for consideration in the traditional grant programs of NIH. Applications judged responsive will be reviewed initially for scientific merit by DRG study sections and secondly by the National Cancer Advisory Board.

DRG will not accept an application in response to a CREG announcement that is identical to one concurrently being considered by NCI or other NIH awarding units.

For further information potential applicants may contact Dr. Vincent T. Oliverio, Division of Cancer Treatment, National Cancer Institute.

TITLE - *INVESTIGATION OF CANCER RESEARCH INFORMATION TRANSFER  
MECHANISMS*

*SCIENTIFIC PROGRAM REQUIREMENTS* The National Cancer Institute (NCI) is accepting applications for support of research projects that will investigate how information (including numeric data) needed for efficient and effective research is transferred and exchanged between cancer researchers (including research clinicians) and how the information transfer process in both basic and clinical areas of cancer research can be improved. The specific types of research projects which will be considered to be responsive to this announcement are listed below:

(1) Research projects involving user studies directed toward identifying in a quantitative way, the information and data needs of researchers and research clinicians in specific areas of cancer research. In some cases, the proposed project might include the identification of existing successful methods of **indexing**, coding, processing, retrieving, reporting, disseminating, and exchanging information which could be applied or modified to meet the identified user needs. When possible, projects should include an experimental trial or development and testing of a pilot system using the selected method(s) along with a careful evaluation of the feasibility, cost, and potential usefulness of the selected method(s).

(2) Research workshops directed toward obtaining a consensus of specialists regarding the most important and significant items of data that should be collected in specific cancer research areas. This would include identification of the optimal number and type of data items that should be collected on patients with specific types of cancer who are treated at multiple centers throughout the U.S. and other countries. These workshops should also identify the specific types of reports containing the collected data items that would be most useful to other specialists working in the same cancer research area.

(3) Research projects designed to identify the most productive and effective mechanisms currently used for transfer of information between individual cancer researchers, and from basic researchers to clinicians engaged in cancer research. This would include studies leading to the identification of key items of information that resulted in significant progress or breakthroughs in the cancer area and how the researcher became aware of and actually used those items of information. Provision must be made in research projects of this type for using the results of the research to develop a set of recommendations for improving information transfer mechanisms used by cancer scientists.

*SIGNIFICANCE TO NCI PROGRAM GOALS* In order for research to be as efficient and as productive as possible, scientists require a constant input of ideas and results of other researchers. This rapid and widespread dissemination of research results between cancer scientists and between basic researchers and clinicians is an integral part of the research process and is essential to the continuing progress of the National Cancer Program.

However, at present there is almost no significant research on this very important process of information transfer between cancer scientists, although the problem of finding useful information published in the growing number of specialty journals and proceedings of scientific meetings is steadily becoming more difficult. With so many researchers working in similar areas, the problem of keeping abreast of the current research activities of all these colleagues is increasingly impossible.

The research to be supported under this announcement in the field of cancer information transfer mechanisms will provide the basis for optimizing existing information exchange mechanisms and for developing new and improved methods that will systematically and efficiently make cancer researchers aware of new research results related to their current research projects.

#### APPLICATION REQUIREMENTS

1. ELIGIBILITY Nonprofit organizations and institutions, State and local governments and their agencies, authorized Federal institutions, and individuals according to NIH grants policies.
2. THE APPLICATION Applicants should propose an individual project. Applicants may elaborate on the purposes, objectives, rationale, and significance stated in this announcement and must complete portions of the applications pertaining to procedural details, the investigator's related experience, facilities available, budgets, and biographical information for key professional personnel. The application should also state the duration of time for which the support is requested. It is anticipated that the project period will not exceed three years, and that the level of effort per year will approximate two professional man-years and 1.5 technician man-years.
3. SUBMISSION Use application form NIH-398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title and the number OIA-1 and the date of publication as the one to which the application responds. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014.
4. RECEIPT DATE Applications must be received in the Division of Research Grants, NIH, no later than October 1, 1975, in order to be considered in the competition under this announcement.

#### REVIEW

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) and NCI staff for responsiveness to this announcement. If an application is judged unresponsive, the applicant will be given an opportunity to withdraw the application or to submit it for consideration in the traditional grant programs of NIH. Applications judged responsive will be reviewed initially for scientific merit by DRG study sections and secondly by the National Cancer Advisory Board.

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DRG will not accept an application in response to a CREG announcement that is identical to one concurrently being considered by NCI or other NIH awarding units.

For further information potential applicants may contact Dr. John Schneider, International Cancer Research Data Bank (ICRDB) Program, Office of International Affairs, National Cancer Institute.



TITLE - *ROLE OF GLYCOPROTEIN SHEDDING FROM MAMMARY CARCINOMA  
CELLS IN THE SPREAD OF METASTASIS*

*SCIENTIFIC PROGRAM REQUIREMENT* The National Cancer Institute (NCI) is accepting applications for support of research projects concerning the role of glycoproteins released from the surface of mammary neoplastic cells in the development of metastasis, with or without the presence of the primary lesion. Mammary carcinoma cells of murine origin have been shown to possess high molecular weight glycoproteins on their surface, and some of these glycoproteins are closely related to human blood group N antigen. (Naturwissenschaften 61:38; 457, 1974). A large amount of this material may be released into the circulation, and the ability of some tumors to metastasize appears to correlate with the degree of glycoprotein dissociation from the plasma membrane. (Proc. Nat. Acad. Sci. USA 72: 1012, 1975, FEBS Lett. 44: 313, 1974). The presence of these glycoproteins on the cell membrane may mask surface histocompatibility antigens. Supporting this hypothesis is the finding of a loss of strain specificity in a subline of mammary carcinoma shedding glycoproteins, while another subline of the same tumor, which does not release surface glycoproteins, maintains strain specificity (J. Nat. Cancer Inst. 51: 585, 1973; Proc. Nat. Acad. Sci. USA 71: 1224, 1974). On the other hand, the shedding of membrane-bound antigens into the circulation may provide the neoplastic cells with an escape route from the immunosurveillance system of the host and thus be a determining factor in metastasis dissemination (Proc. Nat. Acad. Sci. USA 72: 1012, 1975). Any approach to the analysis of this problem area is of interest provided it may have some relevance to the human disease. Cell populations derived from human mammary carcinomas, maintained in vitro, transplantable and metastasizing in nude-athymic mice are available for participants in the Breast Cancer Task Force Program (NCI).

