

NCI DIET, NUTRITION, AND CANCER PROGRAM ON NUTRITIONAL  
ASPECTS OF CANCER AND ITS ETIOLOGY/PREVENTION,  
TREATMENT, REHABILITATION, AND TRAINING

**ANNOUNCEMENT**

The National Cancer Institute's Diet, Nutrition, and Cancer Program desires to expand its involvement with the nutritional aspects of cancer. The program is seeking applications for related research grants concerned with basic and applied studies related to the respective NCI areas of etiology, treatment, rehabilitation, and training.

Etiology and Prevention of Cancer

The Division of Cancer Cause and Prevention of the National Cancer Institute encourages the submission of research grant applications in the broad areas of diet and nutrition, as these might be related to the: (a) etiology of cancer and (b) prevention of cancer. Examples of studies judged to merit consideration are shown below. However, it is not the intent of this announcement to make or imply any delimitation relative to the nature or scope of the research which might be proposed.

The above mentioned examples follow:

Identification of mutagens/carcinogens in human food, body fluids, and feces.

Relationships between diet and excretion of mutagens/carcinogens.

Evaluation of methods of cooking/processing of human foods relative to the formation of mutagens/carcinogens.

Analysis of human foods for the presence of substances which inhibit the carcinogenesis process. Dietary/nutritional approaches to the inhibition of carcinogenesis.

Determination of whether individual vitamins, administered in excess of the maintenance dose, inhibit or promote the carcinogenesis process.

Studies on the role of dietary fiber in the carcinogenesis process.

Studies on the effect of diet/nutrition on tumor induction, tumor incidence, activation/inactivation of chemical carcinogens.

Relationships between diet and possible hormonal status, which may be related to cancer.

Questions concerning these grant-related activities of the Division of Cancer Cause and Prevention should be addressed to:

Thaddeus J. Domanski, M.D.  
National Cancer Institute  
Room 8C29, Landow Building  
7910 Woodmont Avenue  
Bethesda, Maryland 20014

Telephone: (301) 496-9448

### Treatment of Cancer

The Division of Cancer Treatment of the National Cancer Institute is responsible for the development and validation of treatment modalities for neoplastic diseases. The ultimate goals of this effort are improvement of the quality of life and duration of survival for the patient with cancer. There exists at this time an increasing awareness of the impact of malnutrition upon the quality of patient life, duration of survival, and responsiveness to antineoplastic therapy. For this reason, the Division of Cancer Treatment is expanding its ongoing interest in the nutritional aspects of malignancy and its treatment.

Grant applications are invited for clinical and preclinical research in the general areas of anorexia, cachexia metabolism (including etiology and pathogenesis), nutritional supplementation, and the nutritional complications of antineoplastic therapy.

### Background Information

A state of malnutrition and wasting is a frequent complication of cancer and a common cause of cancer related morbidity. Cachexia is also a common cause of mortality in patients with advanced malignant disease with up to one-fifth of cancer patients dying without identifiable cause other than the cachexia syndrome. Causes of malignant cachexia are frequently multiple in number and include anorexia, metabolic abnormalities precipitated by tumor metabolism, and complications of antineoplastic therapy such as the effects of treatment-related nausea and vomiting or malabsorption. Whatever the causes, malnutrition in the cancer patient is becoming recognized as a serious negative prognostic factor. There are increasing data to suggest decreased tolerance and response to antineoplastic therapies accompanied by a shortened survival in patients who are malnourished at the time of initial treatment. End results in cancer management may well be enhanced by expanding our understanding of the mechanisms of malnutrition in cancer patients, and attempts at therapeutic intervention designed to interrupt these mechanisms and/or provide nutritional support. Specific research areas and suggested approaches are listed below:

- A. Anorexia - Specific etiologic factors are not fully understood. The role of possible altered taste sensation is unclear and deserves further investigation. Treatment-associated learned food aversions may contribute to the anorexia syndrome in cancer patients. Their role requires further clarification. Prevention of food aversions and/or their interruption with the use of behavior modification techniques are potential therapeutic maneuvers that deserve further study.

Pharmacologic treatment of anorexia through the use of appetite stimulants has received very little investigation but is a potentially important area. Adequate diets acceptable to anorectic patients need to be developed. One aspect of this problem might be the development of foods with increased acceptability for these patients.

- B. Host/Tumor Competition - Cachexia Metabolism - Further work is required in the area of carbohydrate, lipid, protein, and overall energy metabolism of the cancer patient. Mechanisms of accelerated protein and fat depletion in these patients require further elucidation. Ineffective utilization of dietary carbohydrates with energy wasting metabolic pathways must be further clarified with the eventual aim being therapeutic intervention. Biochemical or dietary efforts to correct aberrant metabolic pathways might be useful in reversing or preventing malnutrition in patients with malignancy. Impact of enteral or parenteral dietary supplements upon aberrant metabolic pathways should be investigated to determine the most efficient source of calories for the cancer patient.
- C. Consequences of Nutritional Deficiencies and the Role of Dietary Supplementation - The role of enteral nutritional supplements in treatment of the cancer patient is not established. The clinical implications of dietary deficiencies and the potential efficacy of enteral supplements require further study in the following areas:
1. The maintenance of nutritional status of cancer outpatients.
  2. Amelioration of the toxicities of antineoplastic therapy.
  3. Potential enhancement of tumor responsiveness to anti-neoplastic therapies.

The role of parenteral nutrition in the management of the cancer patient requires further evaluation. The development and validation of techniques for efficacious, safe, and cost-effective out-patient parenteral nutrition is required. Studies of less hypertonic parenteral solutions containing lipids as a partial energy source with regard to efficacy and safety are another area worthy of study. Comparison with more conventional parenteral solutions would be an important aspect of these studies. Studies demonstrating nutritional efficacy of parenteral nutrition are also required (i.e., correction of abnormal body composition, reversal of glucose intolerance, and aberrant metabolic pathways). Prospective randomized studies of the effect of nutritional supplementation on the ultimate outcome of aggressive cancer therapy are also needed.

- D. Complications of Antineoplastic Therapy - Both radiotherapy and chemotherapy have an impact upon the nutrition of the cancer patient when anorexia, mucositis, nausea, vomiting, and diarrhea occur. Abdominal radiation had been shown to cause a clinically apparent malabsorption syndrome. Preliminary studies are less convincing for malabsorption secondary to chemotherapy. In many clinical settings these are the dose limiting toxicities

in antineoplastic therapy. Efforts aimed at further characterization, prevention, and correction of these complications of therapy are required. Such efforts might include the use of enteral or parenteral dietary supplementation, development of improved anti-emetic agents for concomitant use with antineoplastic therapy, and experiments with dose scheduling in combined modality treatments designed to reduce gastrointestinal toxicities.

- E. Nutritional Deficiencies as Antineoplastic Therapy - Preclinical in vivo laboratory studies have suggested that dietary exclusion of essential amino acids upon which the host's tumor can be shown to be dependent may inhibit tumor growth. Further work of this type with amino acids and other essential nutrients are required with the eventual goal being clinical evaluation of these modalities.

Questions concerning these grant-related activities of the Division of Cancer Treatment - Diet, Nutrition, and Cancer Program should be addressed to:

Daniel L. Kisner, M.D.  
Division of Cancer Treatment  
National Cancer Institute  
Room 8C08, Landow Building  
7910 Woodmont Avenue  
Bethesda, Maryland 20014

Telephone: (301) 496-2522

#### Rehabilitation

The Division of Cancer Control and Rehabilitation (DCCR) of the National Cancer Institute is seeking interested investigators for the purpose of developing specific nutritional regimens that affect the rehabilitation of cancer patients. In general, rehabilitation in cancer is concerned with prevention of impairment, maintenance of host strength and function, and the early restoration of functional loss as a result of cancer or its treatment.

The following are given as examples of research areas relevant to rehabilitation. These are not meant to be inclusive, but only to illustrate some of the possible topics to be considered.

- Dietary counseling for pediatric patients and their parents.
- Effectiveness of psychological support as an appetite stimulant.
- Consequences of malnutrition in host impairment and its relationship to patient rehabilitation.

Questions concerning these grant-related activities of the Division of Cancer Control and Rehabilitation should be addressed to:

Mr. Laurence Burke  
National Cancer Institute  
Room 617, Blair Building  
8300 Colesville Road  
Silver Spring, Maryland 20910

Telephone: (301) 427-7477

#### Training in Diet/Nutrition Cancer Research

Programs are available for the training of individuals in the broad areas of diet and nutrition research as these might relate to cancer. Two programs - Individual Postdoctoral Fellowships (F-32) and Institutional Training Grants (T-32) provide full-time, long-term support to promising individuals and well-qualified institutions through the National Research Service Act (NRSA) (P.L. 93-348). Additionally, the Cancer Research Career Development Program (RCDA) (KO4) provides support for individuals with demonstrated research potential who require additional experience in preparation for careers in independent research.

Questions concerning these National Cancer Institute grant-related training programs should be addressed to:

Research Manpower Branch  
National Cancer Institute  
5333 Westbard Avenue  
Bethesda, Maryland 20016

Telephone: (301) 496-7803

#### General Information

This announcement leaves the choice of specific research objectives, identification of specific aims, development of appropriate protocols in methodology, and the procedures for analysis and interpretation of data to the investigator's initiative. However, once award is made under this program, any substantial modification of the research originally proposed must be mutually agreed upon by the investigator and the respective NCI division.

#### Application and Review Procedures

The receipt dates for new applications are December 1, 1978; March 1, 1979; and July 1, 1979. Applications for research in the areas of etiology/prevention, treatment, and rehabilitation should be prepared on form PHS 398, the application form for the traditional research grant. Training applications for individual postdoctoral fellowships should be prepared on form PHS 416-1; for institutional training, on form PHS 6025; for RCDAs on form PHS 2557-1. Applications should be sent to:

Division of Research Grants  
National Institutes of Health  
Room 240, Westwood Building  
5333 Westbard Avenue  
Bethesda, Maryland 20016

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All applications will be reviewed by a Division of Research Grants Study Section or a designated NCI Study Section. All applications recommended for approval will compete for available funds with all other approved applications assigned to NCI. The DRG will not accept an application in response to this announcement that is the same as one concurrently being considered by any other NIH awarding unit.

Please identify grant applications submitted in response to this announcement by writing at the top of the face sheet of the application: "SUBMITTED IN RESPONSE TO ANNOUNCEMENT ON DIET, NUTRITION, AND CANCER PROGRAM ON NUTRITIONAL ASPECTS OF CANCER AND ITS ETIOLOGY/PREVENTION, TREATMENT, REHABILITATION, AND TRAINING."