*SIGNIFICANCE TO NCI PROGRAM GOALS* Tumor specific transplantation antigens have been demonstrated in nearly all experimental tumors which have been carefully studied. (Ann. Rev. Med. 15: 167, 1964; Adv. Cancer Res. 12: 167, 1969). Furthermore, tumor immunity has been demonstrated in animals bearing tumors (Cancer Res. 28: 2149, 1968 and 31; 734, 1971; J. Nat. Cancer Inst. 43: 111, 1969). Dissemination of metastasis despite such demonstrable host immunity seems a paradox. Mammary carcinomas of humans usually kill the host by metastatic spreading which often appears several years after removal of the primary lesion. The understanding of the metastasizing capacity of these tumors is a basic objective of the NCI program on Breast Cancer.

APPLICATION REQUIREMENTS

1. ELIGIBILITY Nonprofit organizations and institutions, State and local governments and their agencies, authorized Federal institutions, and individuals according to NIH grants policies.

2. THE APPLICATION Applicants should propose an individual project. Applicants may elaborate on the purposes, objectives, rationale, and significance stated in this announcement and must complete portions of the applications pertaining to procedural details, the investigator's related experience, facilities available, budgets, and biographical information for key professional personnel. The application should also state the duration of time for which the support is requested. It is anticipated that the project period will not exceed three years.

3. SUBMISSION Use application form NIH-398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title and the number DCBD-001 and the date of publication as the one to which the application responds. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014.

4. RECEIPT DATE Applications must be received in the Division of Research Grants, NIH, no later than October 1, 1975, in order to be considered in the competition under this announcement.

#### REVIEW

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) and NCI staff for responsiveness to this announcement. If an application is judged unresponsive the applicant will be given an opportunity to withdraw the application or to submit it for consideration in the traditional grant programs of NIH. Applications judged responsive will be reviewed initially for scientific merit by DRG study sections and secondly by the National Cancer Advisory Board.

DRG will not accept an application in response to a CREG announcement that is identical to one concurrently being considered by NCI or other NIH awarding units.

For further information potential applicants may contact Dr. Irvin C. Plough, Division of Cancer Biology and Diagnosis, National Cancer Institute.

TITLE - *METHODOLOGY FOR PERFORMING MASS RADIODIAMMOGRAPHY WITH  
LESS THAN 150 mR PER EXPOSURE*

*SCIENTIFIC PROGRAM REQUIREMENT* The National Cancer Institute (NCI) is accepting applications for support of research projects to explore the feasibility, development and evaluation of methods for performing mass radiomammography, equal or better in resolution, definition and ability to detect cancer to present radiomammographic equipment, but with a reduction in radiation dose to the skin to less than 150 mR per exposure.

*SIGNIFICANCE TO NCI PROGRAM GOALS* At this time it appears that radiomammography in conjunction with physical examination can detect approximately 90% of extant early cancers of the breast. This is accomplished today with radiation doses, when projected on an annually recurring basis, that give concern for its total safety. This statement is made with the knowledge that the question of safety is not firmly established, nor may this be possible for some time. In addition, there are no modalities of detection available today, other than ionizing radiation, that can reproduce this rate of breast cancer detection. While work on other modalities is in progress, it must be recognized that if radiographic equipment can be produced with the same resolution, definition and ability to detect cancer obtained with present techniques, but with markedly reduced radiation dose, the concern about repeated radiomammography should be much allayed.

APPLICATION REQUIREMENTS

1. *ELIGIBILITY* Nonprofit organizations and institutions, State and local governments and their agencies, authorized Federal institutions, and individuals according to NIH grants policies.
2. *THE APPLICATION* Applicants should propose an individual project. Applicants may elaborate the purposes, objectives, rationale, and significance stated in this announcement and must complete portions of the applications pertaining to procedural details, the investigator's related experience, facilities available, budgets, and biographical information for key professional personnel. The application should also state the duration of time for which support is requested. It is anticipated that the project period will not exceed three years.
3. *SUBMISSION* Use application form NIH-398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the application, identify this CREG announcement by its title and the number DCBD-002 and the date of publication as the one to which the application responds. Mail the application and letter to Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014.
4. *RECEIPT DATE* Applications must be received in the Division of Research Grants, NIH, no later than October 1, 1975, in order to be considered in the competition under this announcement.

REVIEW

Upon receipt, applications will be reviewed by the Division of Research Grants (DRG) and NCI staff for responsiveness to this announcement. If an application is judged unresponsive, the applicant will be given an opportunity to withdraw the application or to submit it for consideration in the traditional grant programs of NIH. Applications judged responsive will be reviewed initially for scientific merit by DRG study sections, and secondly by the National Cancer Advisory Board.

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For further information, potential applicants may contact Dr. Irvin C. Plough, Division of Cancer Biology and Diagnosis, National Cancer Institute.

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